

Abstracts publicaciones internacionales ISI 2007

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ANATOMÍA PATOLÓGICA

SPECTROCHIM ACTA A MOL BIOLOM SPECTROSC. 2007;67(1):230-4.

COMPLEXATION OF QUERCETIN WITH THREE KINDS OF CYCLODEXTRINS: AN ANTIOXIDANT STUDY.

Jullian C, Moyano L, Yáñez C, Olea-Azar C.

The slightly water-soluble flavonoid quercetin (QUE) and its inclusion with either beta-cyclodextrin (beta CD), hydroxypropyl-beta-cyclodextrin (HP-beta CD) or sulfobutyl ether-beta-cyclodextrin (SBE-beta CD) were investigated. The stoichiometric ratios and stability constants describing the extent of formation of the complexes have been determined by phase-solubility measurements; in all cases type-A(L) diagrams have been obtained (soluble 1:1 complexes). The results showed that the inclusion ability of beta CD and its derivatives was the order: SBE-beta CD > HP-beta CD > beta CD. Kinetic studies of DPPH center dot with QUE and CDs complexes were done. The results obtained indicated that the QUE-SBE-beta CD complex was the most reactive form. The scavenging capability of QUE and CDs complexes with DPPH center dot and galvinoxyl was studied using ESR spectroscopy. All complexes showed a higher scavenging capability with both radicals, compare quercetin in water. Beside, these results indicated that the complexes formed maintained the quercetin antioxidant activity.

BANCO DE SANGRE

CYTOKINE & GROWTH FACTOR REV. 2007;18(1-2):171-82.

PARADOXICAL EFFECTS OF CYTOKINES IN TUMOR IMMUNE SURVEILLANCE AND TUMOR IMMUNE ESCAPE.

Salazar-Onfray F, López MN, Mendoza-Naranjo, A.

The role of cytokines in modulating the formation of new tumors is mediated by their ability to regulate antigen-specific anti-tumor responses and by the activation of non-specific mechanisms, including those involved in the processes of inflammation and innate resistance. Cytokines may influence the growth of tumors by acting directly on tumor cells as growth promoting or growth inhibiting factors or indirectly by attracting inflammatory cell types and affecting angiogenesis. Due to the potency and complexity of cytokine activity against tumor growth, the improvement of cloning techniques and the availability of recombinant forms of different cytokines, a great effort has been made in the recent years to exploit this anti-tumor potential for cancer therapy. This important goal has been difficult to achieve in most cases due to toxicity of most cytokines which could not be dissociated from their anti-tumoral functions. Nevertheless, if well designed, treatment protocols and/or modifications of the cytokine molecules may in some situations augment the anti-tumor effects while limiting the toxicity. One of these molecular approaches could be the design of peptides containing the functional domain of certain cytokines, exemplified by IT9302, a peptide homologous to the functional domain of IL-10, which has demonstrated to increase tumor NK cell sensitivity.

INVEST OPHTHALMOL VIS SCI. 2007 MAR;48(3):1219-27.

MELANOCORTIN 1 RECEPTOR IS EXPRESSED BY UVEAL MALIGNANT MELANOMA AND CAN BE CONSIDERED A NEW TARGET FOR DIAGNOSIS AND IMMUNOTHERAPY.

López MN, Pereda C, Ramírez M, Mendoza-Naranjo A, Serrano A, Ferreira A, Poblete R, Kalergis AM, Kiessling R, Salazar-Onfray F.

Purpose: uveal melanoma is the most common primary malignant ocular cancer in adults. This tumor has a distinct expression pattern of markers compared with cutaneous melanoma. MC1R is under study as a potential target for antitumor immunity. Because of the potential immunogenicity of MC1R, it is important to evaluate its expression on uveal melanomas. Methods: two novel monoclonal antibodies (MP1.1C11 and MP1.1B7) were used to examine the expression of MC1R in uveal melanomas. Tissue samples obtained from 17 patients were analyzed for expression of MC1R by immunohistochemistry. Additionally, uveal melanoma cell lines were treated with proinflammatory cytokines, after which MC1R cell surface expression was analyzed by flow cytometry. Results: results demonstrated that MC1R is expressed by uveal melanoma to a significantly greater extent than other melanoma markers. With the use of MP1.1C11 or MP1.1B7, MC1R was detected in 95% of the tested melanoma tissues, including one liver metastasis. In contrast, MART-1, S100-specific protein, and gp-100 were only expressed by 66%, 33%, and 67% of the analyzed samples, respectively. Results also demonstrated that even though MC1R is mainly located intracellularly, its cell surface expression can be promoted by cytokines such as IFN-gamma, TNF-alpha, IL-4, and IL-10. Conclusions: these observations support the inclusion of MC1R in the panel of markers for the diagnosis of uveal melanoma. Therapeutic use of MC1R-specific antibodies targeting cytokine-induced MC1R potentially requires expression of the target molecule on the surfaces of tumor cells. Data presented here support MC1R as a new marker and a putative therapeutic target for uveal melanoma.

J IMMUNOLOG. 2007;178(11):6949-57.

FUNCTIONAL GAP JUNCTIONS FACILITATE MELANOMA ANTIGEN TRANSFER AND CROSS-PRESENTATION BETWEEN HUMAN DENDRITIC CELLS.

Mendoza-Naranjo A, Sáez PJ, Johansson CC, Ramírez M, Mandakovic D, Pereda C, López MN, Kiessling R, Sáez JC, Salazar-Onfray F.

Previously, we found that human dendritic cells (hDCs) pulsed with a melanoma cell lysate (MCL) and stimulated with TNF- α (MCL/TNF) acquire a mature phenotype in vitro and are able to trigger tumor-specific immune responses when they are used in melanoma immunotherapy in patients. In this study, we describe that MCL/TNF induces gap junction (GJ)-mediated intercellular communications and promotes melanoma Ag transfer between ex vivo produced hDCs from melanoma patients. hDCs also exhibit increased expression of the GJ-related protein connexin 43, which contributes to GJ plaque formation after MCL/TNF stimulation. The addition of GJ inhibitors suppresses intercellular tumor Ag transfer between hDCs, thus reducing melanoma-specific T cell activation. In summary, we demonstrate that MCL/TNF-stimulated hDCs can establish functional GJ channels that participate in melanoma Ag transfer, facilitating Ag cross-presentation and an effective dendritic cell-mediated melanoma-specific T cell response. These results suggest that GJs formed between hDCs used in cancer vaccination protocols could be essentials for the establishment of a more efficient antitumor response.

CARDIOVASCULAR

TRANSPLANT PROC. 2007 APR;39(3):622-4.

CYTOMEGALOVIRUS INFECTIONS IN CARDIAC TRANSPLANT PATIENTS: AN EXPERIENCE AT A CLINICAL HOSPITAL, UNIVERSITY OF CHILE.

Sepúlveda L, Llancaqueo M, Zamorano J, Bermúdez C, Cortés C.

Background: Since cytomegalovirus (CMV) infects between 20% and 50% of heart transplant patients, we reviewed our experience in 7 cases of this infection. Methods: A prospective analysis of CMV infection was performed in heart transplant patients who received cyclosporine, azathioprine, or mycophenolate mofetil, and prednisone. An elevated creatinine de novo was managed with antibody induction. Results: between August 2001 and December 2005, we performed 22 heart transplants and 1 heart plus kidney transplant. Twenty-two patients were positive for CMV before transplantation. One patient

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died early because of graft failure. Immunosuppression included cyclosporine and prednisone (100%), azathioprine (52%), or mycophenolate (47%). Two recipients were induced with thymoglobulin and 13 with Daclizumab, while 8 did not receive any antibody. Nineteen patients received prophylaxis for CMV. Seven patients (30%) showed CMV infection, 6 of whom had received prophylaxis. Symptoms started at an average of 107 days posttransplantation in patients with prophylaxis. Three patients had gastritis, 2 pneumonias, and 1 colitis. One patient had concomitant lung aspergillosis. The two patients who received ATG developed CMV infections; 3 of the 12 with Daclizumab; and 2 who did not receive antibody. Of the CMV-infected subjects, 5 were on azathioprine and 2 on mycophenolate. All patients were treated with gancyclovir. The 1 patient with concomitant aspergillosis died. Conclusions: The incidence of infection by CMV was 30%. Prophylaxis seemed to delay infection. Daclizumab induction did not increase the risk for CMV.

TRANSPLANT PROC. 2007 APR;39(3):625-6.

FIRST CASE OF SIMULTANEOUS HEART PLUS KIDNEY TRANSPLANTATION IN CHILE: CASE REPORT.

Sepúlveda L, Zamorano J, Cotera A, Núñez N, Llancaqueo M, Bermúdez C, Castillo R, González M, Álvarez F.

Advanced renal disease is a formal contraindication to heart transplantation, and heart failure may make a patient ineligible for kidney transplantation. The International Society of Heart and Lung Transplantation has reported 336 simultaneous heart and kidney transplantations with a 70% rate of 5 year survival. Herein we have presented the first case of simultaneous heart plus kidney transplantation in Chile. The patient is a 62-year-old man with diabetes mellitus and arterial hypertension who in 1997 had a myocardial infarction with cardiogenic shock and acute renal failure. He underwent a coronary bypass but developed progressive heart failure, with an ejection fraction less than 20% and moderate mitral regurgitation. He required chronic hemodialysis and survived a cardiac arrest, receiving an implantable cardioverter defibrillator. Transplantation was performed in 2004 in 2 phases: initially a heart, followed by kidney transplantation. Immunosuppression included Daclizumab, cyclosporine, mycophenolate mofetil (MMF) and steroids. He developed acute renal failure but did not receive dialysis. He left the hospital at 25 days posttransplantation. Two years following double transplantation, he has not shown acute rejection episodes of either the cardiac or the kidney graft. Both cardiac and renal functions are normal. In conclusion, simultaneous heart plus kidney transplantations offer a good alternative treatment for patients with advanced disease of both organs.

MED HYPOTHESES. 2007;69(6):1242-8.

NON-HYPOXIC PRECONDITIONING OF MYOCARDIUM AGAINST POSTOPERATIVE ATRIAL FIBRILLATION: MECHANISM BASED ON ENHANCEMENT OF THE ANTIOXIDANT DEFENSE SYSTEM.

Rodrigo R, Castillo R, Cereceda M, Asenjo R, Zamorano J, Araya J.

Oxidative stress underlies postoperative atrial fibrillation and electrophysiological remodelling associated with rapid atrial pacing. An increasing body of evidence indicates that the formation of reactive oxygen species (ROS) released following extracorporeal circulation are involved in the structural and functional myocardial impairment derived from the ischemia-reperfusion cycle. ROS behave as intracellular messengers mediating pathological processes, such as inflammation, apoptosis and necrosis, thereby participating in the pathophysiology of atrial fibrillation. Thus, increased superoxide ($O_2^{\cdot-}$) production has been found in isolated atrial cardiomyocytes from patients with atrial fibrillation. Therefore, it seems reasonable to assume that the reinforcement of the antioxidant defense system should protect the heart against functional alterations in the cardiac rhythm. On this line, antioxidant enzyme induction through in vivo exposure to moderate concentration of ROS is associated with a reduction in the susceptibility of myocytes to ROS-induced injury. This response could be due to a prevailing effect of survival over apoptotic pathway. Previously, tissue preconditioning caused by prior exposure to an ischemia/reperfusion cycle has been successfully applied in experimental models and clinical settings associated with oxidative damage by ROS. However, such hypoxic preconditioning method is harmful to be applied to many clinical conditions associated with oxidative stress. In turn, experimental studies have revealed that non-enzymatic antioxidants produce a significant functional amelioration in cardiomyocytes subjected to an oxidative challenge. Moreover, clinical studies with patients scheduled for primary coronary artery bypass graft surgery had a reduced incidence of postoperative atrial fibrillation. We present the hypothesis of non-hypoxic preconditioning based on the association of pretreatment with n-3 polyunsaturated fatty acids followed by ascorbate plus alpha-tocopherol supplementation diminishes the incidence of postoperative atrial fibrillation in patients subjected to cardiac surgery with extracorporeal circulation.

NEUROPHARMACOLOGY. 2007 FEB;52(2):291-6.

DEXKETOPROFEN-INDUCED ANTINOCICEPTION IN ANIMAL MODELS OF ACUTE PAIN: SYNERGY WITH MORPHINE AND PARACETAMOL.

Miranda HF, Puig MM, Dursteler C, Prieto JC, Pinardi G.

The antinociceptive activity of dexketoprofen was studied in mice using the acetic acid writhing test (acute tonic pain), the tail flick test (acute phasic pain) and the formalin assay (inflammatory pain). Isobolographic analysis was used to study the antinociceptive interactions between morphine and paracetamol co-administered with dexketoprofen. In the writhing test, the intraperitoneal administration of dexketoprofen or ketoprofen resulted in parallel dose-response curves with equal efficacy, but higher relative potency for dexketoprofen. In the tail flick test, the curves were parallel with similar efficacy and potency. The administration of morphine or paracetamol in both tests resulted in dose-response curves not parallel with that of dexketoprofen, which showed a potency between morphine and paracetamol. In the formalin assay, the antinociceptive activity of morphine during phase I was 122, 295 and 1695 times higher than dexketoprofen, ketoprofen and paracetamol, respectively. Isobolographic analysis demonstrated that the combination of sub-analgesic doses of dexketoprofen with morphine or with paracetamol was strongly synergic in all three tests. Synergistic drug combinations should improve effective pharmacological treatment of pain, minimizing drug specific adverse effects. These findings are undoubtedly worthy of additional controlled clinical trials in severe pain syndromes.

MOL CELL BIOCHEM. 2007 SEP;303(1-2):73-81.

RELATIONSHIP BETWEEN (NA + K)-ATPASE ACTIVITY, LIPID PEROXIDATION AND FATTY ACID PROFILE IN ERYTHROCYTES OF HYPERTENSIVE AND NORMOTENSIVE SUBJECTS.

Rodrigo R, Bächler JP, Araya J, Prat H, Passalacqua W.

Oxidative stress may play a role in the pathogenic mechanism of essential hypertension. Lipid peroxidation can alter the cellular structure of membrane-bound enzymes by changing the membrane phospholipids fatty acids composition. We investigated the relationship between (Na + K)-ATPase activity, lipid peroxidation, and erythrocyte fatty acid composition in essential hypertension. The study included 40 essential hypertensive and 49 healthy normotensive men (ages 35-60 years). Exclusion criteria were obesity, dyslipidemia, diabetes mellitus, smoking, and any current medication. Patients underwent 24-h ambulatory blood pressure monitoring and blood sampling. Lipid peroxidation was measured in the plasma and erythrocytes as 8-isoprostane or malondialdehyde (MDA), respectively. Antioxidant capacity was measured as ferric reducing ability of plasma (FRAP) in the plasma and as reduced/oxidized glutathione (GSH/GSSG ratio) in erythrocytes. (Na + K)-ATPase activity and fatty acids were determined in erythrocyte membranes. Hypertensives had higher levels of plasma 8-isoprostane, erythrocyte MDA, and relative percentage of saturated membrane fatty acids, but lower plasma FRAP levels, erythrocyte GSH/GSSG ratio, (Na + K)-ATPase activity and relative percentage of unsaturated membrane fatty acids, compared with normotensives. Day-time systolic and diastolic blood pressures correlated positively with lipid peroxidation parameters, but negatively with (Na + K)-ATPase activity. These findings suggest that the modulation of (Na + K)-ATPase activity may be associated with changes in the fatty acid composition induced by oxidative stress and provide evidence of a role for this enzyme in the pathophysiology of essential hypertension.

