

EDITORIAL

DICLOFENAC EPOLAMINE TOPICAL PATCH FOR THE TREATMENT OF PAING. AFFAITATI¹, M.A. GIAMBERARDINO¹, D. LAPENNA¹ and R. COSTANTINI²

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Topical nonsteroidal anti-inflammatory drugs produce local pain relief while avoiding systemic adverse events, thanks to minimal systemic absorption. This review evaluates the effectiveness and safety of a topical diclofenac preparation, diclofenac epolamine (DHEP) patch 1.3% or diclofenac epolamine patch with heparin as excipient (DHEP+H) in treating mild-to-moderate pain. DHEP patch was associated with significant pain relief and improved function in numerous pain conditions, from minor soft tissue injuries to osteoarthritis and myofascial pain syndromes. Tolerability was good-to-excellent in all studies, with no serious adverse events. DHEP+H further improved efficacy without affecting tolerability. This patch is effective and safe for localized mild-to-moderate somatic pain.

EDITORIAL

TIME TO LOOK PAST TNF AND THALIDOMIDE FOR CACHEXIA - COULD MAST CELLS AND FLAVONOIDS BE THE ANSWER?L. KING¹, I. TSILIONI² and T.C. THEOHARIDES^{2,3,4}

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Cachexia is a wasting condition associated with late stages of many chronic illnesses and may be present in up to 80% of patients with advanced cancers. Cachexia is a metabolic derangement resulting in a disturbance to the homeostasis of muscle breakdown and synthesis, favoring catabolism and muscle loss. Despite making strides in treating cancer itself, there have been no major advances in the treatment of cachexia pharmacologically or nutritionally. Clinical trials using anti-TNF biologics and thalidomide have largely failed. A new approach may be to focus on other possible waste-inducing mediators, possibly derived from mast cells, and the beneficial action of select natural flavonoids.

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EDITORIAL

**NEW CONCEPTS IN NEUROINFLAMMATION: MAST CELLS
PRO-INFLAMMATORY AND ANTI-INFLAMMATORY CYTOKINE MEDIATORS**

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The activation of brain nociceptors and neurons may lead to neurogenic inflammation, an event that involves immune cells including mast cells (MCs). Microglia are similar to macrophages and secrete pro-inflammatory IL-1 family members and TNF. TNF is rapidly released (first 10 minutes from MC granules) and is subsequently secreted along with other pro-inflammatory cytokines with a new synthesis after several hours. MC-derived TNF is a very powerful pro-inflammatory cytokine which mediates sensitization of the meningeal nociceptors. Here, we report the involvement of MCs in neuroinflammation, the role of inflammatory cytokine IL-1 family members, and of TNF, as well as the potential inhibition of IL-37.

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EFFECTS OF SOYBEAN ISOFLAVONES ON Wnt/ β -CATENIN AND THE TGF- β 1 SIGNALING PATHWAY IN RENAL TISSUE OF TYPE 2 DIABETIC RATS

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To observe the effect of Soyisoflavones (SI) on the expression of Wnt/ β -catenin signaling pathway elements, transforming growth factor- β (THGF- β) and its related proteins in the renal interstitia of diabetic nephropathic (DN) rats, 48 DN rats were randomly divided into 4 groups: DN model group (group DN), soybean isoflavone treatment group (group DA), DN model group + losartan treatment group (group DL), DN model group + soybean isoflavones combined with losartan treatment group (group SL). Each group comprised 12 rats. Twelve healthy Wistar rats were selected as normal controls (group N). After 12 weeks of continuous administration of soybean isoflavone or losartan or those two combined, the body weight of rats was recorded and serum urea nitrogen (BUN) and creatinine (Scr) were measured. The expression of Wnt4, β -catenin, and TGF- β ₁ proteins, as well as mRNA, in the renal interstitium were detected by immunohistochemistry and real-time quantitative PCR (FQ-PCR). In all the groups, Wnt4, β -catenin and TGF- β ₁ protein were only expressed in renal interstitial and renal tubular epithelial cells. There was no significant difference between group DA and group DL ($P > 0.05$). FQ-PCR results showed that Wnt4, β -catenin and TGF- β ₁ mRNA were consistent with the expression of these proteins in the renal tissue of each group. Soy isoflavones can reduce 24-h urinary protein quantification, alleviate renal interstitial pathological damage, and regulate the expression of Wnt4, β -catenin and TGF- β ₁ in the renal interstitium. This suggests that soybean isoflavones could delay the process of renal interstitial fibrosis in DN rats by decreasing the expression of Wnt4, β -catenin and TGF- β ₁ in the renal interstitium, thus demonstrating that soybean isoflavones plus losartan have the best protective effects against diabetes-induced renal fibrosis.

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THE ROLE FOR CYCLIC GLYCINE-PROLINE, A BIOLOGICAL REGULATOR OF INSULIN-LIKE GROWTH FACTOR-1 IN PREGNANCY-RELATED OBESITY AND WEIGHT CHANGES

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Cyclic Glycine-Proline (cGP) regulates the homeostasis of insulin-like growth factor (IGF)-1 function and cGP/IGF-1 ratio determines IGF-1 bioactivity *in vitro* and *in vivo*. Plasma IGF-1 represents largely inactive IGF-1 and weakly associated with human obesity and hypertension. We evaluated the regulatory role for cGP in pregnancy-related obesity and hypertension, and in obesity status between pregnancy and postpartum. Women were recruited in their first pregnancy. A cross-sectional study compared plasma concentration of cGP, IGF-1 and IGF binding protein (IGFBP)-3 in women with obesity and/or hypertension to normal controls 6-year postpartum using UPLC-MS and ELISA. A longitudinal study compared the changes of these peptides from 15-week gestation to 6-year post-partum in the women who remained normal weight, remained obese or changed to obese or to normal respectively. Study 1 is a cross-sectional study. The obese group had lower IGF-1 ($p = 0.001$), higher cGP/IGF-1 ratio ($p = 0.0055$) and the hypertensive group had lower IGFBP-3 ($p = 0.046$) and cGP ($p = 0.043$) than the controls. Study 2 is a longitudinal study. Women with weight loss had increased cGP/IGF-1 ratio ($p = 0.0026$) and decreased IGFBP-3 ($p = 0.0001$) compared with women whose weight remained normal. Women with weight gain had lower IGFBP-3 ($p < 0.0001$) only. Women who remained obese had increased cGP/IGF-1 ratio ($p = 0.006$) only. Increase in cGP/IGF-1 ratio is associated with obesity, but not hypertension. Changes of IGFBP-3 and/or cGP/IGF-1 ratio are associated with weight changes. The data suggest the role for cGP in obesity through autocrine regulation of IGF-1.

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EXPRESSION OF PROTEOGLYCANS IN TWO TYPES OF AMELOBLASTOMA: NOVEL IMMUNOHISTOCHEMICAL FINDINGS

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Alterations in cellular and extracellular matrix components play an important role during tumorigenesis; proteoglycans are included among these components. Ameloblastomas are odontogenic tumors distinguished as invasive and infiltrative neoplasms and are divided into different histological types, the most common of which are the unicystic ameloblastoma and the conventional ameloblastoma. The aim of this study was to identify the presence of two proteoglycans, perlecan and biglycan, in different types of ameloblastoma. Using immunohistochemistry, we determined the presence of both proteins in 28 unicystic ameloblastomas and 23 conventional ameloblastomas. We identified the cytoplasmic and nuclear presence of perlecan and the cytoplasmic presence of biglycan in both types of ameloblastoma. The mean values of immunoexpression were higher in the conventional type compared to the unicystic type. Neither the presence of biglycan in ameloblastomas nor the nuclear presence of perlecan in any odontogenic tumor has previously been reported. The differential immunoexpression of perlecan and biglycan in these types of ameloblastomas suggests their participation in the developmental process of these tumors.

