El material que se presenta a continuación proviene de los datos proporcionados por la OAIC (Oficina de Apoyo a la Investigación Clínica de nuestro Hospital) así como de la que nos facilitaron los servicios en respuesta a nuestra solicitud en diciembre del 2009.

Abstracts de publicaciones internacionales ISI 2009

OFICINA DE APOYO A LA INVESTIGACIÓN CLÍNICA - OAIC

J CLIN ONCOL. 2009 FEB 20;27(6):945-52.

PROLONGED SURVIVAL OF DENDRITIC CELL-VACCINATED MELANOMA PATIENTS CORRELATES WITH TUMOR-SPECIFIC DELAYED TYPE IV HYPERSENSITIVITY RESPONSE AND REDUCTION OF TUMOR GROWTH FACTOR BETA-EXPRESSING T CELLS.

López MN, Pereda C, Segal G, Muñoz L, Aguilera R, González FE, Escobar A, Ginesta A, Reyes D, González R, Mendoza-Naranjo A, **Larrondo M**, Compán A, Ferrada C, Salazar-Onfray F.

PURPOSE: The aim of this work was to assess immunologic response, disease progression, and post-treatment survival of melanoma patients vaccinated with autologous dendritic cells (DCs) pulsed with a novel allogeneic cell lysate (TRIMEL) derived from three melanoma cell lines. PATIENTS AND METHODS: Forty-three stage IV and seven stage III patients were vaccinated four times with TRIMEL/DC vaccine. Specific delayed type IV hypersensitivity (DTH) reaction, ex vivo cytokine production, and regulatory T-cell populations were determined. Overall survival and disease progression rates were analyzed using Kaplan-Meier curves and compared with historical records. RESULTS: The overall survival for stage IV patients was 15 months. More than 60% of patients showed DTH-positive reaction against the TRIMEL. Stage IV/DTH-positive patients displayed a median survival of 33 months compared with 11 months observed for DTH-negative patients (P = .0014). All stage III treated patients were DTH positive and remained alive and tumor free for a median follow-up period of 48 months (range, 33 to 64 months). DTH-positive patients showed a marked reduction in the proportion of CD4+ transforming growth factor (TGF) beta+ regulatory T cells compared to DTH-negative patients (1.54% v 5.78%; P < .0001). CONCLUSION: Our findings strongly suggest that TRIMEL-pulsed DCs provide a standardized and widely applicable source of melanoma antigens, very effective in evoking antimelanoma immune response. To our knowledge, this is the first report describing a correlation between vaccine-induced reduction of CD4+TGFbeta+ regulatory T cells and in vivo antimelanoma immune response associated to improved patient survival and disease stability.

DEPARTAMENTO DE ANATOMÍA PATOLÓGICA

UROL ONCOL. 2009 MAY 16.

THE EXPRESSION OF SYNDECAN-1 AND -2 IS ASSOCIATED WITH GLEASON SCORE AND EPITHELIAL-MESENCHYMAL TRANSITION MARKERS, E-CADHERIN AND β-CATENIN, IN PROSTATE CANCER.

Hector R. Contreras, Rodrigo A. Ledezma, Jorge Vergara, Federico Cifuentes, Cristina Barra, Pablo Cabello, **Ivan Gallegos**, Bernardo Morales, **Christian Huidobro**, Enrique A. Castellón.

The epithelial-mesenchymal transition (EMT) is considered a key step in tumor progression, where the invasive cancer cells change from epithelial to mesenchymal phenotype. During this process, a decrease or loss in adhesion molecules expression and an increase in migration molecules expression are observed. The aim of this work was to determine the expression and cellular distribution of