CLÍNICA PSQUIÁTRICA

ACTAS ESP PSIQUIATR. 2007 NOV-DEC;35(6):387-92.

SEROTONIN TRANSPORTER POLYMORPHISM AND FLUOXETINE EFFECT ON IMPULSIVENESS AND AGGRESSION IN BORDERLINE PERSONALITY DISORDER.

Silva H, Iturra P, Solari A, Villarroel J, Jerez S, Vielma W, Montes C, Pumarino L, Roa N.

Introduction: impulsiveness and aggressiveness are characteristics of borderline personality disorder and are associated to a serotonergic system dysfunction. Serotonin transporter polymorphisms have been linked to aggressive and impulsive behaviors. The short allele (S) in depression is associated to a worse response to selective serotonin reuptake inhibitors (SSRI). This study aims to study these polymorphisms to predict the response of aggressive and impulsive behaviors to SSRIs in borderline personality disorder. Method: fifty-nine patients with DSM-IV borderline personality disorder in accordance with

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the International Personality Disorder Examination (IPDE) and without axis 1 disease were treated with flexible doses of fluoxetine for 12 weeks. The patients were evaluated with the Overt Aggression Scale Modified (OAS-M) at the beginning and at 2, 4, 8 and 12 weeks of treatment. Polymorphisms L and S of the serotonin transporter promoter region were determined. Response to fluoxetine of the LL carriers versus the S carriers (LS+SS) was compared. Results: LL carriers had a better response than S carriers in the reduction of total OAS-M scores and on the aggressiveness and irritability components of the OAS-M. Conclusions: L-allele carriers responded better to fluoxetine than S carriers, in a similar way as in depression. The S allele may represent a common factor of bad response to SSRI in diseases associated to serotonergic system dysfunction.

ACTAS ESP PSIQUIATR. 2007 DEC 4.

GENDER-RELATED DIFFERENCES IN FUNCTIONAL ASSESSMENT OF SEROTONERGIC SYSTEM IN HEALTHY YOUNG SUBJECTS.

Silva H, Nieto R, Montes C, Paredes A, Rentería P, Ramírez A, Jerez S.

Introduction. Prolactin stimulation test with serotonergic stimulants has been widely used in the study of diverse psychiatric disorders. However, the characterization of this response in normal subjects is still incomplete. Objective. To compare the response to serotonin stimulation using dexfenfluramine, a specific serotonergic agent, in young healthy men and women, controlling the menstrual cycle. Methods. A total of 10 women and 9 men, who were given 30 mg of dexfenfluramine orally, were studied and their levels of prolactin were measured on an hourly basis for a five-hour period. Baseline, maximum and delta values of prolactin were compared for both groups. Results. According to the age groups studied (mean age for men: 19.9 +/- 2.5 years old; mean age for women: 20 +/- 1.5 years old), the prolactin maximum level and the response to prolactin (DPRL) were significantly higher in women (p-values: 0.02 and 0.04, respectively). Conclusions. Young healthy women show a greater response to stimulation with dexfenfluramine than young healthy men. Clinical and biological implications of this observation are discussed in the context of the currently available research papers.

LANCET. 2007 NOV 10;370(9599):1629-37.

TREATMENT OF POSTNATAL DEPRESSION IN LOW-INCOME MOTHERS IN PRIMARY-CARE CLINICS IN SANTIAGO, CHILE: A RANDOMISED CONTROLLED TRIAL.

Rojas G, Fritsch R, Solis J, Jadresic E, Castillo C, González M, Guajardo V, Lewis G, Peters TJ, Araya R.

Background: the optimum way to improve the recognition and treatment of postnatal depression in developing countries is uncertain. We compared the effectiveness of a multicomponent intervention with usual care to treat postnatal depression in low-income mothers in primary-care clinics in Santiago, Chile. Methods: 230 mothers with major depression attending postnatal clinics were randomly allocated to either a multicomponent intervention (n=114) or usual care (n=116). The multicomponent intervention involved a psychoeducational group, treatment adherence support, and pharmacotherapy if needed. Usual care included all services normally available in the clinics; including antidepressant drugs, brief psychotherapeutic interventions, medical consultations, or external referral for specialty treatment. The primary outcome measure was the Edinburgh postnatal depression scale (EPDS) score at 3 and 6 months after randomisation. Analysis was by intention to treat. This study is registered with ClinicalTrials.gov, number NCT00518830. Findings: 208 (90%) of women randomly assigned to treatment groups completed assessments. The crude mean EPDS score was lower for the multicomponent intervention group than for the usual care group at 3 months (8.5 [95% CI 7.2-9.7] vs 12.8 [11.3-14.1]). Although these differences between groups decreased by 6 months, EPDS score remained better in multicomponent intervention group than in usual care group (10.9 [9.6-12.2] vs 12.5 [11.1-13.8]). The adjusted difference in mean EPDS between the two groups at 3 months was -4.5 (95% CI -6.3 to -2.7; p<0.0001). The decrease in the number of women taking antidepressants after 3 months was greater in the intervention group than in the usual care group (multicomponent intervention from 60/101 [59%; 95% CI 49-69%] to 38/106 [36%; 27-46%]; usual care from 18/108 [17%; 10-25%] to 11/102 [11%; 6-19%]). Interpretation: our findings suggest that low-income mothers with depression and who have newly born children could be effectively helped, even in low-income settings, through multicomponent interventions. Further refinements to this intervention are needed to ensure treatment compliance after the acute phase.

PSYCHOSOM MED. 2007 DEC;69(9):864-9.

STABILITY OF SOMATOFORM SYMPTOMS-IMPLICATIONS FOR CLASSIFICATION.

Rief W, Rojas G.

Objective: to investigate the stability of somatoform symptoms/disorders. Methods: a literature search was done to select studies reporting data on stability of medically unexplained physical symptoms. Results: whereas individual symptoms vary over time, grouping symptoms into syndromes seems to create stable features. There are substantial problems with the use of lifetime diagnosis, favoring classification approaches that require only present state symptoms. Further, doctors' ratings that symptoms are "medically unexplained" are highly problematic and reduce interrater reliability. Misdiagnoses and overlooking of organic conditions are in the same range as for other psychiatric (and many organic) disorders; therefore, this does not seem to reduce the stability of the diagnoses of somatoform disorders. Conclusions: these results indicate how the classification of somatoform disorders can be improved. Some new diagnostic criteria are suggested that could be considered in the revision of Diagnostic and Statistical Manual of Mental Disorders-V (DSM-V).

LANCET. 2007 SEP 15;370(9591):991-1005.

TREATMENT AND PREVENTION OF MENTAL DISORDERS IN LOW-INCOME AND MIDDLE-INCOME COUNTRIES.

Patel V, Araya R, Chatterjee S, Chisholm D, Cohen A, De Silva M, Hosman C, McGuire H, Rojas G, van Ommeren M.

We review the evidence on effectiveness of interventions for the treatment and prevention of selected mental disorders in low-income and middle-income countries. Depression can be treated effectively in such countries with low-cost antidepressants or with psychological interventions (such as cognitive-behaviour therapy and interpersonal therapies). Stepped-care and collaborative models provide a framework for integration of drug and psychological treatments and help to improve rates of adherence to treatment. First-generation antipsychotic drugs are effective and cost effective for the treatment of schizophrenia; their benefits can be enhanced by psychosocial treatments, such as community-based models of care. Brief interventions delivered by primary-care professionals are effective for management of hazardous alcohol use, and pharmacological and psychosocial interventions have some benefits for people with alcohol dependence. Policies designed to reduce consumption, such as increased taxes and other control strategies, can reduce the population burden of alcohol abuse. Evidence about the efficacy of interventions for developmental disabilities is inadequate, but community-based rehabilitation models provide a low-cost, integrative framework for care of children and adults with chronic mental disabilities. Evidence for mental health interventions for people who are exposed to conflict and other disasters is still weak-especially for interventions in the midst of emergencies. Some trials of interventions for prevention of depression and developmental delays in low-income and middle-income countries show beneficial effects. Interventions for depression, delivered in primary care, are as cost effective as antiretroviral drugs for HIV/AIDS. The process and effectiveness of scaling up mental health interventions has not been adequately assessed. Such research is needed to inform the continuing process of service reform and innovation. However, we recommend that policymakers should act on the available evidence to scale up effective and cost-effective treatments and preventive interventions for mental disorders.

J AFFECT DISORD. 2007 SEP;102(1-3):237-43.

WHAT DOES CHILEAN RESEARCH TELL US ABOUT POSTPARTUM DEPRESSION (PPD)?

Jadresic E, Nguyen Dn, Halbreich U.

Background: in Chile, a country with a so called emerging market-economy, where rapid social and life style changes are taking place, women and the more socially disadvantaged are more at risk of becoming depressed. Methods: results of several studies are summarized in the context of a review of the literature. Results: a third of Chilean women have depressive and/or anxiety symptoms during midpregnancy, while prevalence figures both in the early and the late postpartum period increase up to 50% in most studies. If strict operational criteria describing well defined depressive disorders are used postnatally, differences in prevalence and incidence figures arise depending on socioeconomic status. Whereas incidence rates for postpartum depression (around 9%) are very similar to those found in the northern hemisphere and do not appear to vary across different socioeconomic levels, higher prevalence rates are found among women from lower socioeconomic status. Limitations: the studies focused on current diagnostic entities and did not consider different clusters or dimensions. Conclusion: a shared biological etiology may be triggered by the physiology of childbirth and account for similarities in incidence across different socioeconomic levels. In turn, we hypothesize that the higher prevalence of postpartum depression (PPD) in Chilean women from lower socioeconomic status is the result of pre-existing depression and is not caused by more new cases of the illness.

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J AFFECT DISORD. 2007 SEP;102(1-3):159-76.

CULTURALLY-SENSITIVE COMPLAINTS OF DEPRESSIONS AND ANXIETIES IN WOMEN.

Halbreich U, Alarcón RD, Calil H, Douki S, Gaszner P, Jadresic E, Jasovic-Gasic M, Kadri N, Kerr-Correa F, Patel V, Sarache X, Trivedi JK.

Background: current classifications of Mental Disorders are centered on Westernized concepts and constructs. "Cross-cultural sensitivity" emphasizes culturally-appropriate translations of symptoms and questions, assuming that concepts and constructs are applicable. Methods: groups and individual psychiatrists from various cultures from Asia, Latin America, North Africa and Eastern Europe prepared descriptions of main symptoms and complaints of treatment-seeking women in their cultures, which are interpreted by clinicians as a manifestation of a clinically-relevant dysphoric disorder. They also transliterated the expressions of DSM IV criteria of main dysphoric disorders in their cultures. Results: in many non-western cultures the symptoms and constructs that are interpreted and treated as dysphoric disorders are mostly somatic and are different from the Western-centered DSM or ICD systems. In many cases the DSM and ICD criteria of depression and anxieties are not even acknowledged by patients. Limitations: the descriptive approach reported here is a preliminary step which involved local but Westernized clinicians-investigators following a biomedical thinking. It should be followed by a more systematic-comprehensive surveys in each culture. conclusions: westernized concepts and constructs of mental order and disorders are not necessarily universally applicable. Culturally-sensitive phenomena, treatments and treatment responses may be diversified. Attempts at their cross-cultural harmonization should take into consideration complex interactional multi-dimensional processes.

SOC PSYCHIATRY PSYCHIATR EPIDEMIOL. 2007 NOV;42(11):874-80.

SMOKING AND COMMON MENTAL DISORDERS: A POPULATION-BASED SURVEY IN SANTIAGO, CHILE.

Araya R, Gaete J, Rojas G, Fritsch R, Lewis G.

Background: smoking and common mental disorders (CMD), anxiety and depression, tend to co-exist and are important public health challenges for countries at all levels of development. We aimed to study the association between smoking and common mental disorders after adjusting for alcohol, illicit drug use and other confounders. Methods: cross-sectional household survey. CMD were assessed with a detailed psychiatric interview and smoking, alcohol, and illicit drug use with self-reported questionnaires. results: about 3,870 randomly selected adults were interviewed of whom 12.9% (95% CI 12-15) met criteria for ICD-10 CMD diagnoses. 38% (36-40) of the respondents were current smokers and 11% (10-13) ex-smokers. There was a robust association between heavier smoking and the presence and severity of CMD. However there were no major differences between non-smokers, ex-smokers and light smokers. In the fully adjusted models those individuals with ICD-10 CMD were significantly more likely to be current smokers [OR 1.6 (1.1-2.2)]. Smoking was also strongly associated with drinking heavily [OR 5.4 (4.0-7.3)] and illicit drug use [(OR 2.1 (1.1-4.1)] but there were no significant interactions. Conclusions: smoking is highly prevalent and associated with CMD and other addictive behaviours in Chile. These are major public health problems in need of urgent action.

BR J PSYCHIATRY. 2007 MAY;190:394-401.

COMMON MENTAL DISORDERS AND THE BUILT ENVIRONMENT IN SANTIAGO, CHILE.

Araya R, Montgomery A, Rojas G, Fritsch R, Solis J, Signorelli A, Lewis G.

Background: there is growing research interest in the influence of the built environment on mental disorders. AIMS: To estimate the variation in the prevalence of common mental disorders attributable to individuals and the built environment of geographical sectors where they live. Method: a sample of 3870 adults (response rate 90%) clustered in 248 geographical sectors participated in a household cross-sectional survey in Santiago, Chile. Independently rated contextual measures of the built environment were obtained. The Clinical Interview Schedule was used to estimate the prevalence of common mental disorders. Results: there was a significant association between the quality of the built environment of small geographical sectors and the presence of common mental disorders among its residents. The better the quality of the built environment, the lower the scores for psychiatric symptoms; however, only a small proportion of the variation in common mental disorder existed at sector level, after adjusting for individual factors. Conclusions: findings from our study, using a contextual assessment of the quality of the built environment and multilevel modelling in the analysis, suggest these associations may be more marked in non-Western settings with more homogeneous geographical sectors.

CIRUGÍA

OBESITY (SILVER SPRING). 2007 JAN;15(1):24-31.

POLYUNSATURATED FATTY ACID PATTERN IN LIVER AND ERYTHROCYTE PHOSPHOLIPIDS FROM OBESE PATIENTS.

Elizondo A, Araya J, Rodrigo R, Poniachik J, Csendes A, Maluenda F, Díaz JC, Signorini C, Sgherri C, Comporti M, Videla LA. Objective: our aim was to study the fatty acid (FA) composition of liver phospholipids and its relation to that in erythrocyte membranes from patients with obese nonalcoholic fatty liver disease (NAFLD), as an indication of lipid metabolism alterations leading to steatosis. Research Methods and Procedures: eight control subjects who underwent antireflux surgery and 12 obese patients with NAFLD who underwent subtotal gastrectomy with a gastro-jejunal anastomosis in Roux-en-Y were studied. The oxidative stress status of patients was assessed by serum F2-isoprostanes levels (gas chromatography/negative ion chemical ionization tandem mass spectrometry). Analysis of FA composition of liver and erythrocyte phospholipids was carried out by gas-liquid chromatography. Results: patients with NAFLD showed serum F2-isoprostanes levels 84% higher than controls. Compared with controls, liver phospholipids from obese patients exhibited significantly 1) lower levels of 20:4n-6, 22:5n-3, 22:6n-3 [docosahexaenoic acid (DHA)], total long-chain polyunsaturated FA (LCPUFA), and total n-3 LCPUFA, 2) higher 22:5n-6 [docosapentaenoic acid (DPAn-6)] levels and n-6/n-3 LCPUFA ratios, and 3) comparable levels of n-6 LCPUFA. Levels of DHA and DPAn-6 in liver were positively correlated with those in erythrocytes ($r = 0.77$ and $r = 0.90$, respectively; $p < 0.0001$), whereas DHA and DPAn-6 showed a negative association in both tissues ($r = -0.79$, $p < 0.0001$ and $r = -0.58$, $p < 0.01$, respectively), associated with lower DHA/DPAn-6 ratios. Discussion: obese patients with NAFLD showed marked alterations in the polyunsaturated fatty acid pattern of the liver. These changes are significantly correlated with those found in erythrocytes, thus suggesting that erythrocyte FA composition could be a reliable indicator of derangements in liver lipid metabolism in obese patients.