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TETRAMETHYLPYRAZINE INHIBITED HYPOXIA-INDUCED EXPRESSION OF CALCIUM-SENSING RECEPTORS IN PULMONARY ARTERY SMOOTH MUSCLE CELLS IN CHICKENS

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Tetramethylpyrazine (TMP) is a biologically active ingredient, which is isolated from a popular Chinese medicinal plant. It has been used effectively to treat ischemic heart problems, cerebrovascular and thrombotic vascular diseases. This study was designed to evaluate the effect of TMP on calcium-sensing receptors in pulmonary artery smooth muscle in chickens. For this purpose forty day-old chicks were distributed into five groups: the control group, the hypoxia group (kept under low Oxygen treatment), and TMP groups (kept under low Oxygen treatment along with treatment of different concentrations of TMP). The pulmonary artery smooth muscle cells were also cultured on 6-well plates in high glucose culture medium and divided into the same five groups. We used *in vivo* and *in vitro* study models by applying immunohistochemistry, RT-qPCR assay and Western blotting analysis. Our results showed that pre-incubation with hypoxia markedly stimulated the activation of calcium-sensing receptor (CaSR) in pulmonary artery smooth muscle cells (PASMCs). The TMP decreased the mRNA and protein levels of CaSR. Treatment with TMP clearly inhibited the activation of all CaSR in a dose-dependent manner. Our data demonstrated that TMP can down-regulate the expression of CaSR. Therefore, these findings provide a new target to treat pulmonary arterial hypertension (PAH) under hypoxic conditions.

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REGULATION OF VITAMIN D RECEPTOR AND GENISTEIN ON BONE METABOLISM IN MOUSE OSTEOBLASTS AND THE MOLECULAR MECHANISM OF OSTEOPOROSIS

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The aim of this work was to study the mechanisms of vitamin D receptor (VDR) and Genistein (Gen) on the regulation of bone metabolism of phytoestrogens from cellular and epidemiological perspectives. MC3T3-E1 cells were treated with different concentrations of Gen, and the cell-proliferation rate was detected by an MTT colorimetric assay. The effect of the VDR receptor blocker ZK159222 on the Gen effect was then observed; after adding Gen to MC3T3-E1 cells, we detected the expression of VDR protein via Western blotting. After adding estrogen receptor α -blocker MPP and estrogen receptor β -blocker PHTPP, we observed the effect of Gen on the regulation of the VDR protein. DNA was extracted from the blood samples of 200 postmenopausal women in the early epidemiological survey, and the restriction fragment length polymorphism of VDR gene Apa I and Bsm I in each sample was observed. The results were analyzed using dietary survey and bone mineral density examination. The results show that 10^{-8} mol/L Gen can promote the proliferation of MC3T3-E1 cells ($P < 0.05$). This effect can be canceled by the VDR blocker ZK159222. By analyzing the Apa I and Bsm I genotypes of VDR restriction sites, we discovered no significant difference in bone mineral density (BMD) between different genotypes ($P > 0.05$). In addition, there was no significant correlation between dietary phytoestrogen intake and BMD in different genotypes ($P > 0.05$). In conclusion, VDR can mediate the effect of Gen on the proliferation of MC3T3-E1 cells. The up-regulated expression of VDR protein in Gen is not mediated by the estrogen receptor. Moreover, the VDR gene polymorphism is not related to the BMD in various parts and is not related to the bone metabolism effect of the dietary plant estrogen intake.

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miR-145 IS CRITICAL FOR MODULATION OF VASCULAR SMOOTH MUSCLE CELL PROLIFERATION IN HUMAN CAROTID ARTERY STENOSIS

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miR-145 is highly expressed in vascular cells, where it regulates phenotypic switching and vascular homeostasis, but its role in carotid artery stenosis (CAS) is controversial. In the present study, the expression of miR-145 was assessed by real time quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) in human samples (both plasma and/or endarterectomy samples) from patients with symptomatic CAS and in controls without CAS. The mouse carotid artery ligation (CAL) model was used to determine the role of miR-145 on vascular smooth muscle cells *in vivo* (VSMCs) by using a mimic of or an inhibitor of miR-145. We found that miR-145 expression was significantly reduced in the plasma and plaque from patients with CAS ($p < 0.01$). The expression of miR-145 in the mouse CAL model, as assessed by qRT-PCR, was significantly reduced compared to the carotid arteries of the control group ($p < 0.01$). *In vitro*, enhancement or inhibition of miR-145 in VSMCs demonstrated that miR-145 significantly inhibited proliferation of VSMCs ($p < 0.05$); *in vivo*, enhancement of miR-145 significantly inhibited neointimal formation in the CAL model ($p < 0.01$). These results demonstrate that the expression of miR-145 is reduced in human CAS, miR-145 plays a critical role in CAS by modulation of VSMC proliferation, suggesting that miR-145 may present a potential therapeutic option for treating CAS.

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AMINO ACID AND HYALURONIC ACID MIXTURES DIFFERENTIALLY REGULATE EXTRACELLULAR MATRIX GENES IN CULTURED HUMAN FIBROBLASTS

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The aim of this screening study was to evaluate the efficacy of different proprietary mixtures of amino acid and hyaluronic acid (HA) in stimulating the production of extracellular matrix (ECM) components, particularly the neo-synthesis of elastin, and in promoting a more efficient deposition of elastic fibres (elastogenesis), while at the same time maintaining the stimulation of collagen. The study has allowed identification of the optimal ratios between the amino acids (AA) for the production of collagen and elastin. Human primary dermal fibroblasts from a 44-year-old female donor were used as a test system in an experimental design based on the evaluation of the expression of relevant ECM genes using a transcriptomic dynamic approach. The expression of ECM genes was evaluated by RTqPCR from 24 to 120 hours in the presence of the test items. Moreover, the production of ECM proteins was verified by Western blot analysis after a 120 h treatment period. In addition to elastin, collagen IV, a fundamental structural component of the basal lamina responsible for epithelial and connective tissue anchoring, was analysed as potential target for the modulation of ECM protein production by human fibroblast. The first phase of the study demonstrated that alanine and valine are essential to promote production of elastin, of which they are important constituents. The second phase of the study, which was conducted to clarify the interactions between the different clusters of AA, demonstrated that it is necessary to choose a mixture that contains specific amounts of amino acids of both proteins, collagen and elastin, to give a significant response and a significant production of both. This also proves the existence of a ratio between the 2 clusters (AA elastin/AA collagen) that guarantees an adequate and balanced response to gene expression and production by fibroblasts, collagen and elastin. The study has allowed identification of the optimal ratios between the AA for the production of collagen and elastin.

ROLE OF APC-MEDIATED MDR-1/CLCX-1 SIGNALING PATHWAY IN OVARIAN TUMORS

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We explored the role of APC-mediated MDR-1/CLCX-1 signaling pathway in ovarian tumors. In this study, ovarian tumor cell lines SKOV-3, ES-2 and MCV-152 were used to conduct the research. Fluorescence quantitative PCR and Western-blotting were used to investigate the effects of MDR-1/CLCX-1 signaling pathway in ovarian tumors. The effects of the APC gene silencing and overexpression on proliferation and apoptosis of ovarian tumor cells were detected by flow cytometry. Compared to normal cells, the expression of APC gene mRNA in ovarian tumor cells was significantly decreased ($p<0.05$). Western-blotting results showed that the level of APC protein in ovarian tumor cells was significantly lower than that in normal tissue, while MDR-1/CLCX-1 related proteins levels were significantly increased ($p<0.05$). In the APC gene silenced ovarian tumor cell lines, the expression of MDR-1/CLCX-1 was significantly higher than that of the untreated group ($p<0.05$), and apoptosis of ovarian tumor cells decreased. However, in ovarian tumor cell lines that over-expressed APC gene, the expression of MDR-1/CLCX-1 was significantly lower than that of the untreated group ($p<0.05$), and apoptosis of ovarian tumor cells was increased. There is a certain correlation between the APC gene and ovarian tumors, and the APC gene mediates the apoptosis of tumor cells through the MDR-1/CLCX-1 signaling pathway.