syndecan-1 and -2 (migration molecules) and E-cadherin and β-catenin (adhesion molecules) in different stages of prostate cancer progression. A quantitative immunohistochemical study of these molecules was carried out in tissue samples from benign prostatic hyperplasia and prostate carcinoma, with low and high Gleason score, obtained from biopsies archives of the Clinic Hospital of the University of Chile and Dipreca Hospital. Polyclonal specific antibodies and amplification system of estreptavidin-biotin peroxidase and diaminobenzidine were used. Syndecan-1 was uniformly expressed in basolateral membranes of normal epithelium, changing to a granular cytoplasmatic expression pattern in carcinomas. Syndecan-2 was observed mainly in a cytoplasmatic granular pattern, with high immunostaining intensity in areas of low Gleason score. E-cadherin was detected in basolateral membrane of normal epithelia showing decreased expression in high Gleason score samples. β-Catenin was found in cell membranes of normal epithelia changing its distribution toward the nucleus and cytoplasm in carcinoma samples. We concluded that changes in expression and cell distribution of E-cadherin and β-catenin correlated with the progression degree of prostate adenocarcinoma, suggesting a role of these molecules as markers of progression and prognosis. Furthermore, changes in the pattern expression of syndecan-1 and -2 indicate that both molecules may be involved in the EMT and tumor progression of prostate cancer.

DEPARTAMENTO DE CARDIOLOGÍA

FUNDAM CLIN PHARMACOL. 2009 FEB;23(1):81-8.

EFFECTS OF TRAMADOL AND DEXKETOPROFEN ON ANALGESIA AND GASTROINTESTINAL TRANSIT IN MICE.

Miranda HF, Puig MM, Romero MA, **Prieto JC**.

The purpose of the present study was to evaluate the nature of the antinociceptive interaction among dexketoprofen (DEX), a mixed inhibitor of the cyclo-oxygenases, and tramadol (TRAM), a weak opioid with monoaminergic activity that inhibits norepinephrine and serotonin re-uptake. We assessed antinociception in the acetic acid writhing test, the tail flick and the formalin (FT) tests, and gastrointestinal transit (GIT) after the administration of a charcoal meal. The analysis of the interaction was carried out using isobolograms and interaction indexes or the fixed-dose method GIT. The administration of DEX or TRAM individually induced dose-dependent antinociception in all the algesiometric tests. In the three tests, TRAM was between 5.2 (FT, phase I) and 35 times (FT, Phase II) more potent than DEX. When testing combinations at different potency ratios (1 : 1, 1 : 3, 3 : 1), we could demonstrate synergy in all algesiometric tests, only when drugs were combined in a 1 : 1 proportion. Interestingly, the proportion of the drugs in the combination could change the type of interaction from synergy to antagonism. On the inhibition of GIT, a dose-related inhibition was established for TRAM, but not for DEX. Using a fixed-dose protocol, we could demonstrate antagonism between DEX and TRAM on the inhibition of GIT. The results of the present study suggest that a combination of DEX and TRAM in a 1 : 1 proportion could be adequate to use in future clinical trials in humans.

PHARMACOL BIOCHEM BEHAV. 2009 APR;92(2):314-8.

SYNERGISM BETWEEN NSAIDS IN THE OROFACIAL FORMALIN TEST IN MICE.

Miranda HF, Sierralta F, **Prieto JC**.

Opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are used to relieve acute and chronic pain. The purpose of this study was to determine the degree of interaction between dexketoprofen and NSAID examples of COXs inhibitors using the isobolographic analysis in the formalin orofacial test in mice. The drugs, i.p., induced a dose-dependent antinociception with different potencies in both test phases. Combinations of dexketoprofen with naproxen, nimesulide, ibuprofen or paracetamol on the basis of the fixed ratio (1:1) of their ED(50)'s values alone demonstrated synergism in both phases. This is important since the orofacial pain is a test not currently used in mice; the drugs are all analgesic for humans and phase II is representative of inflammatory pain. The synergism was: COX-3>COX-2>COX-1 inhibitors, this is particularly interesting since the inhibitor of COX-3, paracetamol, displayed a robust anti-inflammatory activity in an assay of acute and inflammatory pain that mimics inflammatory pain in humans. In conclusion, the synergism of the dexketoprofen/NSAID combinations may improve this type of therapeutic profile, since with low doses of the components, side effects are not likely to occur, and they may be used in long-term treatments

CAMB Q HEALTHC ETHICS. 2009 SUMMER;18(3):236-40.