OBES SURG. 2007 MAY;17(5):608-16.

CHANGES IN RESTING ENERGY EXPENDITURE AND BODY COMPOSITION AFTER WEIGHT LOSS FOLLOWING ROUX-EN-Y GASTRIC BYPASS.

Carrasco F, Papapietro K, Csendes A, Salazar G, Echenique C, Lisboa C, Díaz E, Rojas J.

Background: the objective of this study was to evaluate changes in resting energy expenditure (REE), body composition and metabolic parameters, and to investigate predictors of the results in seriously obese patients after Roux-en-Y gastric bypass (RYGBP). Methods: 31 patients (BMI 44.4 +/- 4.8 kg/m²; 27 female, 4 male; 37.3 +/- 11.1 y) were evaluated at baseline and 6 months after RYGBP. Weight, REE, waist circumference (WC), fat mass (FM) and fat-free mass (FFM), physical activity, food intake, fasting glucose (GLU), insulin (INS), HOMA-IR and lipid concentrations were measured. Results: at 6 months, percentage of weight loss (%WL) was 29.0 +/- 4.4% and percentage of excess weight loss was (%EWL) 59.7 +/- 12.3%. FM loss corresponded to 77.1 +/- 12.2% of the weight loss. REE decreased from 33.4 +/- 4.1 to 30.1 +/- 2.6 kcal/kg FFM ($P < 0.05$). Significant decreases ($P < 0.001$) were observed in GLU, INS, HOMA-IR, LDL-cholesterol and triglycerides. %EWL was correlated with baseline INS ($r = 0.44$; $P = 0.014$), baseline HOMA ($r = 0.43$; $P = 0.017$), change in %FM ($r = 0.67$; $P < 0.001$) and change in WC ($r = 0.5$; $P < 0.01$). Decrease in REE/FFM (%) was positively correlated with baseline REE/FFM% ($r = 0.51$; $P < 0.005$) and change in %FM ($r = 0.69$; $P < 0.001$). Initial REE/FFM, baseline energy balance and FM change explain 90% of REE/FFM decrease. Conclusion: RYGBP was an effective procedure to induce significant weight loss, fat mass loss and improvement in metabolic parameters in the short term. Metabolic adaptation was not related to FFM wasting but to a higher baseline REE. Fasting hyperinsulinemia was the best single predictor of weight loss after RYGBP.

OBES SURG. 2007 NOV;17(11):1442-50.

LAPAROSCOPIC SLEEVE GASTRECTOMY: SURGICAL TECHNIQUE, INDICATIONS AND CLINICAL RESULTS.

Braghetto I, Korn O, Valladares H, Gutiérrez L, Csendes A, Debandi A, Castillo J, Rodríguez A, Burgos AM, Brunet L.

Background: laparoscopic sleeve gastrectomy (LSG) has been introduced as a multipurpose restrictive procedure for obese patients. Variations of the surgical technique may be important for the late results. Methods: 50 patients submitted to LSG from January 2005 to December 2006 were studied. Mean age was 38.2 years, preoperative weight was 103.4 +/- 14.1 kg (78 to 146 kg), and preoperative BMI was 37.9 +/- 3.4 (32.9 to 46.8). Important co-morbidities were present in 39 patients (78%). Results: operative time was 110 +/- 15 min. Intraoperative difficulties were observed in 7 patients. Volume of the resected

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specimen was 760 +/- 55 ml and capacity of the gastric remnant was 108.5 +/- 25 ml. There was no conversion to open surgery. Histology of the resected stomach was normal in 8 patients, while chronic gastritis was found in 42 patients. At 6 and 12 months postoperatively, weight loss was 28.0 +/- 6.4 kg and 32.6 +/- 6.8 kg respectively. In the 18 patients who have reached 1 year follow-up, % excess BMI loss reached 85 +/- 0.7%. Most of the medical diseases associated with the obesity resolved after 6 to 12 months. conclusion: LSG may be an acceptable operation. It is easy to perform, safe, and has a lower complication rate than other bariatric operations. Further studies are necessary for the clinical results at long-term follow-up.

NUTR HOSP. 2007 JUL-AUG;22(4):410-6.

AGREEMENT BETWEEN MEASURED AND CALCULATED BY PREDICTIVE FORMULAS RESTING ENERGY EXPENDITURE IN SEVERE AND MORBID OBESE WOMEN.

Carrasco F, Rojas P, Ruz M, Rebolledo A, Mizón C, Codoceo J, Inostroza J, Papapietro K, Csendes A.

Objective: to compare measured resting energy expenditure (REE) with that predicted by formulas derived from populations with normal weight or obesity and from women with severe and morbid obesity. Material and Methods: 66 women (aged 35.6 +/- 10.3 y and BMI of 44.7 +/- 4.9 kg/m²) were evaluated by indirect calorimetry with a metabolic monitor Deltatrac (Datex Inst., Finland), before undergoing gastric bypass. REE was calculated with the following equations: Harris-Benedict's with both actual and adjusted weight, Ireton-Jones', Mifflin's, and Carrasco's Fast Estimation, which corresponds to 16.2 kcal x kg actual weight. Results: (mean +/- sd). Measured REE was 1797 +/- 239 kcal/day. All formulas, except Harris-Benedict's with adjusted weight, overestimated REE. The Ireton-Jones' equation presented the greater overestimation (689 +/- 329 kcal/day), whereas Mifflin's equation overestimated REE only by 6 +/- 202 kcal/day. No significant differences were detected between measured and calculated REE by Mifflin's and Carrasco's Fast Estimation. Accuracy (defined as difference between calculated and measured REE within +/- 10%) was greater with Mifflin's equation (68%), followed by Harris-Benedict's with actual weight (64%) and Carrasco's Fast Estimation (61%). By using the Bland-Altman analysis, significant correlations were observed between calculated-measured REE and mean REE (calculated + measured/2) with all equations except Carrasco's Fast Estimation. This means that all but one formula underestimate or overestimate REE depending on the level of measured REE. Conclusion: in severe and morbid obese women, Mifflin's and Carrasco's Fast Estimation equations provided the best performance to estimate REE. Before recommending an equation in an a subset of individuals it is necessary to make previous validation studies to determine that equation with the best predictive power for this particular group of patients.

NUTRITION. 2007 MAR;23(3):277-80.

PERSISTENT ANEMIA AFTER ROUX-EN-Y GASTRIC BYPASS.

Mizón C, Ruz M, Csendes A, Carrasco F, Rebolledo A, Codoceo J, Inostroza J, Papapietro K, Pizarro F, Olivares M.

Objective: we report the case of a 42-y-old morbidly obese woman who presented persistent anemia as result of Roux-en-Y gastric bypass. methods: The surgical procedure conducted in 1999 consisted of horizontal gastropasty with truncular vagotomy, Roux-en-Y gastrojejunal anastomosis with an alimentary limb of 60 cm, and cholecystectomy. In 2000 a second surgery (subtotal gastrectomy, i.e., 90%, with a 50-mL gastric pouch) was performed because of failed gastropasty. Anemia was detected approximately 1 y after the second surgery. This condition worsened significantly after an abdominal lipectomy performed in 2001. Since then, different oral iron compounds were used for treatment, but with unsatisfactory results. The subject was anemic for 4 y. Results: the condition was corrected only after intravenous iron administration. Iron absorptions from 3 mg of iron as ferrous ascorbate and from a standardized diet that also contained 3 mg of iron were 48.4% and 39.9%, respectively. Conclusion: Iron absorption tests provided evidence that the reduction of intestinal iron absorption capacity was the most probable cause of the persistent anemia.

J GASTROINTEST SURG. 2007 OCT;11(10):1294-7.

BEHAVIOR OF THE COMMON BILE DUCT DIAMETER BEFORE AND 12 YEARS AFTER CHOLEDOCHOSTOMY FOR CHOLECYSTOLITHIASIS AND CHOLEDOCHOLITHIASIS. A PROSPECTIVE STUDY.

Csendes A, Csendes P, Burdiles P, Díaz JC, Maluenda F, Burgos AM.

Introduction: in patients with common bile duct (CBD) stones, the diameter of the CBD is usually dilated. After surgery, the behavior of CBD diameter is not clearly known. OBJECTIVE: to determine at a late follow-up the width of CBD before and after choledochostomy for CBD stones. Material and Methods: in this prospective study, 39 patients with gallstones and CBD stones were included. They were 30 women and 9 men with a mean age of 52.6 years. In all ultrasound, determination of the

CBD caliber before and 12 years after surgery was performed. RESULTS: the mean value of the inner diameter of the CBD before surgery was 11.6 and 12.3 mm in patients below or above 60 years, respectively. Measurement 12 years after surgery showed a mean decrease of nearly 50% of preoperative values, which was highly significant ($p < 0.0001$). However, either below or above 60 years, only 75% of the patients showed this decrease, whereas 25% remained unchanged. conclusion: the dilated preoperative CBD returns to normal or near normal values in 3/4 of the patients after surgical exploration of the CBD and extraction of the stones.

SURGERY. 2007 FEB;141(2):222-8.

ANATOMY OF THE BOERHAAVE SYNDROME.

Korn O, Oñate JC, López R.

Background: spontaneous rupture of the esophagus (Boerhaave syndrome) occurs almost invariably at the same anatomic site. A weakness of the distal esophageal wall is suspected but has not been confirmed by anatomic studies. The aim of this work was to determine the existence of a structural abnormality in the esophageal wall. Material And Methods: in six fresh human cadavers, the left lung was removed and the esophagus was insufflated in situ with air until it burst. The mucosa of the specimens was stripped off, allowing the fibers of the inner muscular coat to be seen. In addition a specimen from a patient who died from this cause was submitted to the same procedure. Results: the site of the experimental rupture matched the clinical case. The tear was located at the margin of contact between "clasp" and oblique fibers, and extends upwards. Conclusions: the connective tissue of the junction between clasp and oblique fibers appears to constitute a weak point in the lower esophagus.

SURG LAPAROSC ENDOSC PERCUTAN TECH. 2007 OCT;17(5):369-74.

LAPAROSCOPIC ANTERIOR CARDIOMYOTOMY PLUS ANTERIOR DOR FUNDOPLICATION WITHOUT DIVISION OF LATERAL AND POSTERIOR PERIESOPHAGEAL ANATOMIC STRUCTURES FOR TREATMENT OF ACHALASIA OF THE ESOPHAGUS.

Braghetto I, Korn O, Valladares H, Rodríguez A, Debandi A, Brunet L.

Laparoscopic cardiomyotomy is the treatment of choice for patients with achalasia of the esophagus. Several different techniques and modifications have been reported concerning the approach (thoracoscopic or laparoscopic), type and length of the myotomy, with or without fundoplication, type of fundoplication, etc. In this prospective study, we report our simplified technique for anterior cardiomyotomy with Dor fundoplication and the results obtained using this procedure. Only the anterior wall of the esophagus was exposed without dissection of the lateral or posterior periesophageal anatomic structures for the technique. Twenty-five patients were operated by a single surgeon. The diagnosis was based on the clinical, radiologic, endoscopic, and functional esophageal tests. Achalasia was classified into 3 types: achalasia type I was diagnosed in 5 patients, type II in 6 patients, and type III in 14 patients. Manometry demonstrated a mean resting pressure of 33.5 mm Hg (range, 18 to 55), associated with incomplete relaxation. The hospital stay was 3 days; the median operative time was 115 minutes (range, 90 to 150), 2 small mucosal perforations occurred which were immediately sutured during surgery without conversion into open technique and no postoperative complications occurred. After operation, lower esophageal sphincter pressure returned to normal values and complete relaxation in all patients. In type II and III achalasia, the esophageal body diameter decreased more than 50% ($P=0.001$) compared with the preoperative diameter, and the internal diameter of the esophagogastric junction increased significantly ($P=0.001$). Only 2 patients presented occasional heartburn and 2 patients received 1 session of hydrostatic dilatation due to mild residual dysphagia. No late recurrence of dysphagia has been observed to the present time (1 to 5 y of follow-up). In conclusion, the goals of the surgery for achalasia are obtained with this simplified technique.

AESTHETIC PLAST SURG. 2007 SEP-OCT;31(5):514-8.

COMPOSITION OF POSTABDOMINOPLASTY SEROMA.

Andrades P, Prado A.

Background: this study aimed to analyze the composition of postabdominoplasty seroma fluid at different intervals, compare it with blood and lymph, and determine whether it meets the criteria for being considered an exudate. Methods: the study enrolled 18 female patients with postabdominoplasty seroma diagnosed by clinical and ultrasound evaluation. All the patients had a Matarasso type 4 anterior abdominal wall deformity. None of the patients were overweight, and none had comorbidities. They all underwent a classical abdominoplasty procedure. Fluid samples were taken from the drains between postoperative days 5 and 7, and from needle aspiration between postoperative days 15 and 20. The fluids were assayed in the clinical

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laboratory at the University of Chile Clinical Hospital for chemical and cellular composition. Blood, lymph, and seroma values were compared by independent group analysis using a Tukey multiple comparison test with an alpha error of 0.05. Results: the total protein, lactate dehydrogenase (LDH), and cholesterol levels for the early and late seroma fluids were lower than in the blood, but higher than in the lymph. The total protein seroma-to-plasma ratio was approximately 0.5; the LDH seroma-to-plasma ratio was approximately 0.6; and the cholesterol seroma-to-plasma ratio was 0.32. The platelet level was very low in the late seroma fluid, showing no statistical differences with the lymph level. The leukocyte level was low in the seroma fluid, with a higher percentage of neutrophils than found in the blood or the lymph. Conclusions: the serous fluid formed under the flap after an abdominoplasty seems to be an exudate. In the early postoperative period, it is an inflammatory exudate that slowly turns into an exudate with some characteristics similar to those of lymph.

OBES SURG. 2007 JAN;17(1):28-34.

ENDOSCOPIC AND HISTOLOGIC FINDINGS OF THE FOREGUT IN 426 PATIENTS WITH MORBID OBESITY.

Csendes A, Burgos AM, Smok G, Beltrán M.

Background: roux-en-Y gastric bypass is the most frequent bariatric operation. In this operation, the distal bypassed stomach is left in situ. We studied pre-operative clinical, endoscopic and histologic findings in a consecutive group of morbidly obese patients prior to bariatric surgery. Methods: a prospective study was conducted from August 1999 until May 2004, which consisted of 426 patients with morbid obesity. There were 94 men and 332 women, with mean age 39.5 years. In all patients prior to surgery, upper endoscopy was performed and biopsy samples were taken distal to squamo-columnar junction (cardiac biopsies), and in 232 of them also in at the antrum. Results: pathological findings at the esophagus were seen in 55% of the patients, mainly related to reflux esophagitis. Barrett's esophagus was seen in 5.8%. In the stomach, pathological findings were seen in 32% of the patients. Active peptic ulcer was demonstrated in 2.6% of the cases. At the duodenum, pathologic findings were detected in 13.4% of the patients, showing an ulcer in 2.6%. At the stomach, chronic inactive gastritis and atrophic gastritis with intestinal metaplasia were found in 8.6% and 6.5% respectively. Antral adenoma with low-grade dysplasia was found in 1 patient, and 1 carcinoid tumor. H. pylori was present in 53% of the patients, mainly in the antrum. Conclusion: in candidates for bariatric surgery, upper endoscopy with biopsy samples and determination of H. pylori should be routinely performed. If present, H. pylori should be eradicated. After surgery, if Barrett's esophagus was present, endoscopic surveillance is recommended.