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DIFFERENCES IN EXPRESSION OF YKL-40 AND TLR4 IN NASAL SINUS MUCOSA OF CHRONIC SINUSITIS PATIENTS WITH AND WITHOUT NASAL POLYPS

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This work studies the expression differences of YKL-40 and TLR4 in nasal sinus mucosa of chronic sinusitis patients with and without nasal polyps and its clinical significances. Fifty chronic sinusitis patients with nasal polyps and 50 chronic sinusitis patients without, accepted by our hospital during February 2016-February 2017, were included and taken as group A and group B, respectively. In addition, another 50 patients with nasal deviation were taken as group C (control group). The ostiomeatal complex mucosa of group A and B and the inferior turbinate mucosa of group C were taken and the fluorescence quantitative PCR method was applied to detect the expression of YKL-40, TLR4 and NF- κ B of the mucosa and explore and influence of YKL-40 and TLR4 on NF- κ B. There was a negative correlation between YKL-40 and TLR4 in group A, and the difference was statistically significant ($P < 0.05$) while there was no relationship between YKL-40 and TLR4 expression in group B. The level of YKL-40 protein in group A was higher than that in group B, which was statistically significant ($P < 0.05$). YKL-40 and TLR4 were positively correlated in group A while there was no correlation between YKL-40 and TLR4 expression in group B. The expression of YKL-40, TLR4 and NF- κ B in chronic sinusitis patients with nasal polyps was high. In addition, there was a negative correlation between YKL-40 and TLR4 expression in chronic sinusitis patients with nasal polyps. YKL-40 and TLR4 interacted with each other to activate NF- κ B and promote disease progression.

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THE INVOLVEMENT AND MECHANISM OF FEBUXOSTAT IN NON-ALCOHOLIC FATTY LIVER DISEASE CELLS

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It has been proved that hyperuricemia is associated with non-alcoholic fatty liver disease (NAFLD). The xanthine oxidase (XO) inhibitor, febuxostat, decreases free fatty acids-induced fat accumulation in HFDT-fed mice. Here, it is shown that febuxostat attenuates fat accumulation and reactive oxygen species (ROS) in HepG2 cells. It was further found that the underlying mechanism is related to the reduction in expression of NLRP3/caspase-1/IL-18/IL-1beta and improved insulin resistance (IR). This finding highlights the possible molecular pathways involving NLRP3 activation for management of ROS and insulin IR. In conclusion, febuxostat may be a promising potential treatment for patients with NAFLD.

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DIFFERENT MOLECULAR SUBTYPES OF BREAST INVASIVE DUCTAL CARCINOMA

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This study aims to analyze the clinical characteristics of breast invasive ductal carcinoma (BIDC) in patients with different molecular subtypes and identify possible correlation to prognosis. miR-10b expression level was detected using real-time quantitative polymerase chain reaction (RT-PCR). Tissue sections were collected and stained using the immunohistochemical method. The samples were grouped into human epidermal growth factor receptor 2, (HER2) overexpression, Triple negative, Luminal A and Luminal B groups. Age, tumor size, breast cancer molecular subtype, clinical stage, miR-10b positive expression, positive expression of Ki-67 and survival rate of patients diagnosed with BIDC were analyzed. The expression of miR-10b was down-regulated in the breast carcinoma tissues. Age and clinical stage were distinctly different among patients with different molecular subtypes of BIDC ($p < 0.05$). Tumor size was not remarkably different ($p > 0.05$) among different subtypes. The positive expression rate of miR-10b was lowest in patients with Luminal B BIDC; the positive expression of Ki-67 was in different correlation with the expression of different receptors, and there was a remarkable difference ($p < 0.05$); moreover, the survival rate of patients with Luminal A and B BIDC was significantly higher compared to patients with other molecular subtypes ($p < 0.05$). Clinical characteristics and prognosis of BIDC vary among different molecular subtypes. This study provides valuable input on BIDC therapy.

LETTER TO THE EDITOR

PERCUTANEOUS TRANSFORAMINAL ENDOSCOPIC DISCECTOMY AND MINI-INCISION SURGERY IN THE TREATMENT OF LUMBAR INTERVERTEBRAL DISC PROTRUSIONHX. NING¹, YW. YUAN², QY. ZHANG³, ZZ. SUN¹, HY. NING⁴ and P. WANG¹

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Lumbar intervertebral disc protrusion (LIDP) is a frequently occurring disease and 10-20% of patients require surgical treatment. Percutaneous transforaminal endoscopic discectomy (PTED) and mini-incision surgery are currently the most common surgeries for patients. To analyze the efficacy of PTED and mini-incision surgery in the treatment of lumbar intervertebral disc protrusion, this study selected 216 patients with LIDP who were admitted to the hospital between February 2014 and June 2015. The subjects were randomly divided into an observation group and a control group, 108 each. Patients in the observation groups were treated by PTED, while patients in the control group were treated by mini-incision surgery, and treatment efficacy of the two groups was observed. The results demonstrated that the duration of surgery and length of hospital stay of the observation group were significantly shorter than those of the control group, the intraoperative blood loss of the observation group was significantly less than that of the control group and the size of surgical incision of the observation group was much smaller than that of the control group ($P<0.05$). As to clinical efficacy, in accordance with the Japanese Orthopaedic Association (JOA) score and the Visual Analogue Scale (VAS) score, results of the observation group were superior to those of the control group at 3 months after surgery ($P<0.05$). In conclusion, treating patients with LIDP through PTED can significantly improve treatment efficacy, shorten surgical and healing time and relieve pain. This therapy is worth clinical promotion.

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LETTER TO THE EDITOR

PRE- AND POST-TREATMENT COMPUTED TOMOGRAPHIC FINDINGS OF A PRIMARY INTRANASAL TRANSMISSIBLE VENEREAL TUMOR IN A CANINE PATIENT

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A two-year-old, female intact, cross-breed dog presented with a two-month history of nasal discharge. Computed tomography (CT) demonstrated obliteration of both nasal cavities by soft tissue density, destruction of the nasal and ethmoidal turbinates, and lysis of the frontal and palatine bones and maxilla. Frontal sinuses and maxillary recesses were obscured by soft tissue/fluid density. Histopathological examination of the mass was diagnostic of transmissible venereal tumor. The dog was clinically normal 3 months after treatment initiation with vincristine sulphate and amoxicillin/clavulanate. Six months after the completion of treatment no mass-like lesion was demonstrated in CT sections. Nasal cavities, maxillary recesses and frontal sinuses were filled with air. The reticular turbinate nasal plexus appeared atrophic with focal loss of the nasal turbinates on both sides. The ethmoidal turbinates were well-defined; however, focal loss of turbinates was also seen. Lysis of the frontal and palatine bones were still evident.

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*LETTER TO THE EDITOR***EFFECT OF SILDENAFIL ON PULMONARY HYPERTENSION ASSOCIATED WITH LEFT HEART FAILURE**

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This study aims to evaluate the effect of sildenafil on pulmonary hypertension (PH) associated with chronic left heart failure. Twenty patients with PH and left heart failure were divided into treatment group (10 cases, with an oral dose of sildenafil 75 mg daily for 8 weeks) and control group (10 cases, with treatment of cardiac glycosides, diuretics, angiotensin-converting enzyme inhibitor, angiotensin II receptor blocker and beta-blockers). Left ventricular systolic function (LVEF), the pulmonary artery systolic pressure (PH), the left ventricular fraction shortening (LVFS), the left atrium diameter (LAD) and the left ventricular end-diastolic diameter (LVD) were measured by echocardiography, the left ventricular mass index (LVMI) was also calculated. The level of N-terminal pro-brain natriuretic peptide (NT-proBNP) was detected by electrochemiluminescence and high sensitivity C-reactive protein (hsCRP) by immune transmission. The walking distance in 6-minute walk test (6-MWT) was calculated. Before treatment, there were no significant differences in LVEF, LVFS, NT-proBNP, hsCRP, 6-MWT, LVD, LAD and LVMI between the treatment group and control group. After four weeks intervention in the treatment group, LVEF, FS and 6-MWT were significantly increased, while NT-proBNP, hsCRP, 6-MWT, LVD and LVMI were significantly decreased, when compared with the control group. In conclusion, sildenafil can improve cardiac function and reduce pulmonary artery pressure. In addition, it can attenuate myocardial remodeling through its anti-inflammatory effect.