DEACTIVATING CARDIAC PACEMAKERS AND IMPLANTABLE CARDIOVERTER DEFIBRILLATORS IN TERMINALLY ILL PATIENTS.

Beca JP, Rosselot E, **Asenjo R,** Anguita V, Quevedo R.

A 68-year-old patient who suffered from gastric cancer diagnosed 8 months earlier presented with multiple peritoneal and hepatic metastasis, despite several rounds of chemo- and radiotherapy. After admission to hospital, his general condition quickly became severely compromised. He was nearly emaciated, despite being on partial parenteral feeding. Four years earlier, due to a cardiac arrhythmia that was refractory to medication, the patient had a cardiac pacemaker (CPM) implanted, regulated to go off at

frequencies of below 70 beats per minute. Given the patient's terminal situation, the team started developing some doubts about the pacemaker's effects during his dying process. The patient had mentioned his intention to donate his pacemaker after his death, but had not asked for its deactivation. The specialists were not sure about the effect of the pacemaker in unnecessarily prolonging the patient's final hour. Nevertheless, they opposed deactivation, which they considered ethically uncertain. The family, who had been initially for the deactivation, decided against it. The patient's condition was progressively deteriorating, as he was falling into a state of sopor and, later, into a coma.

BASIC CLIN PHARMACOL TOXICOL. 2009 MAR;104(3):211-5.

(TTA)N POLYMORPHISM IN 3-HYDROXY-3-METHYLGLUTARYL-COENZYME A AND RESPONSE TO ATORVASTATIN IN CORONARY ARTERY DISEASE PATIENTS.

Noriega V, Pennanen C, Sánchez MP, Chiong M, **Llancaqueo M**, Lavandero S, **Prieto JC.**

3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors have been used clinically for lowering total and low-density lipoprotein cholesterol. Interindividual pharmacological differences observed with this treatment have been attributed to genetic differences. The aim of this study was to assess the association in the low-density lipoprotein cholesterol reduction by atorvastatin and (TTA) n polymorphism in the 3-hydroxy-3-methylglutaryl-coenzyme A reductase gene in patients with coronary artery disease. Changes in total cholesterol levels, triglycerides, high-sensitivity C-reactive protein and free F(2)-isoprostanes were also evaluated. In an open study, patients received 40 mg atorvastatin daily for 8 weeks. Genotyping was done through polymerase chain reaction. The genotype distribution of the 3-hydroxy-3-methylglutaryl-coenzyme A reductase (TTA)n polymorphism was: >10/>10 in 22 out of 64 patients (34%), >10/10 in 14 out of 64 patients (22%) and 10/10 in 28 out of 64 patients (44%). The reduction of low-density lipoprotein cholesterol levels by atorvastatin was not different between allelic variants (TTA)n repeat polymorphism. Reductions in high-sensitivity C-reactive protein were observed in atorvastatin-treated patients with alleles >10/>10 and 10/10. Free F(2)-isoprostanes and total cholesterol were also significantly lower after treatment for all alleles, irrespective of type of polymorphism. In conclusion, the changes induced by atorvastatin treatment on low-density lipoprotein cholesterol, total cholesterol, triglycerides, high-sensitivity C-reactive protein and free F(2)-isoprostane concentrations were not related to the presence of 3-hydroxy-3-methylglutaryl-coenzyme A reductase polymorphism (TTA)n.

DEPARTAMENTO DE CIRUGÍA

ARCH SURG. 2009 OCT;144(10):921-7.

LATE RESULTS OF THE SURGICAL TREATMENT OF 125 PATIENTS WITH SHORT-SEGMENT BARRETT ESOPHAGUS.