CIR ESP. 2007 FEB;81(2):64-9.

SCIENTIFIC FOUNDATIONS FOR MEDICAL TREATMENT BASED ON MODIFYING DIET, LIFESTYLE HABITS, AND PATIENT ATTITUDES IN CHRONIC GASTROESOPHAGEAL REFLUX DISEASE.

Csendes A, Burdiles P.

In most patients with chronic gastroesophageal reflux disease, treatment is medical. Among the main elements involved in treatment are general dietary measures, lifestyle habits, and patients' attitudes to symptom control. The present article summarizes the scientific foundations that support these measures: head elevation during nighttime sleep, smoking cessation, losing weight, avoiding rigorous exercise, and reducing or eliminating alcohol consumption. Dietary therapy is mainly based on avoiding fatty foods, chocolate, coffee, mint, and irritating fizzy drinks. Although each patient's response to these measures is highly individual, the mechanisms through which symptoms are reproduced is gradually becoming clearer: a large percentage of patients with uncomplicated gastroesophageal reflux disease will gain considerable relief simply by eliminating some of these habits.

PLAST RECONSTR SURG. 2007 SEP 15;120(4):935-46.

PROGRESSIVE TENSION SUTURES IN THE PREVENTION OF POSTABDOMINOPLASTY SEROMA: A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND CLINICAL TRIAL.

Andrades P, Prado A, Danilla S, Guerra C, Benítez S, Sepúlveda S, Sciarraffa C, De Carolis V.

Background: the purpose of this study was to evaluate the seroma reduction capabilities of progressive tension sutures and compare them with the conventional use of drains. Methods: sixty female patients were randomized into four groups: group 1 (control, no drains, and no progressive tension sutures), group 2 (progressive tension sutures alone), group 3 (drains alone), and group 4 (progressive tension sutures and drains). All patients underwent a classic abdominoplasty and drains were left for 7 days in the corresponding groups. Clinical and ultrasound assessments

were performed 2 weeks after the operation by blinded evaluators. Punctures, volumes, nonseroma complications, and aesthetic outcome were also measured. results: surgical time was 50 minutes longer in groups 2 and 4. Drain outputs were higher in group 3 than in group 4. The clinical and ultrasound seroma frequency was 35 percent and 90 percent respectively, without significant differences among the groups. The control group was interrupted at 10 patients because of considerably larger seromas and an increased amount of punctures needed for treatment. No differences were found in the other groups. There were no differences with respect to complication rates and aesthetic outcome after follow-up. Conclusions: progressive tension sutures increase surgical time, reduce drain outputs, and have the same clinical and ultrasound seroma frequency as the use of drains alone. The combination of both methods simultaneously does not add any advantages. However, complications and interventions increase if at least one of them is not used. The mechanism of action of progressive tension sutures could be the compartmentalization of the fluid collection under the flap facilitating absorption.

AESTHETIC PLAST SURG. 2007 JUL-AUG;31(4):317-9.

IMPLICATIONS OF TRANSAXILLARY BREAST AUGMENTATION: LIFETIME PROBABILITY OF BREAST CANCER DEVELOPMENT AND SENTINEL NODE MAPPING INTERFERENCE.

Prado A, Andrades P, Leniz P.

After the "fifth-generation" breast implants with ultracohesive silicone gel technology are introduced, the Food and Drug Administration (FDA) will sooner or later retire the ban on the use of these devices in the United States. When this happens, the plastic surgery community must be prepared to face a massive demand for reoperations to change saline-filled breast implants because cohesive gel devices have the potential to provide a more natural breast shape, to minimize the risk of postoperative rippling, and to provide a greater degree of safety if the implant loses its integrity. Despite these advantages and extensive use throughout the rest of the world during the ban in the United States, silicone implants also have disadvantages. One drawback is that transaxillary breast augmentation with more "rigid" gel-filled implants may produce trauma to the armpit, may interfere with sentinel node mapping for breast cancer treatment, and may have future medicolegal implications.

PLAST RECONSTR SURG. 2007 APR 15;119(5):1481-90.

A NEW TECHNIQUE OF "DOUBLE-A" BILATERAL FLAPS BASED ON PERFORATORS FOR THE TREATMENT OF SACRAL DEFECTS.

Prado A, Ocampo C, Danilla S, Valenzuela G, Reyes S, Guridi R.

Background: myocutaneous and fasciocutaneous flaps can provide stable coverage of sacral defects. For neurologically intact patients, sensate innervated gluteal artery perforator flaps are the ideal solution. For patients with spinal cord injury, soft-tissue coverage can be performed with a variety of noninnervated flaps. Methods: between 1997 and 2004, the authors operated on 30 patients, 21 men and nine women, using bilateral gluteal distal fasciocutaneous and proximal musculocutaneous vertical vector rotation-advancement flaps, based on perforators with V-Y closures. The ages of the patients ranged from 32 to 74 years. Twenty-five patients had spinal cord injuries and all had sacral pressure sores extending to the bone. Three patients had low-grade malignant tumors (sacral chordomas); one had a sacral radiation-induced necrosis and two senile patients with large sacral defects had chronic renal failure and multiple sclerosis. No comorbidities were found in the sample. results: all the lesions were closed successfully. After follow-up of 1 to 8 years, 27 patients never required repeated surgery after wound complications. Three patients had infection and partial dehiscence of the flaps that healed after reoperation with V-Y readvancement; three died as a result of their primary diseases. conclusions: this flap design has been used only in selected cases because, after its elevation, use of other gluteal-based flaps for future sacral reconstructions may not be possible. Five neurologically intact patients were found to have good sensitive protection of the flaps and adequate cushion contour after surgery because the authors conserved the gluteal arteries, perforators, and their corresponding sensory nerves.

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PLAST RECONSTR SURG. 2006 MAY;117(6):1725-35.

NONRESECTIVE SHRINKAGE OF THE SEPTUM AND FAT COMPARTMENTS OF THE UPPER AND LOWER EYELIDS: A COMPARATIVE STUDY WITH CARBON DIOXIDE LASER AND COLORADO NEEDLE.

Prado A, Andrades P, Danilla S, Castillo P, Benítez S.

background: the purpose of this article is to describe an alternative nonresective treatment of the fat-septum component of the eyelids during blepharoplasty, using shrinkage desiccation with two low-energy modalities: a carbon dioxide laser and a low-range grid of electrocautery with a Colorado microdissection needle. methods: thirty-six patients underwent a four-lid blepharoplasty. During surgery, after exposure (not opening) of the septum and assessment of the amount of bulging by gentle globe compression, a grid spray of electrocautery (right eye) and carbon dioxide laser (left eye) was applied over the entire septum until shrinkage and correction of the bulging was achieved. Preoperative, postoperative day 15, and 1-year follow-up photographs were evaluated using an objective grading system by blinded surgeons. For statistical analysis, the Wilcoxon matched-pairs signed-ranks test was used, with $p < 0.05$ indicating statistical significance. results: all the patients completed the 15-day evaluation, but only 32 completed the 1-year follow-up. No major eye or eyelids complications were observed. There were no statistical differences in surgical time and postoperative pain on either side. In this study, laser fat-septum shrinkage achieved substandard results compared with electrocautery when analyzed as a continuous variable, but it did not influence the categorical Strasser scale final result in the short- and long-term follow-up. Conclusions: the method described is simple and safe, and provides a subtle but long-lasting, adequate result. No statistical clinical differences were observed between the electrocautery and laser fat-septum shrinkage techniques.

ANESTHESIOLOGY. 2007 FEB;106(2):339-45.

NEOSAXITOXIN AS A LOCAL ANESTHETIC: PRELIMINARY OBSERVATIONS FROM A FIRST HUMAN TRIAL.

Rodríguez-Navarro AJ, Lagos N, Lagos M, Braghetto I, Csendes A, Hamilton J, Figueroa C, Truan D, García C, Rojas A, Iglesias V, Brunet L, Álvarez F.

Background: neosaxitoxin is a phycotoxin that reversibly blocks the voltage-gated sodium channels at the neuronal level. Its activity results in blocking the axonal conduction, stopping the propagation of the nerve impulse. The objective of the present work was to evaluate neosaxitoxin as a local anesthetic in a human trial. Methods: the authors conducted a randomized, double-blind, placebo-controlled trial with 10 healthy volunteers. Subcutaneous injections were made in the middle posterior skin of the calf: one leg received 50 microg neosaxitoxin, and the contra-lateral leg received placebo. The anesthetic effect was evaluated using a standardized human sensory and pain model. TSA II Neurosensory Analyzer (Medoc Ltd, Minneapolis, MN) and von Frey technique were used to evaluate five parameters: sensory threshold for warm and cold, pain thresholds for heat and cold, and mechanical touch perception threshold. Measurements were made 0, 1, 3, 6, 9, 12, 16, 24, and 48 h after the injections. Results: for all the patients, effective and complete blocking of the evaluated parameters was obtained. As the blocking began to revert gradually, heat pain was the first to return to normal values after 3 h. Cold pain was the longest sensation abolished, achieving 24 h of blockade. The toxin was undetected in blood and urine samples. No adverse reactions to neosaxitoxin were detected. conclusions: neosaxitoxin showed an effective local anesthetic effect when injected in the subcutaneous plane. The efficacy of a 50-microg dose of neosaxitoxin was shown. This is the first report of neosaxitoxin as a local anesthetic in a human trial.

COLORECTAL DIS. 2007 SEP;9(7):619-24.

TREATMENT OF CHRONIC ANAL FISSURE BY GONYAUTOXIN.

Garrido R, Lagos N, Lagos M, Rodríguez-Navarro AJ, García C, Truan D, Henríquez A.

Objective: the use of gonyautoxin has been reported to be safe and effective in healing acute and chronic anal fissures. This study was designed to show better efficacy in healing patients with chronic anal fissure by increasing the frequency of toxin injection. Method: twenty-three chronic anal fissure patients were treated with doses of 100 units of gonyautoxin, which was intrasphincteric, infiltrated. The frequency of injection was every 4 days. Anorectal manometries were performed before and 4 min after infiltration. Results: total remissions were achieved within 7-14 days. The patients healed with a mean time of 8.2 ± 2.4 days. No relapsed were observed during the 10-month follow up. Neither faecal incontinence nor other side effects were observed. All patients showed immediate sphincter relaxation detected by clinical examination. The maximum anal resting pressures, recorded 4 min after injections decreased to 62.9 ± 27.7 mmHg, being $65.3 \pm 29.6\%$ of baseline. Immediately after infiltration, patients reported anaesthetic effect with a fall down of the postdefecatory pain. Conclusion:

although, gonyautoxin anal fissures treatment recently published proved to be safe and effective, this study shows a better protocol for anal fissure treatment, showing better efficacy by shorting the healing time with better perception of healing by patients. Gonyautoxin anal sphincter infiltration proves to be safe and effective, reducing discomfort and healing time, advantageously comparing with alternative therapeutic approaches for chronic anal fissure.

ENDOCRINOLOGÍA

DIABETES RES CLIN PRACT. 2007 AUG;77(2):245-50.

FABP2 ALA54THR POLYMORPHISM AND DIABETES IN CHILEAN ELDERS.

Albala C, Villarroel A, Santos JL, Ángel B, Lera L, Liberman C, Sánchez H, Pérez-Bravo F.

Objective: the FABP2 Ala54Thr polymorphism has been associated with insulin resistance and diabetes in several populations. The aim of this study was to estimate the prevalence of FABP2 genotypes in 223 Chilean subjects (136 women and 87 men aged 65-79 years) and its association with type 2 diabetes in a 4 years follow-up. Methods: glucose, Insulin and lipids were measured in fasting plasma samples. Insulin resistance was estimated through the homeostasis model assessment. Diabetes was diagnosed according ADA criteria. The Ala54Thr allelic variant was determined by polymerase chain reaction and restriction fragment-length polymorphism analysis. Logistic regression techniques were used to assess gene-disease associations. Results: genotype frequencies were estimated as 30.5, 49.3 and 20.2% for the Ala/Ala, Ala/Thr and Thr/Thr, respectively. The crude OR for the association between Thr54 carriers and diabetes was estimated as 2.18 (1.12-4.24). The corresponding OR for the association between Thr54 carriers with Metabolic Syndrome was 1.06 (0.59-1.88). After adjustment by BMI and age, a significant association persists for Thr54Thr carriers and diabetes (OR 2.70; 95% CI 1.113-6.527). The 4-year cumulative incidence of diabetes was higher in Thr carriers than in non-carriers (20.1% versus 8.5%; $p < 0.04$). The adjusted association between Thr54Thr polymorphism and diabetes incidence was OR 3.84 (95% CI: 1.140-12.910) Conclusion: our results strongly suggest an association between the Ala54Thr polymorphism of FABP2 with diabetes, revealing a genetic dosage effect regarding its association with diabetes in Chilean elders.

GASTROENTEROLOGÍA

TRANSPLANT PROC. 2007 APR;39(3):612-4.

ORAL ULCERS PRODUCED BY MYCOPHENOLATE MOFETIL IN TWO LIVER TRANSPLANT PATIENTS.

Naranjo J, Poniachik J, Cisco D, Contreras J, Oksenberg D, Valera JM, Díaz JC, Rojas J, Cardemil G, Mena S, Castillo J, Rencoret G, Godoy J, Escobar J, Rodríguez J, Leyton P, Fica A, Toledo C.

Oral ulcers are a frequent problem in transplant medicine. It is important to consider infectious etiologies, exacerbated by the immunosuppressive treatment, but other etiologies are also possible, like adverse drug reactions. Mycophenolate mofetil (MMF) is an immunosuppressive medication that has been used in combination with calcineurin inhibitors and steroids. Reports of renal transplant patients with oral ulcers related to MMF have appeared lately and herein we have described 2 cases in liver transplant patients. Their oral ulcers resolved quickly after suspension of the medication. Our 2 cases in liver transplant patients represented.

DIG DIS SCI. 2007 MAR;52(3):702-10.

PATTERNS OF SMALL INTESTINAL MOTOR ACTIVITY DURING INTRALUMINAL INFUSION OF ELEMENTARY DIETS IN DOGS.

Defilippi C.

During continuous intrainestinal infusion of elementary diets, periodic fluctuation of the frequency of contractions has been observed. This study sought to characterize the temporospatial organization of this pattern and the influence of cholinergic input. Studies were performed on unanesthetized dogs with a duodenal cannula. Motor activity was recorded by means of infused catheters and external transducers. Nutrients were infused continuously at the duodenum and jejunal levels. Studies were repeated after administration of atropine. Six to 14 periodic variations of frequency of contractions during 10 basal infusion experiments were observed in random order. During duodenal infusion, atropine significantly increased the number

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of these events, associated with a synchronous pattern. Frequency and amplitude of contractions during jejunal infusion were significantly lower compared to duodenal infusion. Cyclic pattern elicited by nutrient infusion is related to a cholinergic mechanism; changes depend on the level of infusion.