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LETTER TO THE EDITOR

**VEGF-A EXPRESSION IN SOFT TISSUES REPAIRED BY SHOCKWAVE THERAPY:
DIFFERENCES BETWEEN MODALITIES**

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Shockwave therapy has found its place in the medical treatment of various diseases of the locomotor system such as acute fracture, nonunion, chronic tendinitis and pseudarthrosis. Focused shock waves enable maximum energy in the therapeutic zone, and depth of penetration can be adjusted. Radial shockwave therapy primarily affects superficial tissues, so its application in medicine is doubtful. Our study aimed to assess long bone fracture healing in regard to soft tissues. For this investigation, 84 female Wistar rats were divided into a focused shockwave group (n=36), a radial shockwave group (n=36) and a control group (n=12). Conclusively, long bone fracture repair was enhanced in the shockwave groups. Comparison between focused shock waves and radial shock waves suggested that this latter strongly stimulated the processes of the healing, as 75% of vascular spaces were VEGF-A positive on the 5th day of bone healing, and 85% on the 22nd day of healing.

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LETTER TO THE EDITOR

**PURE RED CELL APLASIA WITH T-CELL LARGE GRANULAR LYMPHOCYTIC
LEUKEMIA**

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Pure red cell aplasia (PRCA) develops as a result of erythroid precursors failing to reach maturity in the bone marrow, which eventually leads to anemia. Here we present a case of a 64-year-old Asian male with a medical history of colorectal adenocarcinoma who had been treated with 6 cycles of oxaliplatin and capecitabine four years ago. The patient was diagnosed with PRCA and T-cell large granular lymphocyte leukemia.

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LETTER TO THE EDITOR

**AUTOLOGOUS PLATELET-RICH PLASMA FOR TREATMENT OF VENOUS LEG
ULCERS: A PROSPECTIVE CONTROLLED STUDY**D. ETUGOV¹, V. MATEEVA² and G. MATEEV¹*¹Department of Dermatology and Venereology, Medical University Sofia, Bulgaria; ²Department of Dermatology and Venereology, Military Medical Academy Sofia, Bulgaria**Received December 5, 2017 – Accepted March 12, 2018*

Venous leg ulcers (VLUs) are chronic difficult-to-treat wounds which affect around 1-2% of the world population. Conventional methods for treatment such as mechanical debridement, occlusive dressings and local antibiotics in case of infection, often lack effectiveness. Autologous platelet-rich plasma (PRP) is an alternative method in the treatment of chronic wounds. PRP contains inflammatory mediators, growth factors, and cytokines that modulate the wound microenvironment to create a better chance for healing. The aim of this prospective clinical study was to evaluate the efficacy of intralesional injection of PRP in the management of VLUs. This study included 23 patients with VLUs. For each patient, two ulcers located in the same anatomical zone and at the same clinical stage were selected. One was treated with a single application of autologous PRP. The other ulcer was used as a control and was treated by conventional methods. The size of the ulcers was assessed at baseline (visit 0), 15 days (visit 1) and 30 days after the procedure (visit 2). Results showed a significant reduction of the size of the ulcer both in the group treated with PRP (mean surface 1368.2 mm² at visit 0 and 596.3 mm² at visit 2) and in the control group (mean surface 880.3 mm² at visit 0 and 582.8 mm² at visit 2). Statistical analysis showed a significant change in the size of the ulcer between visit 0 and visit 2 in both groups ($p < 0.0001$). The application of PRP in difficult-to-treat venous leg ulcers may be a promising new method for therapy of this condition. The results of this study correlate with the data from the majority of previous studies and confirm the effectiveness of PRP. Nevertheless further research in the area is needed to evaluate the therapeutic significance of the method and eventually show its superiority to conventional treatments in larger cohorts.

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LETTER TO THE EDITOR

COMPARATIVE STUDY OF METHOTREXATE AND HUMAN UMBILICAL CORD MESENCHYMAL STEM CELL TRANSPLANTATION IN THE TREATMENT OF RHEUMATOID ARTHRITISYH. WANG¹, ZQ. YANG¹, SF. ZHU¹ and Y. GAO²

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In this study, a collagen-induced arthritis (CIA) model was established to simulate rheumatoid arthritis (RA) using two intradermal injections of bovine type II collagen and Freund's complete adjuvant mixture given at two-week intervals. Subsequently, the transplantation of human umbilical cord mesenchymal stem cells (hUC-MSCs) was used to treat RA and the treatment efficacy, as well as the possible regulatory mechanism underlying hUC-MSC transplantation, was observed. During the study, forty rats were randomly divided into four groups and their blood samples were collected at different time points to measure levels of serum cartilage oligomeric matrix protein (COMP). Based on the symptoms and pathological features of the rats, a total success rate of 83% was achieved by the treatment. Furthermore, the improvement of joint symptoms was more obvious when methotrexate and MSC transplantation were used. In summary, it was concluded that MSC transplantation relieved the symptoms of arthritis by down-regulating the expression of COMP on the synovial membrane and in the serum of CIA rats.

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*LETTER TO THE EDITOR***EFFECTS OF HOUSEHOLD BLEACH ON SPUTUM SMEAR MICROSCOPY TO CONCENTRATE ACID FAST BACILLI FOR THE DIAGNOSIS OF PULMONARY TUBERCULOSIS**

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Tuberculosis (TB) is one of the major public health problem among contagious diseases in Pakistan. TB diagnosis mainly depends on sputum smear microscopy. The main objective of this study was to evaluate the effects of household bleach on sputum smear microscopy to concentrate acid fast bacilli for the diagnosis of pulmonary tuberculosis. Sputum specimens of 200 suspected TB patients were collected for the study. Smears were prepared from the purulent part of sputum sample before and after bleach treatment, heat fixed and stained with the ZN technique. The obtained data were analyzed by chi-squared test using SPSS software. Out of 200 isolates, 22 (11%) patients had positive smears for acid fast bacilli (AFB) by direct ZN staining. After treatment with household bleach (NaOCL) and centrifugation, the number of AFB positive patients were increased from 22 (11%) to 37 (18.5%). The bleach-concentration method for sputum samples significantly increased the TB detection rate as compared to direct sputum smear microscopy. Thus, a shift from direct sputum microscopy to bleach-concentration technique should be considered a better method for detection of AFB in sputum through smear microscopy.

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LETTER TO THE EDITOR

COMPARISON OF GEFITINIB AND PLATINUM-BASED CHEMOTHERAPY AND ONLY PLATINUM-BASED CHEMOTHERAPY TO TREAT LUNG ADENOCARCINOMA

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To study the curative effects and safety for patients who adopt both gefitinib and platinum-based chemotherapy or only platinum-based chemotherapy in the treatment of lung adenocarcinoma, 80 EGFR mutation-positive lung adenocarcinoma patients in stage IIIB/IV were divided into two groups. Half of them received both gefitinib and standard chemotherapy (group A), and the others (group B) received only standard chemotherapy. Overall response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS) and the related toxicities of both groups were recorded in order to take certain nursing measures for a variety of toxicities. Next, statistical methods were used to analyze the curative effects and safety of the two treatments. The results showed that ORR, DCR and median progression-free (mPFS) survival of the two groups of patients showed no statistical difference ($P>0.05$). However, group A (18.56 months) had a longer median overall survival (mOS) than group B (14.87 months), which was of statistical significance ($P<0.05$). Nausea and loss of appetite were common mild adverse reactions, and anemia and leukocytopenia were moderate common adverse reactions. The difference between these two groups of patients regarding adverse reactions was not statistically significant ($P>0.05$). In conclusion, the two treatments have similar safety, but lung adenocarcinoma patients with drug resistance during stage IIIB/IV after using first-line gefitinib therapy have lower survival benefits than patients who take both gefitinib and platinum-based chemotherapy.