Csendes A, Braghetto I, Burdiles P, Smok G, Henríquez A, **Burgos AM.**

HYPOTHESIS: The results of surgical treatment of patients with long-segment Barrett esophagus (BE) have been extensively reported. However, few publications refer to the results of surgery 5 years after the fact among patients with short-segment BE. This study aimed to determine the late results of 3 surgical procedures in patients with short-segment BE by subjective and objective measurements. DESIGN: Prospective, nonrandomized study starting on March 1, 1987, and ending on December 31, 2005. SETTING: A prospective, descriptive study of a group of patients. PATIENTS: A total of 125 patients with short-segment BE underwent 3 operations in different periods: duodenal switch plus highly selective vagotomy and antireflux technique in 31 patients, vagotomy plus partial gastrectomy and Roux-en-Y loop with antireflux surgery in 58 patients, and laparoscopic Nissen fundoplication in 36 patients. MAIN OUTCOME MEASURES: Late subjective and objective outcomes of the 3 different surgical procedures. RESULTS: No operative mortality and only 2 postoperative complications (1.6%) occurred. The regression from intestinal metaplasia to cardiac or oxyntocardiac mucosa occurred in 60.8% to 65.4% of the patients, at a mean time of 39 to 56 months after surgery. Visick grading showed Visick grade I or II in 86.3% to 100.0% of the patients. No progression to low- or high-grade dysplasia or adenocarcinoma occurred. CONCLUSIONS: On the basis of these results, laparoscopic Nissen fundoplication seems to be the surgical option for patients with short-segment BE because it is less invasive, has fewer side effects, and produces good results in the long-term follow-up.

BIOCHIM BIOPHYS ACTA. 2009 NOV;1792(11):1080-6.

ENHANCEMENT IN LIVER SREBP-1C/PPAR-ALPHA RATIO AND STEATOSIS IN OBESE PATIENTS: CORRELATIONS WITH INSULIN RESISTANCE AND N-3 LONG-CHAIN POLYUNSATURATED FATTY ACID DEPLETION.

Pettinelli P, Del Pozo T, Araya J, Rodrigo R, **Araya AV, Smok G, Csendes A, Gutiérrez L**, Rojas J, **Korn O, Maluenda F, Diaz JC**, Rencoret G, **Braghetto I, Castillo J, Poniachik J**, Videla LA.

Sterol receptor element-binding protein-1c (SREBP-1c) and peroxisome proliferator-activated receptor-alpha (PPAR-alpha) mRNA expression was assessed in liver as signaling mechanisms associated with steatosis in obese patients. Liver SREBP-1c and PPAR-alpha mRNA (RT-PCR), fatty acid synthase (FAS) and carnitine palmitoyltransferase-1a (CPT-1a) mRNA (real-time

RT-PCR), and n-3 long-chain polyunsaturated fatty acid (LCPUFA)(GLC) contents, plasma adiponectin levels (RIA), and insulin resistance (IR) evolution (HOMA) were evaluated in 11 obese patients who underwent subtotal gastrectomy with gastro-jejunal anastomosis in Roux-en-Y and 8 non-obese subjects who underwent laparoscopic cholecystectomy (controls). Liver SREBP-1c and FAS mRNA levels were 33% and 70% higher than control values (P<0.05), respectively, whereas those of PPAR-alpha and CPT-1a were 16% and 65% lower (P<0.05), respectively, with a significant 62% enhancement in the SREBP-1c/PPAR-alpha ratio. Liver n-3 LCPUFA levels were 53% lower in obese patients who also showed IR and hipoadiponectinemia over controls (P<0.05). IR negatively correlated with both the hepatic content of n-3 LCPUFA (r=-0.55; P<0.01) and the plasma levels of adiponectin (r=-0.62; P<0.005). Liver SREBP-1c/PPAR-alpha ratio and n-3 LCPUFA showed a negative correlation (r=-0.48; P<0.02) and positive associations with either HOMA (r=0.75; P<0.0001) or serum insulin levels (r=0.69; P<0.001). In conclusion, liver up-regulation of SREBP-1c and down-regulation of PPAR-alpha occur in obese patients, with enhancement in the SREBP-1c/PPAR-alpha ratio associated with n-3 LCPUFA depletion and IR, a condition that may favor lipogenesis over FA oxidation thereby leading to steatosis.