GENÉTICA

HEALTH POLICY. 2007 OCT;83(2-3):295-303.

COST-EFFECTIVENESS OF A FOLIC ACID FORTIFICATION PROGRAM IN CHILE.

Llanos A, Hertrampf E, Cortés F, Pardo A, Grosse SD, Uauy R.

Objective: periconceptional intake of folic acid reduces the risk of neural tube defects (NTDs), a frequent birth defect that can cause significant infant mortality and disability. In Chile, fortification of wheat flour with folic acid has resulted in significant reduction in the risk of anencephaly and spina bifida. We investigated the cost-effectiveness implications of this policy. Methods: we conducted an ex-post economic analysis of this intervention. Estimates of the effect of fortification in decreasing NTDs and deaths were derived from a prospective evaluation. The costs of fortification and provision of medical care to children with spina bifida in Chile were based on primary data collection. Findings: the intervention costs per NTD case and infant death averted were I\$ 1200 and 11.000, respectively. The cost per DALY averted was I\$ 89, 0.8% of Chile's GDP per capita. Taking into account averted costs of care, fortification resulted in net cost savings of I\$ 2.3 million. Conclusion: fortification of wheat flour with folic acid is a cost-effective intervention in Chile, a middle income country in the post-epidemiological transition. This result supports the continuation of the Chile fortification program and constitutes valuable information for policy makers in other countries to consider.

IMAGENOLÓGÍA

SURG TODAY. 2007;37(3):183-6.

EVOLUTIVE RADIOLOGICAL CHANGES OF THE ESOPHAGUS IN PATIENTS WITH ACHALASIA WHO DID NOT RECEIVE TREATMENT.

Csendes P, Csendes A, Cortés C, Burgos AM.

Purpose: the radiological features of achalasia of the esophagus are well known and have been described. However, very little is known concerning the natural history of this disease. We aimed to determine the evolutive radiological changes of the esophagus in a group of patients with achalasia who had not previously undergone any treatment. Methods: we undertook a prospective study of 14 patients with achalasia from a group of 205 patients. They included 9 women and 5 men who did not receive any treatment at the initial diagnosis. Two radiological parameters were evaluated: (a) the maximal internal diameter of the middle third of the thoracic esophagus in millimeters and (b) the internal diameter of the esophagogastric junction in millimeters. Results: at a mean follow-up of 5-years without any treatment, there was a significant increase in the diameter of the thoracic esophagus, with a rate of "dilatation" of 6.1 mm/year. In addition, there was a significant decrease of the internal diameter of the esophagogastric junction, with a rate of "stenosis" of 1 mm/year. The lower esophageal sphincter was hypertensive in all with an incomplete relaxation. Conclusion: these results suggest that there is a progressive deterioration in the radiological parameters of the esophagus in patients with achalasia not treated over a 5-year period of observation.

J ENDOUROL. 2007 NOV;21(11):1361-6.

CHARACTERIZING TUNA ABLATIVE TREATMENTS OF THE PROSTATE FOR BENIGN HYPERPLASIA WITH GADOLINIUM-ENHANCED MAGNETIC RESONANCE IMAGING.

Mynderse LA, Larson B, Huidobro C, Meyer JJ, Busel D, Hanson DP, Larson T.

Background And Purpose: transurethral Needle Ablation of the prostate TUNA has been accepted as an office-based treatment for benign prostatic hyperplasia (BPH) for many years. Clinical outcomes have been reported, but the amount and location of the necrosis produced have yet to be characterized. The necrosis caused by TUNA was evaluated by gadolinium-enhanced magnetic resonance imaging (MRI) of the pelvis. Patients and Methods: twelve patients with BPH/lower urinary-

tract symptoms underwent standard TUNA, and MRI scans with gadolinium enhancement were performed before and 1 week after treatment. The images were studied using Analyze software to quantify the amount of necrosis compared with the prostatic volume. Transverse, coronal, and sagittal images were obtained to identify the location of the necrosis. Results: new gadolinium defects were seen in all patients after TUNA. The lesions coalesced into continuous areas of necrosis and correlated with the site of needle placement. The mean volume of necrosis was 6.84 cc and equated to 8.6% of the prostate volume. No lesions were found near the apex, urethra, or rectum; and none extended beyond the prostate capsule. Conclusions: gadolinium-enhanced MRI demonstrates new vascular defects representing necrosis caused by TUNA of the prostate. This therapy for BPH produces necrotic lesions that can be placed strategically by the surgeon. The standard protocol produces lesions that coalesce to create larger lesions. This MRI study has characterized, for the first time, the heating pattern and intraprostatic necrosis of a complete TUNA procedure.

INFECTOLOGÍA

TRANSPL INFECT DIS. 2007 SEP;9(3):203-10.

INMUNOHISTOCHEMICALLY PROVEN CYTOMEGALOVIRUS END-ORGAN DISEASE IN SOLID ORGAN TRANSPLANT PATIENTS: CLINICAL FEATURES AND USEFULNESS OF CONVENTIONAL DIAGNOSTIC TESTS.

Fica A, Cervera C, Pérez N, Marcos MA, Ramírez J, Linares L, Soto G, Navasa M, Cofan F, Ricart MJ, Pérez-Villa F, Pumarola T, Moreno A.

We studied the main clinical features, outcome, and laboratory parameters in a group of solid organ transplant (SOT) patients with immunohistochemically proven cytomegalovirus (CMV) disease. Confirmed CMV cases were obtained through databases. Demographics, clinical data, transplantation type, immunosuppressive regimens, donor and recipient CMV serostatus, therapy, outcome and laboratory results, pp65 antigenemia, and qualitative polymerase chain reaction (PCR) for CMV were analyzed. From 1995 to 2004, 31 cases with complete medical records were identified. Disease appeared between 24 and 2538 days after transplantation but most cases presented in the first 100 days. Gastrointestinal CMV disease was the most frequent form (71%), while thrombocytopenia was present in 50% of cases, and leukopenia was less common (35.5%). CMV pp65 antigenemia was positive in 58% of patients, but its sensitivity increased to 71% if performed during the first 6 months. A qualitative CMV PCR technique gave similar results during this period (71.4%). Most patients were treated with intravenous ganciclovir (n=25; 80.6%). In 4 cases (19.4%), use of foscarnet alone or a sequential regimen with ganciclovir-foscarnet was deemed necessary. Surgical procedures were necessary in 5 patients (16%). The death rate reached 13%. CMV end-organ disease can be a life-threatening infection in SOT patients. Gastrointestinal disease was the most frequent end-organ disease. CMV antigen detection is best suited for the early period after transplantation.

LABORATORIO ENDOCRINOLOGÍA Y REPRODUCCIÓN

DEVELOPMENT. 2007 MAR;134(5):945-57.

FXNA, A NOVEL GENE DIFFERENTIALLY EXPRESSED IN THE RAT OVARY AT THE TIME OF FOLLICULOGENESIS, IS REQUIRED FOR NORMAL OVARIAN HISTOGENESIS.

García-Rudaz C, Luna F, Tapia V, Kerr B, Colgin L, Galimi F, Dissen GA, Rawlings ND, Ojeda SR.

In rodents, the formation of ovarian follicles occurs after birth. In recent years, several factors required for follicular assembly and the growth of the newly formed follicles have been identified. We now describe a novel gene, Fxna, identified by differential display in the neonatal rat ovary. Fxna encodes an mRNA of 5.4 kb, and a protein of 898 amino acids. Fxna is a transmembrane metallopeptidase from family M28, localized to the endoplasmic reticulum. In the ovary, Fxna mRNA is expressed in granulosa cells; its abundance is maximal 48 hours after birth, i.e. during the initiation of follicular assembly. Reducing Fxna mRNA levels via lentiviral-mediated delivery of short hairpin RNAs to neonatal ovaries resulted in substantial loss of primordial, primary and secondary follicles, and structural disorganization of the ovary, with many abnormal follicles containing more than one oocyte and clusters of somatic cells not associated with any oocytes. These abnormalities were

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not attributable to either increased apoptosis or decreased proliferation of granulosa cells. The results indicate that Fxna is required for the organization of somatic cells and oocytes into discrete follicular structures. As an endoplasmic reticulum-bound peptidase, Fxna may facilitate follicular organization by processing precursor proteins required for intraovarian cell-to-cell communication.

FERTIL STERIL. 2007 FEB;87(2):321-8.

SEX HORMONE-BINDING GLOBULIN EXPRESSION IN THE ENDOMETRIA OF WOMEN WITH POLYCYSTIC OVARY SYNDROME.

Maliqueo M, Bacallao K, Quezada S, Clementi M, Gabler F, Johnson MC, Vega M.

OBJECTIVE: to evaluate the protein and messenger RNA expression of sex hormone-binding globulin (SHBG) in endometria from women with polycystic ovary syndrome (PCOS). DESIGN: case-control study. SETTING: Hospital research unit. Patient(S): thirty-three women with PCOS, and 17 fertile, healthy women of similar age to those with PCOS. intervention(s): endometrial and blood samples were obtained from women with PCOS (PCOSEs) and from control women (CEs) during the proliferative phase of the menstrual cycle. Main Outcome Measure(S): expression studies for SHBG (immunohistochemistry and reverse transcription-polymerase chain reaction). Hormonal studies for determining sex steroids (T, P, and E(2)) and SHBG concentration. Insulin sensitivity was assessed by composite insulin sensitivity index (ISI(composite)). Result(S): In stroma, the protein expression of SHBG was lower in PCOSEs than in CEs. Epithelial cells had a similar expression of SHBG protein in both groups. Messenger RNA of variant 548 base pairs (wild-type) tended to be lower in PCOSEs compared to CEs. When PCOSEs were classified by insulin resistance, the PCOSEs with normal insulin sensitivity showed an expression of stromal SHBG similar to that observed in CEs. conclusion(s): the low SHBG expression in the stromal compartment of endometria from women with PCOS with insulin resistance may contribute to generate an abnormal steroid milieu in the endometria of these women.

GYNECOL ONCOL. 2007 FEB;104(2):290-5.

DEREGULATION OF TISSUE HOMEOSTASIS IN ENDOMETRIA FROM PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME WITH AND WITHOUT ENDOMETRIAL HYPERPLASIA.

Villavicencio A, Bacallao K, Gabler F, Fuentes A, Albornoz J, Casals A, Vega M.

Objective: to study the proteins involved in endometrial homeostasis in PCOS women. Methods: protein expression of Ki67, Bcl-2, Bax, Pro-Caspase-3 and Caspase-3 by immunohistochemistry and/or Western blot, and DNA fragmentation using in situ 3'-end labeling of apoptotic cells, was measured in 9 samples of normal endometrium (NE), 12 PCOS endometria without treatment (PCOSE), 7 endometria from PCOS women with endometrial hyperplasia (HPCOSE) and 9 endometria from patients with endometrial hyperplasia (HE). Results: cell proliferation was higher in epithelium from PCOSE ($P < 0.05$), HPCOSE and HE vs NE. A higher Bcl-2/Bax relative ratio in PCOSE and HPCOSE was observed, in absence of active Caspase-3 and scarce DNA fragmentation in the four groups of endometria studied. Conclusion: as the apoptosis was scarce in all of the groups studied, endometrial homeostasis deregulation in PCOS could be a result of increased proliferation. Therefore, the onset of endometrial hyperplasia in PCOS endometrium could be linked to inadequate cell proliferation, and concomitantly to inadequate cell survival.

MEDICINA NUCLEAR

EUR J NUCL MED MOL IMAGING. 2007 NOV;34(11):1735-46.

COMPARISON OF RADIONUCLIDE VENTRICULOGRAPHY USING SPECT AND PLANAR TECHNIQUES IN DIFFERENT CARDIAC CONDITIONS.

Massardo T, Jaimovich R, Lavados H, Gutiérrez D, Rodríguez JC, Saavedra JM, Alay R, Gatica H.

Purpose: accurate assessment of ventricular function is required to optimize therapeutic management of cardiac diseases. The aim of this study was to correlate planar equilibrium multigated acquisition (MUGA) with tomographic ventriculography (SPECT) in patients with diverse volumes and wall motion abnormalities. Methods: eighty-three studies in 80 patients (56+/-14 years; 56% women) were classified according to ventricular dilation, wall motion abnormalities and systolic dysfunction. Left and right ventricular ejection fraction (LVEF and RVEF) and end-diastolic and end-systolic left ventricular volumes (EDV and

ESV) were obtained using a commercial QBS program for SPECT. On planar acquisition, LVEF and RVEF were obtained using standard techniques and volumes were determined using the count-based method, without blood sampling. Results: a. Total group: with the planar method, LVEF was 44+/-17%, RVEF 42+/-13%, left EDV 147+/-97 ml (range 31-487 ml) and left ESV 93+/-85 ml (range 15-423 ml); with SPECT the corresponding values were 40+/-20%, 49+/-16%, 131+/-95 ml and 91+/-89 ml, respectively (p=NS for all but RVEF). Linear correlation was 0.845 for LVEF, 0.688 for RVEF, 0.927 for left EDV and 0.94 for left ESV, with good intra-class correlation. B. Subgroups: global and intra-class correlations between planar imaging and SPECT were high for volumes, RVEF and LVEF in all subgroups, except in patients with normal wall motion and function, who showed smaller volumes with SPECT. The group with diffuse wall motion abnormalities had a lower EDV on SPECT. In the abnormal left ventricle, RVEF was higher with SPECT. Conclusion: good correlation and agreement exist between SPECT and planar MUGA with respect to LVEF and left ventricular volumes. SPECT is useful in patients with functional abnormalities, but less reliable in those with normal small cavities. A combined technique is still necessary, and RVEF should be interpreted cautiously.

NEFROLOGÍA

PERIT DIAL INT. 2007 MAY-JUN;27(3):359-63.

COST/UTILITY STUDY OF PERITONEAL DIALYSIS AND HEMODIALYSIS IN CHILE.

Pacheco A, Saffie A, Torres R, Tortella C, Llanos C, Vargas D, Sciaraffia V.

In Chile the reimbursement/patient/year for chronic peritoneal dialysis (PD) is US\$14,654 and for chronic hemodialysis (HD) US\$10,909. However, no study comparing global (direct plus indirect) costs has been performed in our country. Our research objective was to compare global costs and quality of life between the two therapies. Patients (n = 159) from five selected dialysis units in Chile [57 patients on PD (50 on automated PD) and 102 on standard HD (3 x 4 hours weekly)] were retrospectively studied. No patient had previously received the alternate therapy. Items analyzed were quality of life, customer satisfaction, direct and indirect costs, annual global costs, and cost/utility index. Mean age on HD was 54.14 +/- 16.01 years and on PD 49.76 +/- 18.88 years (p > 0.05). No differences in the distribution of diabetic patients between the therapies were found. Hemodialysis and PD groups did not have differences in the quality of life index, although there was better customer satisfaction with PD than with HD. Direct and indirect costs were calculated. We found significant differences in favor of PD in erythropoietin consumption (2.24 +/- 1.57 vials/week on HD and 1.35 +/- 0.85 vials/week on PD, p < 0.05) and working time (31.0 +/- 13.3 hours/week on HD and 38.5 +/- 12.2 hours/week on PD, p < 0.05). The quality life index (Health-Related SF-36 Health Survey) was 65.75 on HD and 66.88 on PD. Annual global costs were US\$20,803 for HD and US\$20,742 for PD. The cost/utility index was 3.16 for HD and 3.10 for PD. Patients on PD have an advantage related to erythropoietin consumption and working capacity compared with HD patients. Addition of related indirect costs to reimbursements gives a more accurate insight into treatment costs. Considering all these parameters, we did not find significant differences between HD and PD in quality life index, cost/utility index, or annual global cost in this Chilean end-stage renal disease population.