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LETTER TO THE EDITOR

ANTI-TUMOR MECHANISM OF IL-21 USED ALONE AND IN COMBINATION WITH 5-FLUOROURACIL *IN VITRO* ON HUMAN GASTRIC CANCER CELLS

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To study the effect and related mechanism of IL-21 alone and in combination with 5-Fluorouracil on the proliferation and growth, transferability, and apoptosis of gastric cancer cells, we cultivated gastric cancer cell SGC-7901 and created four experimental groups with varying concentrations of IL-21 and 5-Fluorouracil: IL-21 group (IL-21 100ng/ml), semi-combination group (5-Fluorouracil 25µg/ml+IL-21 100ng/ml), 5-Fluorouracil group (5-Fluorouracil 50µg/ml), and combination group (5-Fluorouracil 50µg/ml+IL-21 100ng/ml). The MTT (3-(4, 5)-dimethylthiazoliazol-2-yl)-2, 5-diphenyltetrazolium bromide) assay was used to detect the inhibitory effect of each group on the proliferation and growth of gastric cancer cells. A scratch-wound assay was carried out to detect the inhibitory effect of each group on transferability. TUNEL assay was used to detect the effect of each group on the apoptosis of the gastric cancer cells, and Western blot was used to detect the expression of caspase-3, caspase-8, bcl-2, and c-myc, which are the proteins related to apoptosis, after the drug effect in each group. The results show that, compared to the 5-Fluorouracil group, the inhibitory effects after 24 h of the IL-21 group and the semi-combination group on SGC-7901 were weaker ($P < 0.001$). However, if the effect lasted 48 h, then the inhibition in the semi-combination group had no significant difference compared to the 5-Fluorouracil group ($P > 0.05$). The scarification test showed that all groups could inhibit the transferability of SGC-7901 and that the effect increased successively from the IL-21 group, the semi-combination group, the 5-Fluorouracil group, to the combination group. The TUNEL assay indicated that all groups could promote the apoptosis of SGC-7901. The percentage of cell apoptosis increased, and the Western blot showed that the expression of caspase-3, caspase-8, and c-myc, respectively, in the semi-combination group, the 5-Fluorouracil group, and the combination group increased successively and that the successive increasing of c-myc was the most significant. The expression of bcl-2 tended to decrease. In conclusion, IL-21 used alone and in combination with 5-Fluorouracil are anti-tumor mechanisms in SGC-7901.

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LETTER TO THE EDITOR

EFFECT OF MANNOSE ON THE LUNG FUNCTION OF RATS WITH ACUTE PANCREATITIS

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The present study aimed to investigate the mechanisms by which mannose protects the lung injury induced in rats with acute pancreatitis (AP). An AP combined with Acute Lung Injury (ALI) model was established. A total of 90 healthy adult male Sprague-Dawley rats (300±50g weight) were randomly divided into three groups: sham operation group (SO group), severe acute pancreatitis lung injury group (SAP group), and mannose intervention group (MT group). Subsequently, each group was divided into two subgroups based on the time passed from intervention, namely 6 and 12 h. Each subgroup comprised 15 rats. The ratio of wet/dry weight of the lung tissue exhibited no significant change at different time points in the SO group. This parameter was significantly increased in the SAP group compared with the SO group at each time point of the treatment ($P < 0.05$) and it was significantly lower in the MT group than that in the AP group ($P < 0.05$) and it was significantly increased in the AP group at each time ($P < 0.05$) compared with the SO group. The levels of TNF- α in the lung tissue in the SO group exhibited no significant change at different time points, but they were significantly decreased in the MT group at each time point ($P < 0.05$) compared with the SAP group. The mannose receptor (MR) mRNA and protein levels in the lung tissues exhibited no significant change at different time points. The mRNA and protein levels of MR in the SAP group were significantly decreased at each time point ($P < 0.05$) compared with the SO group. The mRNA and protein levels of MR, in the lung tissue of the MT group were significantly increased at each time point compared with the SAP group ($P < 0.05$). Mannose could reduce the injury caused to the lung tissue of rats with severe acute pancreatitis by up-regulation of the expression of MR mRNA and protein.

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LETTER TO THE EDITOR

SALINE CONDITIONS ALTER MORPHO-PHYSIOLOGICAL INTENSIFICATION IN PURSLANE (*PORTULACA OLERACEA* L.)S. ZAMAN¹, S-B. SHAH², Y-T. JIANG³ and S-Q. CHE¹

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In this study, primary investigations of selected cultivar of purslane named as Tall Green under particular salinity stress were evaluated to understand the basic concept of different mechanisms of physiological attributes which will play an important role for molecular and proteomic level research. The evaluation of morphological and physiological attributes under 0 mM (without salt addition) 100 mM and 200 mM salt stress changed dramatically. The results showed high salt stress at 200 mM significantly decreasing the morphological attributes and performance of leaves, stems, and roots. At moderate salt stress levels, 100 mM, the ratio of Fv/Fm slightly increased compared to high stress. In addition, salt stress significantly decreased the total chlorophyll content (chl a+b) at 200 mM. The relative water content percentage was high at 0 mM. Moreover, the electrolyte leakage (EL) significantly increased with increasing salinity stress compared to control 0 mM.

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*LETTER TO THE EDITOR***CONTINUOUS FEMORAL NERVE BLOCK AND PATIENT-CONTROLLED INTRAVENOUS POSTOPERATIVE ANALGESIA ON Th1/Th2 IN PATIENTS UNDERGOING TOTAL KNEE ARTHROPLASTY**

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The purpose of this study is to observe and compare the effects of continuous femoral nerve block (cFNB) and patient-controlled intravenous analgesia (PCIA) on postoperative analgesia and Th1/Th2 in patients undergoing total knee arthroplasty (TKA). Forty-six TKA were selected and randomly divided into two groups: the cFNB group and PCIA group. Patients in the two groups all underwent general anesthesia using a laryngeal mask. In the cFNB group, the femoral nerve block and catheterization were performed after induction of general anesthesia: 0.375% ropivacaine hydrochloride with a 20 mL loading dose was provided. After the end of the operation, the electronically controlled analgesia pump was connected. In the PCIA group, fentanyl with a 0.05 mg loading dose was provided and the electronic controlled analgesia pump was connected at the end of the operation. Venous blood was collected before anesthesia (T0), 1 h postoperatively (T1), 24 h postoperatively (T2) and 48 h postoperatively (T3). Th1/Th2 was calculated and analyzed by flow cytometry, and other indexes of these time points were recorded. The results show that there was no significant difference between the two groups regarding changes in blood pressure, heart rate and postoperative sedation Ramsay score. There was no significant difference in Th1 percentages (Th1%), Th2 percentages (Th2%) and ratios of Th1-to-Th2 (Th1/Th2) between the two groups at T0, T1 and T2 ($P>0.05$), while the Th1%, Th2% and Th1/Th2 of the PCIA group were lower than those of the cFNB group at T3 ($P<0.05$). It was concluded that cFNB represents a better postoperative analgesia for patients than PCIA, and has a lesser effect on Th1/Th2 balance, which can improve the outcome of patients.

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LETTER TO THE EDITOR

SACCHAROMYCES CEREVISIAE, KEY ROLE OF MIG1 GENE IN METABOLIC SWITCHING: PUTATIVE FERMENTATION/OXIDATION

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Saccharomyces cerevisiae can utilize a wide range of carbon sources; however, in the presence of glucose the use of alternate carbon sources would be repressed. Several genes involved in the metabolic pathways exert these effects. Among them, the zinc finger protein, Mig1 (multicopy inhibitor of GAL gene expression) plays important roles in glucose repression of *Saccharomyces cerevisiae*. To investigate whether the alleviation of glucose effect would result in a switch to oxidative production pathway, MIG1 were disrupted in a haploid laboratory strain (2805) of *S. cerevisiae*. The impact of this disruption was studied under fully aerobic conditions when glucose was the sole carbon source. Our results showed that glucose repression was partly alleviated; i.e., ethanol, as a significant fermentation marker, and acetate productions were respectively decreased by 14.13% and 43.71% compared to the wild type. In Δ MIG1 strain, the metabolic shifting on the aerobic pathway and a significant increase in pyruvate and glycerol production suggested it as an optimally productive industrial yeast strain. However, further studies are needed to confirm these findings.

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LETTER TO THE EDITOR

PHARMACOKINETIC CHANGES INDUCED BY FOCUSED ULTRASOUND IN GLIOMA-BEARING RATS USING DYNAMIC CONTRAST-ENHANCED MRI MEASUREMENTYL. ZHAO¹, X. XIA², CE. LIANG² and XM. LI³

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It has been shown that focused ultrasound (FUS) can be effectively used for brain tumor therapy, and as a noninvasive, targeted drug delivery technique combined with microbubbles. In this study, magnetic resonance imaging (MRI) was used to measure the kinetics of Gadolinium diethylenetriamine Penta acetic acid (Gd-DTPA) in glioma-bearing rats. Ten glioma-bearing rats (9-12 weeks, 290-340 g weight) were used in the study. After the use of dynamic contrast enhancement (DCE)-MRI, the spatial permeability of FUS-induced blood-brain barrier disruption (BBB-D) was evaluated, and the kinetic parameters by the general kinetic model (GKM) were calculated. The results show that mean K_{trans} of the contralateral tumor was significantly lower than the mean K_{trans} of sonicated tumor. Moreover, the transfer constant K_{trans} in ultrasound tumors was closely related to tissue extravasation ($R = 0.95$), suggesting that DCE-MRI can determine drug accumulation in the brain. Except for a few small red blood cell extravasations, there was no macroscopic damage according to the histologic analysis. The study showed that the DCE-MRI can be a valuable tool in quantifying BBB permeability in tumors and monitor the kinetics of FUS-induced BBB-D processes.