OBES SURG. 2009 NOV;19(11):1515-21.

SCINTIGRAPHIC EVALUATION OF GASTRIC EMPTYING IN OBESE PATIENTS SUBMITTED TO SLEEVE GASTRECTOMY COMPARED TO NORMAL SUBJECTS.

Braghetto I, Davanzo C, **Korn O, Csendes A, Valladares H,** Herrera E, González P, **Papapietro K.**

BACKGROUND: Sleeve gastrectomy (SG) has been accepted as an option for surgical treatment for obesity. This operation could be associated with motor gastric dysfunction and abnormal gastric emptying. The purpose of this prospective study is to present the results of gastric emptying to liquids and solids using scintigraphy in patients who underwent SG compared to normal subjects. METHODS: Twenty obese patients were submitted to laparoscopic SG and were compared to 18 normal subjects. Gastric emptying of liquids and solids was measured by scintigraphic technique. Results were expressed as half time of gastric emptying and the percentage of retention at 20, 30, and 60 min for liquids and at 60, 90, and 120 min for solids. RESULTS: In the group of operated patients, 70% of them (n = 14) presented accelerated emptying for liquids and 75% (n = 15) for solids compared to 22.2% and 27.7%, respectively, in the control group. The half time of gastric emptying (T (1/2)) in patients submitted to SG both for liquids and solids were significantly more accelerated compared to the control group (34.9 +/- 24.6 vs 13.6 +/- 11.9 min for liquids and 78 +/- 15.01 vs 38.3 +/- 18.77 min for solids; p < 0.01). The gastric emptying for liquids expressed as the percentage of retention at 20, 30, and 60 min was 30.0 +/- 0.25%, 15.4 +/- 0.18%, and 5.7 +/- 0.10%, respectively, in operated patients, significantly less than the control subjects (p < 0.001). For solids, the percentage of retention at 60, 90, and 120 min was 56 +/- 28%, 34 +/- 22%, and 12 +/- 8%, respectively, for controls, while it was 25.3 +/- 0.20%, 9 +/- 0.12%, and 3 +/- 0.05%, respectively, in operated patients (p < 001). CONCLUSIONS: Gastric emptying after SG is accelerated either for liquids as well as for solids in the majority of patients. These results could be taken in consideration for the dietary indications after surgery and could play a significant role in the definitive results during the late follow-up.

AM J CLIN NUTR. 2009 SEP;90(3):527-32.

IRON ABSORPTION AND IRON STATUS ARE REDUCED AFTER ROUX-EN-Y GASTRIC BYPASS.

Ruz M, Carrasco F, Rojas P, Codoceo J, Inostroza J, Rebolledo A, Basfi-fer K, **Csendes A, Papapietro K**, Pizarro F, Olivares M, Sian L, Westcott JL, Hambidge KM, Krebs NF.

BACKGROUND: Iron deficiency and iron deficiency anemia are common in patients who undergo gastric bypass. The magnitude of change in iron absorption is not well known. OBJECTIVE: The objective was to evaluate the effects of Roux-en-Y gastric bypass (RYGBP) on iron status and iron absorption at different stages after surgery. We hypothesized that iron absorption would be markedly impaired immediately after surgery and would not improve after such a procedure. DESIGN: Anthropometric, body-composition, dietary, hematologic, and iron-absorption measures were determined in 67 severe and morbidly obese women [mean age: 36.9 +/- 9.8 y; weight: 115.1 +/- 15.6 kg, body mass index (BMI: in kg/m(2)); 45.2 +/- 4.7] who underwent RYGBP. The Roux-en-Y loop length was 125-150 cm. Determinations were carried out before and 6, 12, and 18 mo after surgery. Fifty-one individuals completed all 4 evaluations. RESULTS: The hemoglobin concentration decreased significantly throughout the study (repeated-measures analysis of variance). The percentage of anemic subjects changed from 1.5% at the beginning of the study to 38.8% at 18 mo. The proportion of patients with low serum ferritin increased from 7.5% to 37.3%. The prevalence of iron deficiency anemia was 23.9% at the end of the experimental period. Iron absorption from both a standard diet and from a standard dose of ferrous ascorbate decreased significantly after 6 mo of RYGBP to 32.7% and 40.3% of their initial values, respectively. No further significant modifications were noted. CONCLUSION: Iron absorption is markedly reduced after RYGBP with no further modifications, at least until 18 mo after surgery.