NEUROLOGÍA Y NEUROCIRUGÍA

ANN NEUROL. 2007;62(6):666-70.

DYNAMIN 2 MUTATIONS CAUSE SPORADIC CENTRONUCLEAR MYOPATHY WITH NEONATAL ONSET.

Bitoun M, Bevilacqua JA, Prudhon B, Maugenre S, Taratuto AL, Monges S, Lubieniecki F, Cances C, Uro-Coste E, Mayer M, Fardeau M, Romero NB, Guicheney P.

We report four heterozygous dynamin 2 (DNM2) mutations in five centronuclear myopathy patients aged 1 to 15 years. They all presented with neonatal hypotonia with weak suckling. Thereafter, their phenotype progressively improved. All patients demonstrated muscle weakness prominent in the lower limbs, and most of them also presented with facial weakness, open mouth, arched palate, ptosis, and ophthalmoparesis. Electrophysiology showed only myopathic changes, and muscle biopsies showed central nuclei and type I fiber hypotrophy and predominance. Our results expand the phenotypic spectrum of dynamin 2 - related centronuclear myopathy, from the classic mild form to the more severe neonatal phenotype.

ABSTRACTS

ALZHEIMER DIS ASSOC DISORD. 2007 JAN-MAR;21(1):1-7.

NEUROPATHOLOGIC HETEROGENEITY IN HDDD1: A FAMILIAL FRONTOTEMPORAL LOBAR DEGENERATION WITH UBIQUITIN-POSITIVE INCLUSIONS AND PROGRANULIN MUTATION.

Behrens MI, Mukherjee O, Tu PH, Liscic RM, Grinberg LT, Carter D, Paulsmeyer K, Taylor-Reinwald L, Gitcho M, Norton JB, Chakraverty S, Goate AM, Morris JC, Cairns NJ.

Hereditary dysphasic disinhibition dementia (HDDD) describes a familial disorder characterized by personality changes, and language and memory deficits. The neuropathology includes frontotemporal lobar atrophy, neuronal loss and gliosis and, in most cases, abundant Abeta plaques and neurofibrillary tangles (NFTs). A Pick/Alzheimer's spectrum was proposed for the original family (HDDD1). Here we report the clinicopathologic case of an HDDD1 individual using modern immunohistochemical methods, contemporary neuropathologic diagnostic criteria to distinguish different frontotemporal lobar degenerations (FTLDs), and progranulin (PRGN) mutation analysis. Clinical onset was at age 62 years with personality changes and disinhibition, followed by nonfluent dysphasia, and memory loss that progressed to muteness and total dependence with death at age 84 years. There was severe generalized brain atrophy (weight=570 g). Histopathology showed superficial microvacuolation, marked neuronal loss, gliosis, and ubiquitin-positive, tau-negative cytoplasmic and intranuclear neuronal inclusions in frontal, temporal, and parietal cortices. There were also frequent neuritic plaques and NFTs in parietal and occipital cortices. The case met neuropathologic criteria for both FTLD with ubiquitin-positive, tau-negative inclusions (FTLD-U), and Alzheimer disease (Braak NFT stage V). We discovered a novel pathogenic PGRN mutation c.5913 A>G (IVS6-2 A>G) segregating with FTLD-U in this kindred. In conclusion, HDDD1 is an FTLD-U caused by a PGRN mutation and is neuropathologically heterogeneous with Alzheimer disease as a common comorbidity.

STROKE. 2007;38(4):1203-10.

AUTOPSY PREVALENCE OF CORONARY ATHEROSCLEROSIS IN PATIENTS WITH FATAL STROKE.

Góngora-Rivera F, Labreuche J, Jaramillo A, Steg PG, Hauw JJ, Amarencu P.

Background and Purpose-Myocardial infarction (MI) is the leading cause of long-term mortality in patients with stroke, yet the prevalence of coronary atherosclerosis in these individuals is unknown. The objective of the study was to establish the prevalence of coronary atherosclerosis and MI after fatal stroke. Methods-Using an autopsy data bank, we studied the prevalence of coronary plaques and coronary stenoses > 50% and pathologic evidence of MI in 803 consecutive autopsies of neurologic patients. Results-Coronary plaques, coronary stenoses, and MI were present in 72.4%, 37.5%, and 40.8%, respectively, of the 341 patients with stroke and in 26.8%, 10.1%, and 12.8%, respectively, of the 462 patients with other neurologic diseases ($P < 0.001$). Two-thirds of cases of MI were clinically silent and found at autopsy. Compared with other neurologic diseases, and after adjusting for age, gender, and heart weight, the odds ratios (95% confidence intervals) of the presence of coronary plaques, coronary stenosis, and MI in stroke patients were 3.81 (2.66 to 5.46), 2.80 (1.85 to 4.25), and 2.34 (1.58 to 3.46), respectively. The frequency of coronary atherosclerosis and MI was similar between stroke subtypes. The prevalence of coronary plaques, coronary stenosis, and MI was 79.0%, 42.9%, and 46.0%, respectively, in the presence of plaques in any segment of the extracranial and intracranial brain arteries, and 50.8%, 17.9%, and 23.9%, respectively, in the absence of plaques (adjusted $P < 0.01$). Coronary atherosclerosis was also related to the severity of atherosclerosis in any segment of the cerebral arteries (adjusted probability value for linear trend $< .005$). Conclusions-Coronary atherosclerosis and MI are highly prevalent in patients who died from a stroke regardless of the etiology. They are more frequent when atherosclerosis is present in the carotid and cerebral arteries. They are also common in stroke patients with no evidence of carotid or cerebral atherosclerosis.

NEUROSCI LETT. 2007;418(2):181-5.

ASSOCIATION OF GST M1 NULL POLYMORPHISM WITH PARKINSON'S DISEASE IN A CHILEAN POPULATION WITH A STRONG AMERINDIAN GENETIC COMPONENT.

Pérez-Pastene C, Graumann R, Díaz-Grez F, Miranda M, Venegas P, Godoy OT, Layson L, Villagra R, Matamala JM, Herrera L, Segura-Aguilar J.

We have studied the association of a null mutation of Glutathione Transferase M1 (GST M1 *0/0) with Parkinson's disease (MIM 168600) in a Chilean population with a strong Amerindian genetic component. We determined the genotype in 349 patients with idiopathic Parkinson's disease (174 female and 175 male; 66.84 +/- 10.7 years of age), and compared that to 611 controls (457 female and 254 male; 62 +/- 13.4 years of age). A significant association of the null mutation in GST M1 with Parkinson's disease was found ($p = 0.021$), and the association was strongest in the earlier age range. An

association of GSTM1 *0/0 with Parkinson's disease supports the hypothesis that Glutathione Transferase M1 plays a role in protecting astrocytes against toxic dopamine oxidative metabolism, and most likely by preventing toxic one-electron reduction of aminochrome.

STROKE. 2007;38(5):1442-6.

PREVALENCE AND DETERMINANTS OF SUBDIAPHRAGMATIC VISCERAL INFARCTION IN PATIENTS WITH FATAL STROKE.

Abboud H, Labreuche J, Góngora-Rivera F, Jaramillo A, Duyckaerts C, Steg PG, Hauw JJ, Amarenco P.

Background and Purpose - Arterial thromboembolism is a common cause of both visceral and brain infarctions. Because the cause of brain infarction is unknown in up to 39% of patients, the discovery of subdiaphragmatic visceral infarction (SDVI) in this context is important, but its frequency is unknown. We therefore investigated the prevalence of SDVI in subjects who died from stroke. We also evaluated the yield of SDVI diagnosis for stroke subtyping. Methods - We performed a case - control study using a series of 815 consecutive autopsies of patients who had died from a neurological disease, including 350 with stroke (260 infarcts and 90 hemorrhages). We systematically assessed the presence of renal, splenic, and mesenteric infarction (no case of spinal cord was recorded) and analyzed their determinants in patients with stroke. Patients with other neurological diseases served as the control group. Results - Renal infarction was the most frequent SDVI (10.2%), whereas mesenteric infarction was rare (1.1%). At least one SDVI was found in 16.9% of patients with stroke (38.7% of patients with a cardioembolic stroke) and in 5.1% of patients with other neurological diseases (adjusted OR = 2.12; 95% CI = 1.08 to 4.16). Among patients with stroke, a significant heterogeneity in the prevalence of SDVI was found across etiological stroke subgroups with only three patients (3.3%) with hemorrhagic stroke having an SDVI (2 mesenteric and one renal infarction) compared with 56 patients (21.5%) with ischemic stroke ($P < 0.0001$). Among patients with brain infarction and a SDVI, 76.8% had a definite cardiac source of embolism. Conclusions - In patients with fatal brain infarction, the prevalence of SDVI is higher than previously thought, especially in those with stroke attributed to cardiac emboli. Seeking SDVI may assist in the etiologic diagnosis of brain infarction.

NEUROSC LETT. 2007;422(3):193-7.

LRRK2 MUTATIONS IN SOUTH AMERICA: A STUDY OF CHILEAN PARKINSON'S DISEASE.

Pérez-Pastene C, Cobb SA, Díaz-Grez F, Hulihan MA, Miranda M, Venegas P, Godoy OT, Kachergus JM, Ross OA, Layson L, Farrer MJ, Segura-Aguilar.

Pathogenic substitutions in the leucine-rich repeat kinase 2 protein (Lrrk2), R1441G and G2019S, are prevalent causes of autosomal dominant and sporadic Parkinson's disease in the Northern Spanish population. In this study we examined the frequency of these two substitutions in 166 Parkinson's disease patients and 153 controls from Chile, a population with Spanish/European-American admixture. Lrrk2 R1441G was not observed, however Lrrk2 G2019S was detected in one familial and four sporadic Parkinson's disease patients. These findings suggest Lrrk2 G2019S may play an important role in Parkinson's disease on the South American Continent and further studies are now warranted.

AM J PHYSIOL CELL PHYSIOL. 2007;293:C162-C171, 2007.

EFFECTS OF ATP, Mg^{2+} , AND REDOX AGENTS ON THE Ca^{2+} DEPENDENCE OF RYR CHANNELS FROM RAT BRAIN CORTEX.

Bull R, Finkelstein JP, Humeres A, Behrens MI, Hidalgo C.

Despite their relevance for neuronal Ca^{2+} -induced Ca^{2+} release (CICR), activation by Ca^{2+} of ryanodine receptor (RyR) channels of brain endoplasmic reticulum at the [ATP], $[Mg^{2+}]$, and redox conditions present in neurons has not been reported. Here, we studied the effects of varying cis-(cytoplasmic) free ATP concentration ([ATP]), $[Mg^{2+}]$, and RyR redox state on the Ca^{2+} dependence of endoplasmic reticulum RyR channels from rat brain cortex. At pCa 4.9 and 0.5 mM adenylylimidodiphosphate (AMP-PNP), increasing free $[Mg^{2+}]$ up to 1 mM inhibited vesicular $[^3H]$ ryanodine binding; incubation with thimerosal or dithiothreitol decreased or enhanced Mg^{2+} inhibition, respectively. Single RyR channels incorporated into lipid bilayers displayed three different Ca^{2+} dependencies, defined by low, moderate, or high maximal fractional open time (P_o), that depend on RyR redox state, as we have previously reported. In all cases, cis-ATP addition (3 mM) decreased threshold $[Ca^{2+}]$ for activation, increased maximal P_o , and shifted channel inhibition to higher $[Ca^{2+}]$. Conversely, at pCa 4.5 and 3 mM ATP, increasing cis- $[Mg^{2+}]$ up to 1 mM inhibited low activity channels more than moderate activity channels but barely modified

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high activity channels. Addition of 0.5 mM free [ATP] plus 0.8 mM free [Mg²⁺] induced a right shift in Ca²⁺ dependence for all channels so that [Ca²⁺] <30 μM activated only high activity channels. These results strongly suggest that channel redox state determines RyR activation by Ca²⁺ at physiological [ATP] and [Mg²⁺]. If RyR behave similarly in living neurons, cellular redox state should affect RyR-mediated CICR.

OAIC

NEUROSCI LETT. 2007;423(2):172-7.

ENDOSOMAL ABNORMALITIES RELATED TO AMYLOID PRECURSOR PROTEIN IN CHOLESTEROL TREATED CEREBRAL CORTEX NEURONAL CELLS DERIVED FROM TRISOMY 16 MICE, AN ANIMAL MODEL OF DOWN SYNDROME.

Arriagada C, Astorga C, Atwater I, Rojas E, Mears D, Caviedes R, Caviedes P.

The CNh and CTb cell lines are derived from the cerebral cortex of normal and trisomy 16 mice, an animal model of human trisomy 21, Down syndrome (DS), and represent in vitro models to study cellular events associated with the human condition. Amyloid precursor protein (APP) plays an important role in the development of neuropathology associated with DS and cholesterol in the amyloidogenic processing of APP. There is also increasing evidence of alterations in the recycling pathway of the early endosome compartment in nervous tissue from DS. In the present study, we report endosomal abnormalities related to amyloid precursor protein in cholesterol-treated CTb cells. Colocalization studies revealed the presence of APP-derived products in early endosomal compartments in both cell lines. Using internalization and immunoprecipitation techniques, differential effects were observed between the normal and trisomic cell lines when treated with cholesterol. Internalization experiments showed that the CTb cell line accumulates internalized APP in intracellular compartments for longer periods of time when compared to the CNh cell line. Immunoprecipitation revealed a differential interaction between the trafficking-related protein Rab4 and APP in the neuronal cell lines CNh and CTb. The present study suggests a putative mechanism by which overexpressed APP accumulates in intracellular compartments related to the endosomal trafficking pathway in individuals with DS, and highlights the usefulness of the CTb cell line as a model to study altered APP metabolism related to this genetic condition.

OBSTETRICIA Y GINECOLOGÍA

GYNECOL ONCOL. 2007 JAN;104(1):168-75.

NERVE GROWTH FACTOR AND ITS HIGH-AFFINITY RECEPTOR TRKA PARTICIPATE IN THE CONTROL OF VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION IN EPITHELIAL OVARIAN CANCER.

Campos X, Muñoz Y, Selman A, Yazigi R, Moyano L, Weinstein-Oppenheim C, Lara HE, Romero C.

Objectives: to compare the expression of nerve growth factor (NGF) and its high-affinity receptor trkA in normal ovaries and in epithelial ovarian carcinomas. Given NGF acts as an angiogenic factor through a vascular endothelial growth factor (VEGF)-mediated mechanism in several types of tissues, we examined whether NGF regulates the expression of VEGF isoforms in epithelial ovarian cancer (EOC). Methods: the expression and localization of NGF and tyrosine kinase receptor A (trkA) in normal ovarian samples and in ovarian cancer samples were analyzed by RT-PCR and immunohistochemistry. NGF regulates the expression of three VEGF isoforms (VEGF(121), VEGF(165) and VEGF(189)); these were examined using RT-PCR in explants of EOC and ELISA in culture media. Results: TrkA mRNA levels were over-expressed in ovarian cancer compared to normal ovarian samples, whereas NGF mRNA levels remained unchanged. NGF and trkA proteins were absent or found in very low levels in normal ovarian surface epithelium (OSE), whereas they were highly expressed in epithelial cells of EOC. Additionally, NGF stimulated the expression of VEGF isoforms in cancer explants. The effect was dose-dependent and inhibited by a NGF antibody and by K(252a), a trk receptor inhibitor. Conclusion: the abundance of NGF and trkA receptors in epithelial cells of EOC, together with the ability of NGF to increase VEGF expression strongly suggests an autocrine role of NGF in EOC. These findings suggest that blocking neurotrophin action could be a therapeutic target in treating ovarian cancer.