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LETTER TO THE EDITOR

EVALUATION OF SAFETY AND EFFICACY OF DIFFERENT CONTINUOUS BLOOD PURIFICATION METHODS IN TREATING INFANTILE SEPSISW-B. LI¹, L-Y. YIN¹ and X-Q. ZHANG²¹*Department of Infectious Disease, Xuzhou Children's Hospital, Xuzhou, Jiangsu, P.R. China;*²*Intensive Care Unit, Xuzhou Children's Hospital, Xuzhou, Jiangsu, P.R. China**Received August 21, 2017 – Accepted August 24, 2017*

The aim of this study was to compare the safety and the efficacy of two methods of continuous blood purification (CBP), continuous veno-venous hemofiltration (CVVH) and high volume hemofiltration (HVHF), for treatment of infantile sepsis. Eighty-six children with sepsis were enrolled in this study and randomly divided into two groups with 47 cases in the CVVH group and 39 cases in the HVHF group. Survival rate, duration of blood filtration, mean arterial pressure (MAP), mean heart rate and SaO₂, APACHE II score, procalcitonin, hs-CRP and TXB2 were compared between the two groups. Results showed that survival rate, MAP, mean heart rate and SaO₂ in the two groups did not have any significant differences. Duration of blood filtration and APACHE II score in the HVHF group was significantly shorter than that in the CVVH group. After therapy, levels of procalcitonin, hs-CRP and TXB2 declined dramatically in both groups, however this reduction was more significant in the HVHF group. We conclude that HVHF is a safer and more effective method as it produced stable hemodynamics, shorter filtration time, better APACHE II scores and better results in alleviating inflammatory reactions.

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LETTER TO THE EDITOR

TRANSURETHRAL FLUORESCENCE CYSTOSCOPY GUIDANCE FOR TOTAL RESECTION OF BLADDER TUMOR

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The first two Authors contributed equally to this study

The purpose of this work is to investigate the total resection of bladder tumor under transurethral fluorescence cystoscopy. Nineteen patients with bladder tumor, from which we resected a total of 26 tumors, including 16 single tumors with diameters of 0.5~2 cm, were enrolled in the study. All tumors were located in the posterior wall or neck of the bladder. For the surgery, the size and location of tumors in the bladder were observed by fluorescence cystoscopy. Then, plasma electrocision was used to cut the full-thickness of the bladder to the fat outside of the bladder along the near-end of the tumor, then along the left and right side of bladder (to the far-end), and the full-thickness of the tumor was resected. Finally, the far-end tumor was removed and the full-thickness of the bladder at the bottom was completely resected. All operations were completed successfully within 10-40 min. There was little bleeding during surgery and no secondary bleeding after surgery. Tumor staging found 17 patients at T1 stage (20 tumors) and 2 patients at T2 stage (6 tumors). Patients were followed up for 6~12 months without any recurrence. We show here that total resection of bladder tumor can be accomplished under transurethral fluorescence cystoscopy and preventative resection can be conducted on the suspicious bladder wall with precision to eliminate tumor residue that promotes recurrence.

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*LETTER TO THE EDITOR***EFFECTS OF LOW MOLECULAR WEIGHT HEPARIN IN THE TREATMENT OF VENOUS THROMBOEMBOLISM IN PATIENTS WITH GASTROINTESTINAL CANCER**

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This study aimed to observe the safety and effectiveness of different dosing regimens of low molecular weight heparin in the prevention of venous thromboembolism (VTE) and to provide a guideline for the treatment of individualized VTE prophylaxis in patients with postoperative gastrointestinal tumors. Forty patients with high risk for VTE after surgery for gastrointestinal tumors treated in Hongqi Hospital of Mudanjiang Medical University in the period October 2016 to May 2017 were included in the study. The patients were randomly divided into two groups, group A that included 24 patients treated with low molecular weight heparin (LMWH) 5000 IU every 12 hours, and group B comprised of 16 patients treated with LMWH 5000IU every 24 hours. On the seventh day post-surgery anti-Xa activity values reached effective anticoagulation (>0.5 IU/mL) in both groups. In group A, there was one case of anti-Xa activity exceeding 1.0 IU/mL, but no bleeding complications occurred. Using LMWH 5000 IU subcutaneous injection every 12 hours could also prevent postoperative VTE of gastrointestinal tumor, but the risk of bleeding complications is higher compared with 24-hour administration. Monitoring of plasma D-dimer within 7 days after gastrointestinal surgery did not show a great value for VTE monitoring. This study demonstrated that subcutaneous injection of LMWH can prevent VTE after gastrointestinal tumor surgery and provide a new alternative for VTE prevention.

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*LETTER TO THE EDITOR***PREDICTION OF LENGTH OF HOSPITAL STAY AND MORTALITY IN PATIENTS WITH DELIRIUM: A PROSPECTIVE COHORT ANALYSIS OF 200 ICU PATIENTS**

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Delirium develops in most critically ill Intensive Care Unit (ICU) patients and is associated with longer hospital stay, increased rate of mortality and increased cost of healthcare. The purpose of this study was to evaluate the incidence of delirium in non-ventilated ICU patients and demonstrate its clinical association with the hospital/ ICU length of stay and in-patient mortality. A total of 200 ICU patients (aged 18 years or over) who were admitted to the ICU with specific primary diagnoses were selected for the study and followed up until either hospital discharge or death. Delirium status of each patient was assessed every morning by trained study personnel using the Confusion Assessment Method for Intensive Care Unit (CAM-ICU). Data collection included baseline demographics, diagnosis (at the time of admission) and severity of illness using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score. Upon evaluation of the effects associated with age, gender, mortality and other variables, it was found that age had a direct effect on the incidence of delirium, with the probability of delirium increasing with the increase in the age of patients. It was also shown that mortality, either in the ICU or during the hospital stay, was associated significantly with the occurrence of delirium. This study shows that duration of delirium in ICU is an independent predictor of long-term hospital stay and is significantly associated with mortality. These findings are crucial for health care professionals and future research trials dealing with critically ill ICU patients.

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LETTER TO THE EDITOR

PERIPHERAL T LYMPHOCYTE IMMUNITY AND L-DOPAMINE IN PATIENTS WITH PARKINSON'S DISEASEZX. HU¹, WN. SONG², XD. LU¹, ML. ZHOU¹ and JH. SHAO¹¹*Department of Neurology, The Affiliated Hospital of Hangzhou Normal University, Hangzhou, China;*²*Department of Obstetrics, Hangzhou Obstetrics and Gynecology Hospital, Hangzhou, China**Received February 8, 2018 – Accepted April 9, 2018*

This study aimed to evaluate the efficacy of T-cell immune function and L-dopamine (L-DOPA) in patients with Parkinson's disease (PD). Sixty subjects (included in the study group) with PD who were patients of the Neurology Department of The Affiliated Hospital of Hangzhou Normal University from July 2015 to March 2017 were selected. The study group was then categorized into groups according to the age of the patients, severity of disease, level of cognition, and treatment of L-DOPA. The control group (30 cases) was from the healthy population of the check-up center at The Affiliated Hospital of Hangzhou Normal University. The peripheral blood T-lymphocyte subsets of the study group were measured by direct immunofluorescence flow cytometry staining and compared with the control group. At the same time, correlation analysis was carried out on patients with different degrees of disease severity according to staging, different accompanying symptoms, and whether L-DOPA was administered. The results of the study show that the levels of CD4+, CD8+, CD3+, and CD4+/CD8+ peripheral blood in PD patients were significantly lower than those in the control group ($P<0.05$). It was found that the levels of CD4+, CD8+, CD3+, and CD4+/CD8+ decreased with age. The CD4+, CD8+, CD3+, and CD4+/CD8+ in patients with advanced stage PD were more significant than those with low PD stages ($P<0.05$). The levels of CD4+, CD8+, CD3+, and CD4+/CD8+ in the dementia group were significantly lower than those in the non-dementia group ($P<0.05$). The levels of CD4+, CD8+, CD3+, and CD4+/CD8+ in PD patients treated with L-DOPA were higher than those of PD patients without L-DOPA treatment ($P<0.05$). In conclusion, the immune function of T cells in patients suffering from PD is low, and the immune function of T cells in patients with severe disease is lower. Therefore, it is of certain significance to further study the pathophysiological mechanism of PD.