OBES SURG. 2009 SEP;19(9):1262-9.

EVALUATION OF THE RADIOLOGICAL GASTRIC CAPACITY AND EVOLUTION OF THE BMI 2-3 YEARS AFTER SLEEVE GASTRECTOMY.

Braghetto I, Cortes C, Herquiñigo D, **Csendes P,** Rojas A, Mushle M, **Korn O, Valladares H, Csendes A, Maria Burgos A, Papapietro K.**

BACKGROUND: Sleeve gastrectomy is a restrictive procedure for treatment of obese patients with different body mass index (BMI) and presents good results in terms of a reduction of percentage of excess weight loss and BMI. There is no consensus which is the optimal technique regarding to the diameter of the gastric tube, but a capacity of 100-120 ml has been suggested. In this prospective study, we compare the gastric capacity evaluated with barium sulfate or computer-aided tomography (CAT) scan early and 24 months after operation compared to the changes in body weight and BMI reduction in a small group of 15 consecutive patients submitted to sleeve gastrectomy. METHODS: Fifteen successive obese patients submitted to laparoscopic sleeve gastrectomy were included. They were studied in order to measure the residual gastric capacity with barium sulfate and CAT scan early (3 days) and late (2 years) after surgery. RESULTS: The early postoperative gastric volume was 108 +/- 25 ml (80-120 ml) and 116.2 +/- 78.24 assessed with barium sulfate and CAT scan, respectively. The gastric capacity at the late control increased to 250 +/- 85 and 254 +/- 56.8 assessed with the same techniques. However, patients remained stable with a BMI close to 25 without regain of weight at least at the time of observation. CONCLUSIONS: Gastric capacity can increase late after sleeve gastrectomy even after performing a narrow gastric tubulization. It is very important to measure objectively residual gastric volume after sleeve gastrectomy and its eventual increase in order to determine the late clinical results and to indicate eventual strategy for retreatment.

OBES SURG. 2009 DEC;19(12):1672-7.

GASTRIC LEAK AFTER LAPAROSCOPIC-SLEEVE GASTRECTOMY FOR OBESITY.

Burgos AM, Braghetto I, Csendes A, Maluenda F, Korn O, Yarmuch J, Gutierrez L.

BACKGROUND: One of the most serious complications after laparoscopic sleeve gastrectomy (LSG) is gastric leak. Few publications exist concerning the treatment of gastric leak. We sought to determine by way of a prospective study the clinical presentation, postoperative course, and treatment of gastric leak after LSG for obesity. METHODS: From October 2005 to August 2008, 214 patients with different degrees of obesity underwent LSG. During surgery, each patient received saline with methylene blue by way of nasogastric tube and had a drain placed. All patients underwent radiologic study with liquid barium sulphate on postoperative day 3. RESULTS: Seven patients developed gastric leak. Leak in two patients (28.6%) was diagnosed by upper gastrointestinal tract (UGI) study. Two patients had type I leak (28.6%), and five patients had type II leak (71.4%). Four patients underwent reoperation. Three patients were managed medically with enteral or parenteral feeding; the drain was maintained in situ; and collections were drained by percutaneous punctions guided by computed axial tomography. Mean hospital length of stay was 28.8 days, and time to leakage closure was 43 days after surgery. CONCLUSION: Different ways exist to manage gastric leak, depending on the magnitude of the collection and the clinical repercussions. When treatment necessitates reintervention and is performed early, suture repair is more likely to be successful. Leakage closure time will vary.