J ULTRASOUND MED. 2007 SEP;26(9):1215-20.

THREE-DIMENSIONAL POWER DOPPLER SONOGRAPHY IN THE PRENATAL DIAGNOSIS OF A TRUE KNOT OF THE UMBILICAL CORD: VALUE AND LIMITATIONS.

Hasbún J, Alcalde JL, Sepúlveda W.

objective: the purpose of this study was to examine the value of 3-dimensional power Doppler sonography in the prenatal diagnosis of a true knot of the umbilical cord. Methods: cases in which the diagnosis of a true knot of the umbilical cord was suspected by prenatal 2-dimensional sonography were reviewed. The presumably affected segment of the cord was examined with 3-dimensional power Doppler sonography for further characterization. Confirmation of the prenatal diagnosis was sought by reviewing the delivery records and contacting the referring obstetrician and the patients themselves. Results: eight consecutive cases were studied. Three-dimensional power Doppler sonography displayed a vascular spatial configuration pattern consistent with a true knot of the umbilical cord in all of them. However, the prenatal diagnosis was confirmed at delivery in only 5 cases (62.5%). Although there were no cases of a false knot mimicking a true knot of the umbilical cord, all incorrect diagnoses in this series were associated with multiple loops of the umbilical cord in the third trimester. Conclusions: three-dimensional power Doppler sonography seems to be helpful in determining the presence of a true knot of the umbilical cord in utero, especially in the second trimester. However, this should not be considered a definitive method for the diagnosis because multiple loops of the umbilical cord lying close to each other can generate a sonographic image that can be undistinguishable from a true knot of the umbilical cord prenatally, especially when located in a small pocket of amniotic fluid. Therefore, the presumable diagnosis of a true knot of the umbilical cord in utero should be taken with caution.

ULTRASOUND OBSTET GYNECOL. 2007 DEC;30(7):946-51.

SCREENING FOR TRISOMY 21 DURING THE ROUTINE SECOND-TRIMESTER ULTRASOUND EXAMINATION IN AN UNSELECTED CHILEAN POPULATION.

Parra-Cordero M, Quiroz L, Rencoret G, Pedraza D, Muñoz H, Soto-Chacón E, Miranda-Mendoza I.

Objective: to evaluate the performance of a detailed ultrasound examination during the second trimester as a screening test for Down syndrome in an unselected Chilean population. Methods: this was part of an ongoing longitudinal study. Included were 3071 women with singleton pregnancies who underwent routine ultrasound examination between 21 + 0 and 25 + 6 gestational weeks as a screening test for chromosomal abnormalities and major congenital structural defects, and who were diagnosed as having trisomy 21 or being chromosomally normal. Maternal age, and eight soft markers and cardiac defects associated with Down syndrome were evaluated as a screening test using logistic regression analysis. Results: the incidence of Down syndrome was 0.6%, and the mean maternal age was 29.4 +/- 6.2 years. At least one of four soft markers (absent nasal bone, nuchal edema, short femur, echogenic foci) and/or cardiac defects was present in 77.8% of Down syndrome fetuses and in 3.1% of normal fetuses. Furthermore, with a false-positive rate of 1%, the detection rate using the combined model of ultrasound markers and maternal age was 72.2%. Conclusions: second-trimester ultrasound markers are able to detect over 70% of Down syndrome fetuses with only a 1% false-positive rate.

PRENAT DIAGN. 2007 DEC;27(13):1251-7.

FETAL ARTERIAL AND VENOUS DOPPLER PULSATILITY INDEX AND TIME AVERAGED VELOCITY RANGES.

Parra-Cordero M, Lees C, Missfelder-Lobos H, Seed P, Harris C.

Objectives: the aim of this study was to determine the fetal arterial and venous Doppler pulsatility index and time averaged velocity ranges for women undergoing third trimester ultrasound. Methods: one hundred and seventy-two women with singleton pregnancy and clinical indication underwent biometry and fetal Doppler assessment at 23 to 41 weeks. Umbilical artery, middle cerebral artery, thoracic aorta and ductus venosus pulsatility index and time averaged velocity measurements were performed and corrected statistically based on the distribution of estimated fetal weight at the time of the scan. Results: the tables and figures of the several vessels published in this study are broadly comparable to other publications and unlike others, are adjusted for the estimated fetal weight distribution. Conclusions: we present the values of the commonly measured Doppler indices in fetuses with normal growth at the time of scan. The ranges, therefore, have potential utility in the setting where referrals to a fetal assessment unit are made.

ABSTRACTS

BIOCELL. 2007;31(1):51-9.

PREIMPLANTATION EMBRYOTOXICITY AFTER MOUSE EMBRYO EXPOSITION TO REACTIVE OXYGEN SPECIES.

Cebral E, Carrasco I, Vantman D, Smith R.

Exposure of either gametes or embryos to conditions and/or factors that generate oxidative stress has been associated with impaired early embryogenesis. The effects of reactive oxygen species (ROS) on mouse preimplantation development, depending of the ROS-concentration and time of exposition, were studied. Two-cell embryos were incubated with 5, 10, 25 and 50 microM of hydrogen peroxide (H₂O₂) for 30 and 60 minutes of exposition and allowed to develop for 72 h to study the quality of development. The incubation with 50 microM H₂O₂ for 30 or 60 minutes, strongly inhibited the 2-cell embryo development as compared to the control ($p < 0.001$). Twenty-five microM H₂O₂ produced inhibition of blastocyst formation ($p < 0.001$) and 10 microM H₂O₂ significantly decreased the percentages of expanded and hatched blastocysts, which resulted morphologically altered ($p < 0.05$ and $p < 0.01$, respectively). The higher H₂O₂ concentrations were able to elicit necrotic morphology in the 2-cell arrested embryos, while 10 microM H₂O₂ induced moderate damage with the arrested embryos partially fragmented. In conclusion, important causes for defective preimplantation development and for early embryo losses may be due to oxidative stress because early mouse embryos exposed to ROS for short times arrested at the first cellular cycle (2-cell) and/or impaired embryo differentiation and morphogenesis, being these effects ROS-concentration-dependent.

GYNECOL ONCOL. 2007;104(2):290-5.

DEREGULATION OF TISSUE HOMEOSTASIS IN ENDOMETRIA FROM PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME WITH AND WITHOUT ENDOMETRIAL HYPERPLASIA.

Villavicencio A, Bacallao K, Gabler F, Fuentes A, Albornoz J, Casals A, Vega M.

Objective. To study the proteins involved in endometrial homeostasis in PCOS women. Methods. Protein expression of Ki67, Bcl-2, Bax, Pro-Caspase-3 and Caspase-3 by immunohistochemistry and/or Western blot, and DNA fragmentation using in situ 3'-end labeling of apoptotic cells, was measured in 9 samples of normal endometrium (NE), 12 PCOS endometria without treatment (PCOSE), 7 endometria from PCOS women with endometrial hyperplasia (HPCOSE) and 9 endometria from patients with endometrial hyperplasia (HE). Results. Cell proliferation was higher in epithelium from PCOSE ($P < 0.05$), HPCOSE and HE vs NE. A higher Bcl-2/Bax relative ratio in PCOSE and HPCOSE was observed, in absence of active Caspase-3 and scarce DNA fragmentation in the four groups of endometria studied. Conclusion. As the apoptosis was scarce in all of the groups studied, endometrial homeostasis deregulation in PCOS could be a result of increased proliferation. Therefore, the onset of endometrial hyperplasia in PCOS endometrium could be linked to inadequate cell proliferation, and concomitantly to inadequate cell survival.

FERTIL STERIL. 2007;87(2):321-8.

SEX HORMONE-BINDING GLOBULIN EXPRESSION IN THE ENDOMETRIA OF WOMEN WITH POLYCYSTIC OVARY SYNDROME.

Maliqueo M, Bacallao K, Quezada S, Clementi M, Gabler F, Johnson MC, Vega M.

Objective: to evaluate the protein and messenger RNA expression of sex hormone-binding globulin (SHBG) in endometria from women with polycystic ovary syndrome (PCOS). Design: case-control study. Setting: hospital research unit. Patient(s): thirty-three women with PCOS, and 17 fertile, healthy women of similar age to those with PCOS. Intervention(s): endometrial and blood samples were obtained from women with PCOS (PCOSEs) and from control women (CEs) during the proliferative phase of the menstrual cycle. Main Outcome Measure(s): expression studies for SHBG (immunohistochemistry and reverse transcription-polymerase chain reaction). Hormonal studies for determining sex steroids (T, P, and E₂) and SHBG concentration. Insulin sensitivity was assessed by composite insulin sensitivity index (ISI_{composite}). Result(s): in stroma, the protein expression of SHBG was lower in PCOSEs than in CEs. Epithelial cells had a similar expression of SHBG protein in both groups. Messenger RNA of variant 548 base pairs (wild-type) tended to be lower in PCOSEs compared to CEs. When PCOSEs were classified by insulin resistance, the PCOSEs with normal insulin sensitivity showed an expression of stromal SHBG similar to that observed in CEs. Conclusion(s): the low SHBG expression in the stromal compartment of endometria from women with PCOS with insulin resistance may contribute to generate an abnormal steroid milieu in the endometria of these women.

J MATERN FETAL NEONATAL MED. 2007;20(11):793-6.

MATERNAL SERUM SOLUBLE ADHESION MOLECULE LEVELS AT 11(+0)-13(+6) WEEKS AND SUBSEQUENT DEVELOPMENT OF PRE-ECLAMPSIA.

Parra-Cordero M, Turan OM, Kaur A, Pearson JD, Nicolaides KH.

Objectives. We sought to examine whether the maternal serum concentration of soluble vascular cell adhesion molecule 1 (sVCAM-1) and intercellular adhesion molecule 1 (sICAM-1) at 11(+0)-13(+6) weeks of gestation could improve the prediction for subsequent development of pre-eclampsia. Methods. A nested case-control prospective study of pregnancies having uterine artery Doppler routinely at 11(+0)-13(+6) weeks of gestation was conducted to determine the maternal serum concentration of sICAM-1 and sVCAM-1 in peripheral blood samples obtained from 18 women who later developed pre-eclampsia and 60 unaffected women. Results. The mean uterine artery pulsatility index was higher (2.2 +/- 0.6 vs. 1.8 +/- 0.5, $p < 0.05$) in the pre-eclampsia compared with the unaffected pregnancies. There were no significant differences between the groups in the mean serum concentration of either adhesion molecule. Conclusions. These results suggest that there is no endothelial activation before the appearance of clinical signs of preeclampsia. Therefore, these biochemical markers are unlikely to become early predictors of this condition.

N ENG J MED. 2007;357(5):462-9

PROGESTERONE AND THE RISK OF PRETERM BIRTH AMONG WOMEN WITH A SHORT CERVIX.

Fonseca EB, Celik E, Parra M, Singh M, and Fetal Med Fdn Second Trimester Scr.

Background: previous randomized trials have shown that progesterone administration in women who previously delivered prematurely reduces the risk of recurrent premature delivery. Asymptomatic women found at midgestation to have a short cervix are at greatly increased risk for spontaneous early preterm delivery, and it is unknown whether progesterone reduces this risk in such women. Methods: cervical length was measured by transvaginal ultrasonography at a median of 22 weeks of gestation (range, 20 to 25) in 24,620 pregnant women seen for routine prenatal care. Cervical length was 15 mm or less in 413 of the women (1.7%), and 250 (60.5%) of these 413 women were randomly assigned to receive vaginal progesterone (200 mg each night) or placebo from 24 to 34 weeks of gestation. The primary outcome was spontaneous delivery before 34 weeks. Results: spontaneous delivery before 34 weeks of gestation was less frequent in the progesterone group than in the placebo group (19.2% vs. 34.4%; relative risk, 0.56; 95% confidence interval [CI], 0.36 to 0.86). Progesterone was associated with a nonsignificant reduction in neonatal morbidity (8.1% vs. 13.8%; relative risk, 0.59; 95% CI, 0.26 to 1.25; $P=0.17$). There were no serious adverse events associated with the use of progesterone. Conclusions: in women with a short cervix, treatment with progesterone reduces the rate of spontaneous early preterm delivery.

OFTALMOLOGÍA

CELL BIOL INT. 2007;31(2):1350-40.

G2 CHECKPOINT-DEPENDENT DNA REPAIR AND ITS RESPONSE TO CATALASE IN DOWN SYNDROME AND CONTROL LYMPHOCYTE CULTURES.

Pincheira J, Romero P, Marcelain K, Salazar L, De la Torre C.

The amount of DNA lesions repaired in G2 and also G2 timing are controlled by the DNA damage-dependent checkpoint. Down syndrome (DS) lymphocytes showed twice as much constitutive DNA damage in G2 than control ones, when recording it as chromosomal aberrations in metaphase, after caffeine-induced checkpoint abrogation. During G2, DS lymphocytes repaired 1.5 times more DNA lesions than control ones. However the DS cells displayed a decreased threshold for checkpoint adaptation, as the spontaneous override of the G2 to mitosis transition block induced by the checkpoint took place in the DS cells when they had three times more DNA lesions than controls. Catalase addition to cultures scavenges hydrogen peroxide diffused from cells, resulting in subsequent intracellular depletion (Antunes and Cadenas, 2000). The intracellular H₂O₂ level seemed to regulate the G2 checkpoint. Thus, in controls, H₂O₂ depletion (induced by 3.2-50 $\mu\text{g/mL}$ catalase) prevented its functioning: chromosomal damage increased while G2 shortened. Conversely, in the DS lymphocytes, 12.5 $\mu\text{g/mL}$ catalase lengthened G2 and decreased chromosomal damage, in spite that the amount of DNA repaired in G2 was half of that repaired in the catalase-free DS lymphocytes.

ABSTRACTS

ONCOLOGÍA

J CLIN ONCOL. 2007 AUG 1;25(22):3205-9.

CLINICAL BENEFIT WITH DOCETAXEL PLUS FLUOROURACIL AND CISPLATIN COMPARED WITH CISPLATIN AND FLUOROURACIL IN A PHASE III TRIAL OF ADVANCED GASTRIC OR GASTROESOPHAGEAL CANCER ADENOCARCINOMA: THE V-325 STUDY GROUP.

Ajani JA, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, Rodrigues A, Fodor M, Chao Y, Voznyi E, Marabotti C, Van Cutsem E; V-325 Study Group.

Purpose: for patients with advanced gastric or gastroesophageal cancer (AGGEC) providing clinical benefit with improved palliation is highly desirable. However, a prospective evaluation of clinical benefit in AGGEC patients has never before been reported in a phase III setting. Patients and Methods: in a multinational trial (V325), 445 patients were randomly assigned and treated with either docetaxel plus cisplatin and fluorouracil (DCF) or cisplatin and fluorouracil (CF). Clinical benefit was prospectively evaluated in this trial as a secondary end point. The primary measure for clinical benefit analysis was time to definitive worsening by one or more categories of Karnofsky performance status (KPS). Secondary clinical benefit end points included time to 5% definitive weight loss, time to definitive worsening of appetite by one grade, pain-free survival (defined as time to first appearance of pain), and time to first cancer pain-related opioid intake. Clinical benefit assessments were recorded at each clinic visit. Results: clinical benefit assessments were performed in more than 75% of patients throughout V325. DCF significantly prolonged time to definitive worsening of KPS compared with CF (median, 6.1 v 4.8 months; hazard ratio, 1.38; 95% CI, 1.08 to 1.76; log-rank P = .009). Although time to definitive weight loss and time to definitive worsening of appetite favored DCF, the results were not statistically significant. Pain-free survival and time to first cancer pain-related opioid intake were comparable. Conclusion: to our knowledge, V325 is the first phase III trial to report clinical benefit in AGGEC patients. Clinical benefit was assessed beyond protocol-specific chemotherapy. The addition of D to CF not only significantly improved clinical benefit but also improved quality of life, time to progression, and overall survival compared with CF.