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LETTER TO THE EDITOR

APATINIB TREATMENT IN EXTENSIVE METASTATIC ADVANCED THYMIC CARCINOMAY. HE¹, S. LIU², M. E¹, C. WANG¹, M. SHI¹, G. LIU¹ and N. ABIYASI³

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Apatinib is a novel oral, anti-tumor, angiogenic-targeting drug that can selectively target vascular endothelial growth factor receptor-2 (VEGFR-2). In clinical trials, this new tyrosine kinase inhibitor (TKI) has been shown to be an effective and safe treatment for a variety of malignancies. Currently, there is a lack of studies of patients with thymic carcinoma; therefore, we present a case of advanced thymic carcinoma treated with apatinib after chemotherapy failure with multiple lung metastases. This patient has been taking a dose of 500 mg of apatinib per day, and his efficacy has achieved partial response (PR), according to the RECIST 1.1 standard, and progression-free survival (PFS) is 6.3 months at this point. Apatinib will continue as his maintenance treatment. During the treatment, drug-related toxicity and side effects were tolerable. Thus, apatinib may be a meaningful option for the treatment of advanced metastatic thymic carcinoma after chemotherapy failure.

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LETTER TO THE EDITOR

PROTECTIVE EFFECTS OF *HERPETOSPERMUM CAUDIGERUM* EXTRACTS AGAINST LIVER INJURY INDUCED BY CARBON TETRACHLORIDE IN MOUSE

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The first two Authors contributed equally to this study

Herpetospermum caudigerum (*H. caudigerum*; HC), popularly known as “Sejimeiduo” in Tibet, it is widely used in Tibetan traditional medicine for the treatment of dyspepsia, liver and colic diseases. This study was designed to evaluate the effect of *H. caudigerum* extract (HCE) on suppressing liver injury induced by carbon tetra chloride (CCl₄). For this purpose, we used CCl₄ to induce acute liver injury in mouse model. The protective effects of HCE against liver injury were evaluated by biochemical parameters, histopathological and immunohistochemical staining. The results showed that the superoxide dismutase (SOD) activity was significantly increased with the increasing dose of HCE as compared to the CCl₄-treated group (p<0.01); while AST and ALT levels in serum, MDA and MPO in liver were reduced in a dose-dependent manner. The histopathology showed that HCE treatment promoted the recovery of histopathological changes in liver in a dose-dependent way. Meanwhile, there was a higher expression of caspase-3 and NF-κB in the nucleus of several liver cells in the CCl₄-induced group, and a low expression of caspase-3 and NF-κB were found with the increasing dose of HCE. Therefore, the present study suggests that HCE is a potent hepatoprotective agent that can treat acute liver injury and this ability may be attributed towards its anti-inflammatory and antioxidant potential.

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LETTER TO THE EDITOR

PYRAZINAMIDE-RESISTANT MYCOBACTERIUM TUBERCULOSIS ISOLATES FROM KHYBER PAKHTUNKHWA AND *rpsA* MUTATIONS

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Pyrazinamide (PZA) is a key first-line antibiotic used for the short-course treatment of drug-sensitive and multidrug-resistant (MDR) isolates of tuberculosis. PZA exhibits potent action against semi-dormant bacilli in acidic environments. However, mutations that occur in target genes may cause technical difficulties in the diagnosis of PZA resistance during drug susceptibility testing. The objective of the current study is to identify mutations in *pncA*^{WT} *rpsA* and *rpsA*^{WT} *panD* genes among PZA-resistant isolates of *Mycobacterium tuberculosis* (MTB) circulating in the Pashtun dominant region, Khyber Pakhtunkhwa, Pakistan. We selected 18 PZA-resistant *pncA*^{WT} strains from the Provincial Tuberculosis Reference Laboratory (PTRL) Khyber Pakhtunkhwa to investigate mutations in the coding region of *rpsA* and *panD* genes. The experiments were repeated for drug susceptibility testing using MGIT 960 automated system. In addition, eighteen PZA-resistant *rpsA* genes along with 5 susceptible strains and one H37Rv strain were sequenced. All 18 isolates were PZA-resistant. The majority of these isolates exhibited multidrug resistance (MDR) (13/18). We identified 14 non-synonymous and one synonymous mutation in the coding region of *rpsA* in 11 strains. All mutations were scattered throughout the gene and not reported previously. Further, we did not identify any mutation in 7 *rpsA*^{WT} *panD* genes. Mutations in *rpsA* but not in *panD* occur in PZA-resistant *pncA*^{WT} MTB isolates circulating in Khyber Pakhtunkhwa, Pakistan.

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LETTER TO THE EDITOR

COMPARATIVE EFFICACY OF ORAL CONTRACEPTIVE *VERSUS* LOCAL TREATMENT *VERSUS* INTENSE PULSED LIGHT COMBINED WITH VACUUM IN ENDOCRINE ACNE IN WOMEN

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All Authors contributed equally to this study

Acne is the most common affection of adolescents, although it can be also found in adult women. Our study was aimed at the comparative assessment of three different therapies over a three-month period, applied to women with moderate comedogenic and papulo-pustular endocrine acne. In the study 116 female patients with endocrine localized face acne were included and divided into three groups: group I with 42 patients was treated with a combination of contraceptive pill + local treatment + pulsed-vacuum light; group II with 38 patients was treated with contraceptives and pulsed-vacuum light and group III with 36 patients was treated only with local treatment. The acne evaluation was made using the Global Acne Grading System (GAGS). Statistical data processing was carried out using the STATA software. For the comedogenic form of acne, the good and very good results were superior in group I vs group II and III (83.33% vs 31.58% vs 5.56%) at the end of the three months of treatment. For the papulo-pustulous form of acne, good and very good results were similar in groups I and II (92.86% vs 73.68%) both after the first month of treatment and at the end of the study, well above the local treatment group (13.99%). Our study highlighted the superiority of laser treatment combined with hormonal treatment, compared to hormonal and local treatment in the comedogenic form of acne, and the superiority of hormonal treatment combined (or not) with laser treatment in the papulo-pustular form compared to local treatment.

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*LETTER TO THE EDITOR***COMPARISON OF AUTOMATIC AND MANUAL REPOSITION TREATMENT FOR HORIZONTAL SEMICIRCULAR CANAL BENIGN PAROXYSMAL POSITIONAL VERTIGO**

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The purpose of this investigation was to compare the efficacy of automatic to manual reposition treatment for patients with horizontal semicircular canal paroxysmal positional vertigo (BPPV). Sixty patients diagnosed with BPPV were equally and randomly divided into either a manual reposition treatment group or an automatic reposition treatment group. The groups were compared regarding difference in pain [visual analog scale (VAS)], extent of vertigo disorder [dizziness handicap inventory (DHI)], quality of life (SF-36), and therapeutic effect. Improved VAS, DHI and SF-36 were observed in both groups, however the efficacious rate of the automatic reposition group (96.7%) was 13.4% higher than that of the manual reposition group, reaching a statistical significance ($p < 0.05$). In conclusion, in the treatment of BPPV patients, automatic reposition is more effective than manual reposition and can improve the patient's quality of life.