ANN SURG. 2009 FEB;249(2):189-94.

LATEST RESULTS (12-21 YEARS) OF A PROSPECTIVE RANDOMIZED STUDY COMPARING BILLROTH II AND ROUX-EN-Y ANASTOMOSIS AFTER A PARTIAL GASTRECTOMY PLUS VAGOTOMY IN PATIENTS WITH DUODENAL ULCERS.

Csendes A, Burgos AM, Smok G, Burdiles P, Braghetto I, Díaz JC.

INTRODUCTION: After a partial resection of the stomach, the continuity of the gastrointestinal tract can be restored either by a Billroth II gastrojejunal anastomosis or a Roux-en-Y gastrojejunostomy. Each procedure has its advantages and disadvantages. OBJECTIVE: To determine through a prospective and random clinical trial, the clinical outcome and the endoscopic and histologic alterations of the distal esophagus and the gastric remnant in patients who received a partial distal gastrectomy due to duodenal ulcers and a Billroth II or Roux-en-Y reconstruction. MATERIAL AND METHODS: In this prospective random trial, a total of 75 patients with duodenal ulcers were included. A bilateral selective vagotomy and partial distal gastrectomy were performed in all patients. A Billroth II or Roux-en-Y 60-cm-long loop was randomly used for reconstruction of the gastrointestinal tract. During the latest follow-up clinical evaluation, upper endoscopy and biopsy samples from the distal esophagus and gastric remnant were obtained. RESULTS: There was 1 operative mortality and 6 patients had some morbidity. The average follow-up period was 15.5 years (range, 11-21). Patients with Roux-en-Y gastrojejunostomy were significantly more asymptomatic and had greater Visick I grading than patients with Billroth II reconstruction ($P < 0.001$). In the distal esophagus, endoscopic findings were normal in 90% of the Roux-en-Y group, but only in 51% of the Billroth II group ($P < 0.0009$). Nearly 25% of the latter group had the appearance of a short-segment Barrett esophagus compared with 3% of the Roux-en-Y group ($P < 0.0001$). The gastric remnant endoscopic findings were normal in 100% of the Roux-en-Y group and in 18% of the Billroth II group ($P < 0.02$). Histologic analyses showed similar proportions of normal fundic mucosa and chronic active fundic gastritis. However, chronic atrophic fundic gastritis and intestinal metaplasia were

significantly more frequent after Billroth II reconstruction (P < 0.008). Helicobacter pylorus was present in a similar proportion of patients. CONCLUSIONS: This prospective and random study showed that Roux-en-Y gastrojejunostomy is significantly better than a Billroth II reconstruction in patients with duodenal ulcers, through subjective and objective endoscopic and histologic evaluations during the latest follow-up evaluation.

OBESITY (SILVER SPRING). 2009 MAY;17(5):973-9.

LIVER NF-KAPPAB AND AP-1 DNA BINDING IN OBESE PATIENTS.

Videla LA, Tapia G, Rodrigo R, Pettinelli P, Haim D, Santibáñez C, **Araya AV, Smok G, Csendes A, Gutiérrez L, Rojas J, Castillo J, Korn O, Maluenda F, Díaz JC,** Rencoret G, **Poniachik J.**