J CLIN ONCOL. 2007 AUG 1;25(22):3210-6.

QUALITY OF LIFE WITH DOCETAXEL PLUS CISPLATIN AND FLUOROURACIL COMPARED WITH CISPLATIN AND FLUOROURACIL FROM A PHASE III TRIAL FOR ADVANCED GASTRIC OR GASTROESOPHAGEAL ADENOCARCINOMA: THE V-325 STUDY GROUP.

Ajani JA, Moiseyenko VM, Tjulandin S, Majlis A, Constenla M, Boni C, Rodrigues A, Fodor M, Chao Y, Voznyi E, Awad L, Van Cutsem E; V-325 Study Group.

Purpose: therapy of patients with advanced gastric or gastroesophageal junction cancer should provide symptom relief and improve quality of life (QOL) because most patients are symptomatic at baseline. Using validated instruments, we prospectively assessed QOL (even after completion of protocol treatment) as one of the secondary end points of the V325 phase III trial. Patients And Methods: four hundred forty-five patients randomly received either docetaxel 75 mg/m² and cisplatin 75 mg/m² each on day 1 plus fluorouracil 750 mg/m²/d continuous infusion on days 1 to 5 every 3 weeks (DCF) or cisplatin 100 mg/m² on day 1 plus fluorouracil 1,000 mg/m²/d continuous infusion on days 1 to 5 every 4 weeks (CF). The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30) and, where available, the EuroQOL EQ-5D questionnaire were administered every 8 weeks from baseline until progression and then every 3 months. Time to definitive deterioration of QOL parameters was analyzed. Results: the proportions of patients having assessable EORTC QLQ-C30 and EQ-5D questionnaires at baseline were 86.0% and 78.7% with DCF, respectively, and 89.7% and 92.8% with CF, respectively. Time to 5% deterioration of global health status (primary end point) significantly favored DCF over CF (log-rank test, P = .01). QOL was preserved longer for patients on DCF than those on CF for all time to deterioration analyses, demonstrating the statistical superiority of DCF compared with CF. conclusion: V325 represents the largest trial with the longest prospectively controlled evaluations of QOL during protocol chemotherapy and follow-up in patients with advanced gastric or gastroesophageal junction cancer. In V325, advanced gastric or gastroesophageal junction cancer patients receiving DCF not only had statistically improved overall survival and time to tumor-progression, but they also had better preservation of QOL compared with patients receiving CF.

REUMATOLOGÍA

ANN RHEUM DIS. 2007 DEC 4.

MODULATION OF ESTABLISHED MURINE COLLAGEN-INDUCED ARTHRITIS BY A SINGLE INOCULATION OF SHORT-TERM LIPOPOLYSACCHARIDE-STIMULATED DENDRITIC CELLS.

Salazar L, Aravena O, Abello P, Escobar A, Contreras-Levicoy J, Rojas-Colonelli N, Catalán D, Aguirre A, Zúñiga R, Pesce B, González C, Cepeda R, Cuchacovich M, Molina MC, Salazar-Onfray F, Delgado M, Toes RE, Aguilón JC.

The use of regulatory or immature dendritic cells (DCs) as tools for modulating experimental rheumatoid arthritis is very recent. TNF-stimulated DCs have been shown to restore tolerance in experimental autoimmune encephalomyelitis and collagen-induced arthritis (CIA). Objective: we investigated the capacity of short-term lipopolysaccharide (LPS)-stimulated DCs pulsed with type-II collagen (CII) to induce tolerance against established CIA. Methods: Bone marrow-derived DCs were generated in the presence of GM-CSF. After CIA induction, mice were injected at day 35 with a single dose of 4- or 24-hour LPS-stimulated DCs that had been loaded with CII (CII/DCs, 4hLPS/CII/DCs or 24hLPS/CII/DCs). Arthritis progression was monitored by clinical and histologic evaluations. Results: Flow cytometry of 4hLPS/CII/DCs showed intermediate CD40 and CD86 expression, lower than that of 24hLPS/CII/DCs (fully mature) and higher than that of CII/DCs (immature). A functional assay showed that 4hLPS/CII/DCs display increased endocytosis ability with respect to 24hLPS/CII/DCs, indicating a semi-mature state. The single inoculation of 4hLPS/CII/DCs in mice with established CIA reduced significantly disease severity over time. Histologic evaluation of mice treated with 4hLPS/CII/DCs revealed diminished inflammatory synovitis, cartilage damage and fibrosis. Co-cultures of DCs with splenocytes from CIA mice showed that collagen-specific IFN γ production was dramatically inhibited by 4hLPS/CII/DCs. 4hLPS/CII/DCs were high IL-10 producers which could explain the inhibition of arthritis progression in mice receiving this treatment because neither antibodies nor regulatory CD4+CD25+Foxp3+ T lymphocytes were demonstrated to be involved. conclusion: short-term LPS-modulated DCs inoculation interferes with CIA progression when loaded with CII.

J CELL BIOCHEM. 2007 MAY 15;101(2):389-98.

L-TYPE CALCIUM CHANNELS IN GROWTH PLATE CHONDROCYTES PARTICIPATE IN ENDOCHONDRAL OSSIFICATION.

Mancilla EE, Galindo M, Fertilio B, Herrera M, Salas K, Gatica H, Goecke A.

Longitudinal bone growth occurs by a process called endochondral ossification that includes chondrocyte proliferation, differentiation, and apoptosis. Recent studies have suggested a regulatory role for intracellular Ca(2+) (Ca(i) (2+)) in this process. Indirect studies, using Ca(2+) channel blockers and measurement of Ca(i) (2+), have provided evidence for the existence of Ca(2+) channels in growth plate chondrocytes. Furthermore, voltage-gated Ca(2+) channels (VGCC), and specifically L- and T-type VGCCs, have been recently described in murine embryonic growth plates. Our aim was to assess the effect of L-type Ca(2+) channel blockers on endochondral ossification in an organ culture. We used cultures of fetal rat metatarsal rudiments at 20 days post gestational age, with the addition of the L-type Ca(2+) channel blockers verapamil (10-100 microM) or diltiazem (10-200 microM) to the culture medium. Longitudinal bone growth, chondrocyte differentiation (number of hypertrophic chondrocytes), and cell proliferation (incorporation of tritiated thymidine) were measured. Verapamil dose-dependently decreased growth, the number of hypertrophic chondrocytes, and cell proliferation, at concentrations of 10-100 microM. Growth and the number of hypertrophic chondrocytes decreased significantly with diltiazem at 50-100 microM, and proliferation decreased significantly at concentrations of 10-200 microM. Additionally, there was no increase in apoptosis over physiological levels with either drug. We confirmed the presence of L-type VGCCs in rat rudiments using immunohistochemistry, and showed that the antagonists did not alter the pattern of VGCC expression. In conclusion, our data suggest that L-type Ca(2+) channel activity in growth plate chondrocytes is necessary for normal longitudinal growth, participating in chondrocyte proliferation and differentiation.

ABSTRACTS

MOL IMMUNOL. 2007 MAR;44(8):2115-23.

METHOTREXATE REGULATES THE EXPRESSION OF GLUCOCORTICOID RECEPTOR ALPHA AND BETA ISOFORMS IN NORMAL HUMAN PERIPHERAL MONONUCLEAR CELLS AND HUMAN LYMPHOCYTE CELL LINES IN VITRO.

Goecke IA, Álvarez C, Henríquez J, Salas K, Molina ML, Ferreira A, Gatica H.

MTX is an effective therapy for autoimmune-inflammatory diseases. The mechanisms that mediate these actions are not completely clear. It is accepted that many of these effects are mediated through the release of adenosine with the activation of the adenosine receptor A2. MTX is used as a steroid sparing agent. An improved in vitro GC cell sensitivity in GC insensitive asthma patients has been demonstrated after MTX treatment. Most GC actions are mediated by the GCR. The effect of MTX on GCRs expression has not been previously evaluated. Therefore, we evaluate if MTX regulates the expression of glucocorticoid receptors, increasing the expression of the active receptor (GCR alpha) and/or decreasing the expression of the dominant negative receptor (GCR beta). We show that MTX increases the mRNA and protein levels of GCR alpha and decreases or leaves unchanged the protein expression of the GCR beta in CEM cells in culture. This effect was also observed in other lymphocytes (Jurkat and Raji) and in PBMC from healthy volunteers. We also show that upon MTX treatment PBMC from normal volunteers exhibit a higher sensitivity to DEX inhibition on LPS-induced TNF alpha release. To explore if these actions are mediated by adenosine through the adenosine receptor A2 we evaluate the effect of adenosine on the GCRs expression and the effect of an A2 receptor blocker (DMPX) on MTX effects on GCRs expression. Our results show that adenosine does not mimic and DMPX can enhance MTX effects on these receptors. We conclude that MTX increases the GCR alpha/GCR beta ratio of expression in lymphocytes which could mediate its previously reported effects in improving cell glucocorticoid sensitivity. These actions are not mediated by the adenosine receptor A2.

UROLOGÍA

UROLOGY. 2007 OCT;70(4):777-80.

CORRELATION BETWEEN PRIMARY TUMOR PATHOLOGIC FEATURES AND PRESENCE OF CLINICAL METASTASIS AT DIAGNOSIS OF TESTICULAR SEMINOMA.

Valdevenito JP, Gallegos I, Fernández C, Acevedo C, Palma R.

Objectives: to compare several risk factors in the testicular biopsy of patients with pure seminoma with and without clinical metastasis at diagnosis. Methods: we performed a retrospective study of patients with pure seminoma. The retroperitoneum was staged with computed tomography and the thorax with simple radiography and/or computed tomography, taking into account the original reports and clinical stage. The previous reports and original pathology plates were reviewed by pathologists who were unaware of the clinical stage of the patients. Patients with beta-human chorionic gonadotropin greater than 800 mIU/mL were excluded. Results: a total of 86 patients had sufficient data and comprised the study cohort. Of the 86 patients, 62 had clinical Stage I (72%), 20 had Stage II (23%), and 4 had Stage III (5%). On univariate analysis, tumor size greater than 4 cm ($P = 0.0135$), testicular vascular invasion ($P = 0.0042$), rete testis invasion ($P = 0.0002$), tunica albuginea penetration ($P = 0.00001$), base of the spermatic cord invasion ($P = 0.0002$), epididymis invasion ($P = 0.001$), and vascular invasion of the cord ($P = 0.024$) were predictive of metastasis. On multivariate analysis, tumor size greater than 6 cm (odds ratio 6.9, 95% confidence interval 1.3 to 35, $P = 0.02$) and rete testis invasion (odds ratio 6.1, confidence interval 1.2 to 30, $P = 0.025$) remained as important predictors of metastasis (tumor size less than 6 cm was not significant on multivariate analysis). Conclusions: the results of this study have demonstrated that rete testis invasion and tumor size correlate independently with the presence of clinical metastasis at diagnosis of testicular seminoma.

EUR UROL. 2007 FEB;51(2):556-8.

GIANT LITHIASIS IN A FEMALE URETHRAL DIVERTICULUM.

Gómez Gallo A, Valdevenito Sepúlveda JP, San Martín Montes M.

The formation of gallstones in a urethral diverticulum is a rare clinical entity and is usually seen in males. The case of a 50 year old woman is presented, who consults for hard vaginal mass and dyspareunia associated with repeated urinary infections, with radiological images and an interesting photoendoscopic vision of the upper dome of the gallstone. The diverticulum was approached via vaginal way and the local extraction was successful.

FERTIL STERIL. 2007;88(5):1318-26.

AZFc PARTIAL DELETIONS IN CHILEAN MEN WITH SEVERE SPERMATOGENIC FAILURE.

Lardone MC, Parodi DA, Ebensperger M, Penaloza P, Cornejo V, Valdevenito R, Pommer, Castro A.

Objective: to determine the prevalence of AZFc subdeletions in infertile Chilean men with severe spermatogenic impairment. Design: prospective analysis. Setting: University infertility clinic. Patient(s): ninety-five secretory azo/oligozoospermic men without AZFc Y chromosome microdeletions: 71 whose testicular histology showed severe spermatogenic impairment and 24 who exhibited reduced testicular volume and elevated serum FSH levels. As controls, we studied 77 men (50 fertile and/or normozoospermic, and 27 with azoospermia and normal spermatogenesis). Intervention(s): peripheral blood was drawn to obtain genomic DNA for polymerase chain reaction (PCR) digestion assays of DAZ-sequence nucleotide variants and for AZFc-STS PCR after a complete testicular characterization (biopsy, hormonal, and physical evaluation). Main Outcome Measure(s): DAZ genes and AZFc subdeletion types. Result(s): in cases we observed two "gr/gr" subdeletions (2.1%), one with absence of DAZ1/DAZ2 (g1/g2 subtype), and the other with absence of DAZ3/DAZ4 (r2/r4 subtype). Additionally, we found a g1/g3 subdeletion in a patient with Sertoli-cell-only syndrome. In controls, we observed two gr/gr subdeletions with absence of DAZ1/DAZ2 (2.6%) in a fertile/normozoospermic and in an obstructive azoospermic man. Conclusion(s): AZFc subdeletions do not seem to cause severe impairment of spermatogenesis. Moreover, gr/gr-DAZ1/DAZ2 subdeletions do not appear to affect fertility in Chilean men.

ENDOUROLOG. 2007;21(11):1361-6.

CHARACTERIZING TUNA (R) ABLATIVE TREATMENTS OF THE PROSTATE FOR BENIGN HYPERPLASIA WITH GADOLINIUM-ENHANCED MAGNETIC RESONANCE IMAGING.

Mynderse LA, Larson B, Huidobro C, Meyer JJ, Busel D, Hanson DP, Larson T.

Background and Purpose: transurethral Needle Ablation of the prostate (TUNA (R)) has been accepted as an office-based treatment for benign prostatic hyperplasia (BPH) for many years. Clinical outcomes have been reported, but the amount and location of the necrosis produced have yet to be characterized. The necrosis caused by TUNA was evaluated by gadolinium-enhanced magnetic resonance imaging (MRI) of the pelvis. Patients and Methods: twelve patients with BPH/lower urinary-tract symptoms underwent standard TUNA, and MRI scans with gadolinium enhancement were performed before and 1 week after treatment. The images were studied using Analyze (R) software to quantify the amount of necrosis compared with the prostatic volume. Transverse, coronal, and sagittal images were obtained to identify the location of the necrosis. Results: new gadolinium defects were seen in all patients after TUNA. The lesions coalesced into continuous areas of necrosis and correlated with the site of needle placement. The mean volume of necrosis was 6.84 cc and equated to 8.6% of the prostate volume. No lesions were found near the apex, urethra, or rectum; and none extended beyond the prostate capsule. Conclusions: gadolinium-enhanced MRI demonstrates new vascular defects representing necrosis caused by TUNA of the prostate. This therapy for BPH produces necrotic lesions that can be placed strategically by the surgeon. The standard protocol produces lesions that coalesce to create larger lesions. This MRI study has characterized, for the first time, the heating pattern and intraprostatic necrosis of a complete TUNA procedure.