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LETTER TO THE EDITOR

DIAGNOSIS WITH SPIRAL CT IMAGING BEFORE GASTRIC CARCINOMA SURGERY

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This study was carried out to study multi-slice spiral CT imaging for patients with gastric carcinoma and explore the values of multi-slice spiral CT imaging in staging prior to gastric carcinoma (GC) surgery. Forty-eight patients with GC underwent multi-slice spiral CT, and the scanning results were compared with the pathological results. The similarity of the results was observed, and the accuracy was calculated. Of 48 patients, 8 did not undergo surgery because of metastasis. In the diagnosis of the remaining 40 patients, the sensitivity of multi-slice spiral CT in the diagnosis of staging of invasive depth of GC was 77.5%; $\kappa = 0.642$ in the analysis of consistency; there was no significant difference with the pathological results ($p > 0.05$). The overall accuracy of diagnosis for stage N was 80%. The accuracy of multi-slice CT in detecting distant metastasis of GC was 87.5%. Multi-slice spiral CT can determine and evaluate various metastases of GC. The diagnostic results obtained using multi-slice spiral CT was probably consistent with the pathological results.

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LETTER TO THE EDITOR

THE IMPORTANCE OF EXPRESSING PDCD4 AND PDCD5 ANTI-ONCOGENES IN GLIOMA

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Glioma is the most common malignant tumor of the brain, which is difficult to be completely resected. The recurrence and mortality rates are high and the prognosis is poor. The aim of this study was to investigate the expression of anti-oncogene programmed cell death 4 (PDCD4) and programmed cell death 5 (PDCD5) in glioma and their influence on the progression of the disease in order to provide new therapeutic approaches. Reverse transcription polymerase chain reaction (RT-PCR) analysis was used to investigate PDCD4 mRNA and PDCD5 mRNA expression in 66 glioma patients who served as the study group and 22 patients who suffered from craniocerebral injuries or hematencephalon who were used as controls. The experimental group was divided into a low malignant group (tumors grade I - II) and a high malignant group (tumor grades III-IV). The PDCD4 mRNA and PDCD5 mRNA expression in the experimental group was 0.545 ± 0.202 and 0.687 ± 0.174 and in the control group was 0.942 ± 0.131 and 0.868 ± 0.190 , respectively ($P<0.05$). The PDCD4 mRNA and PDCD5 mRNA expressions in the low malignant group were 0.628 ± 0.240 and 0.750 ± 0.198 , respectively, and in the high malignant group were 0.464 ± 0.185 and 0.553 ± 0.170 , respectively ($P<0.05$). The results showed a downregulation of PDCD4 mRNA and PDCD5 mRNA expression in the experimental group compared with the control group. This downregulation was correlated with the pathological grade of glioma. In the high malignant group the PDCD4 mRNA and PDCD5 mRNA expressions were significantly decreased compared with the low malignant group and the control group. PDCD4 mRNA and PDCD5 mRNA expressions are promising targets for the diagnosis and treatment of glioma.

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LETTER TO THE EDITOR

TREATMENT OF SYMPTOMATIC ORAL MUCOSITIS WITH SODIUM HYALURONATE AND SYNTHETIC AMINO ACID PRECURSORS OF COLLAGEN IN PATIENTS UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANTATIONT. RUGGIERO¹, R. POL¹, D. CAMISASSA¹, S. SIMIELE², L. GIACCONE³ and S. CAROSSA⁴

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The purpose of the study is to evaluate the clinical effects of Mucosamin[®] (a spray preparation containing sodium hyaluronate combined with a pool of amino acids of precursor collagen, including L-Proline, L-Leucine, L-Lysine and glycine) on wound healing and pain management of oral mucositis after hematopoietic stem cell transplantation. The importance of professional dental hygiene by dental hygienist in reducing the severity of oral mucositis as unique therapy or in addition to therapy with Mucosamin[®] was also evaluated. One hundred thirty-seven patients undergoing hematopoietic stem cell transplantation were recruited in a case-control study and divided into 4 groups: Group A: professional oral hygiene + Mucosamin[®]; Group B: professional oral hygiene + standard treatment with chlorhexidine 0.20%; Group C: only Mucosamin[®]; Group D: only standard treatment with chlorhexidine 0.20%. The following evaluations were made: WHO mucositis scale, OMAS mucositis scale, VAS, periodontal recording, days of mucositis. Comparing the groups at the onset of OM on WHO scale, it was observed that Group A grade 1 occurrence was more statistically significant than Group B ($p=0.03^*$); comparison between Group A and D showed a statistically significant difference in favour of Group A ($p=0.0002^*$). Also OMAS scale showed a statistically significant difference between groups who assumed Mucosamin, who developed lower OM grade ($p=0.001^*$). There was a statistically significant difference between group A compared with group B over the overall duration of OM ($p=0.02^*$), as well as between group A and group D ($p=0.03^*$). According to the present study the combination of a careful debridement, correct oral hygiene during hospitalization and the use of Mucosamin[®] exponentially reduces the severity and duration of mucositis and consequently the discomfort of the patient. Moreover, it can be stated that the use of Mucosamin[®] also results in a reduction in the extent of chemotherapy lesions. Hyaluronic acid and amino acid-based sprays can be a valuable therapeutic aid in the treatment of mucositis.

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LETTER TO THE EDITOR

SDR® vs TRADITIONAL COMPOSITE IN CLASS II RESTORATIONS IN PRIMARY MOLARS

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This study aims to compare the clinical characteristics of a new flowable resin-based composite with those of a traditional composite when applied to deciduous molars for class II restorations. Twenty-eight children between 6-12 years of age, with paired minimal Class II cavities present on their primary molars, were chosen. The paired cavities were restored with either a microhybrid composite or a new flowable resin-based composite. The composites were assigned to cavities in either the right or left side of the mouth, using random allocation tables. Each pair of restorations were clinically assessed at six-month intervals following the United States Public Health Service criteria. The prevalence of carious lesions was higher in maxillary molars (53.6%) compared to the mandibular molars (46.4%). At 24 months, Charlie or Delta scores in the paired groups were not seen in any patient, thus demonstrating a clinical success. The statistical analysis using Pearson's *chi*-squared test did not reveal significant p-values for any parameter except the proximal contact showing significant p-values for this parameter. SDR appears to be the material of choice for the restoration of deciduous teeth due to its clinical features shown at 24 months as well as its ease and speed of application.

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*LETTER TO THE EDITOR***DEEP INFILTRATION FOR THE TREATMENT OF HYPOMINERALIZED ENAMEL LESIONS IN A PATIENT WITH MOLAR INCISOR HYPOMINERALIZATION: A CLINICAL CASE**L. GIANNETTI¹, A. MURRI DELLO DIAGO¹, E. CORCIOLANI¹ and E. SPINAS²*¹Department Paediatric Dentistry, University of Modena and Reggio Emilia, Italy; ²Department Surgical Sciences, University of Cagliari, Cagliari, Italy**Received March 14, 2018 – Accepted April 12, 2018*

This case report presents the technique of deep infiltration for the treatment of hypomineralized enamel lesions in a patient affected by molar incisor hypomineralization (MIH) with the purpose of obtaining an aesthetic improvement in the affected vestibular enamel. Deep infiltration treatment involves a sequence of steps starting with an initial mechanical abrasion of the outside surface of the enamel, followed by a phase of chemical erosion using 15% hydrochloric acid, penetration through the porosity of the enamel by a very fluid resin, and finally the repair of the thin layer of lost enamel using a composite. The aesthetic improvement of the elements affected by hypomineralized lesions is discernable immediately following treatment and becomes more accentuated with time. At the expense of minimal damage to surface enamel, deep infiltration enables treatment of all types of white spot enamel lesions, regardless of aetiology, offering the possibility of restoring an aesthetically pleasing smile for patients.

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ERRATA CORRIGE

Withdrawal

The article below published in Volume 32 No. 2 has been withdrawn owing to discrepancies in the results found by the co-Authors.

S. Ali, C. Sola, M. Harrison, M. Tahir, A. Sheed Khan, M. Mumtaz, E. Chimara and F. Hassan. Spoligotyping analysis of Mycobacterium tuberculosis with TB-SPRINT technology

Authors

The Authors of the article entitled “Clinical course of severe colitis: a comparison between Crohn’s disease and ulcerative colitis” published in Volume 32 No. 2 p. 415 should read:

E. Sinagra, A. Orlando, F. Mocciaro, V. Criscuoli, L. Oliva, S. Maisano, M. Giunta, F. La Seta, G. Solina, A.G. Rizzo, A. Leone, G. Tomasello, F. Cappello and M. Cottone