Oxidative stress and insulin resistance (IR) are major contributors in the pathogenesis of nonalcoholic fatty liver disease (NAFLD) and in the progression from steatosis to nonalcoholic steatohepatitis (NASH). Our aim was to assess nuclear factor-kappaB (NF-kappaB) and activating protein-1 (AP-1) activation and Toll-like receptor 4 (TLR4) expression as signaling mechanisms related to liver injury in obese NAFLD patients, and examined potential correlations among them, oxidative stress, and IR. Liver NF-kappaB and AP-1 (electromobility shift assay (EMSA)), TLR4 expression (western blot), ferric reducing ability of plasma (FRAP), and IR evolution (HOMA) were evaluated in 17 obese patients who underwent subtotal gastrectomy with gastro-jejunal anastomosis in Roux-en-Y and 10 nonobese subjects who underwent laparoscopic cholecystectomy (controls). Liver NF-kappaB and AP-1 DNA binding were markedly increased in NASH patients (n = 9; P < 0.05) compared to controls, without significant changes in NAFLD patients with steatosis (n = 8), whereas TLR4 expression was comparable between groups. Hepatic NF-kappaB activation was positively correlated with that of AP-1 (r = 0.79; P < 0.0001); both liver NF-kappaB and AP-1 DNA binding were inversely associated with FRAP (r = -0.43 and r = -0.40, respectively; P < 0.05) and directly correlated with HOMA (r = 0.66 and r = 0.62, respectively, P < 0.001). Data presented show enhanced liver activation of the proinflammatory transcription factors NF-kappaB and AP-1 in obese patients with NASH, parameters that are significantly associated to oxidative stress and IR.

OBES SURG. 2009 JUL;19(7):890-3.

INFLAMMATORY RESPONSE MEASURED BY BODY TEMPERATURE, C-REACTIVE PROTEIN AND WHITE BLOOD CELL COUNT 1, 3, AND 5 DAYS AFTER LAPAROTOMIC OR LAPAROSCOPIC GASTRIC BYPASS SURGERY.

Csendes A, Burgos AM, Roizblatt D, Garay C, Bezama P.

BACKGROUND: Morbid obesity is a chronic inflammatory condition due to the production of several cytokines from the adipose tissue. However, what happens with some of these parameters the first days after surgery is unknown. Therefore, the objective of the present study was to determine, through a prospective and descriptive study, the behavior of the C-reactive protein (CRP), the white blood cell count, and the body temperature prior to a gastric bypass and for 5 days afterwards. METHODS: A total of 156 patients with morbid obesity were included in this prospective study. There were 120 women and 36 men, with a mean age of 41 years and a body mass index of 43 kg/m(2). They were submitted either to a laparotomic resectional gastric bypass or to a laparoscopic gastric bypass. Body temperature was measured every 8 h during 5 days. CPR and white blood cells were measured at the first, third, and fifth day after surgery. RESULTS: All patients had a normal postoperative course. Body temperature showed no change. White blood cells increased significantly at the first and third day after surgery but normalized by the fifth day. However, the third day after surgery, laparotomic gastric bypass patients showed a significantly greater increase in the total white blood cell count as well as in segmented neutrophil cells compared to laparoscopic surgery patients. CRP exhibited a similar increase and was more pronounced after a laparotomic approach. CONCLUSION: During the 5 days after gastric bypass, a significant increase in white blood cells and CRP was observed. The increase was significantly greater after a laparotomic bypass compared to the laparoscopic approach.

OBES SURG. 2009 APR;19(4):490-4.

A PROSPECTIVE RANDOMIZED STUDY COMPARING PATIENTS WITH MORBID OBESITY SUBMITTED TO LAPAROTOMIC GASTRIC BYPASS WITH OR WITHOUT OMENTECTOMY.

Csendes A, Maluenda F, Burgos AM.

BACKGROUND: Visceral fat, especially the greater omentum, seems to be an important factor in the development of some metabolic disturbances such as insulin resistance, hyperglycemia, and dyslipidemia. Therefore, we wanted to evaluate the influence of resecting or leaving in situ the greater omentum in a group of patients with morbid obesity. METHODS: Seventy patients with morbid obesity were submitted to laparotomic resectional gastric bypass and an omentectomy was randomly performed in some patients. Body mass index (BMI), serum levels of sugar, insulin, total cholesterol, and triglycerides were determined prior to surgery and followed up on for 2 years afterwards. RESULTS: Two years after surgery, no differences were seen in BMI levels in either group. Blood sugar levels, serum insulin, total cholesterol levels, and serum triglycerides had similar values in both groups. Arterial hypertension had similar behavior. CONCLUSIONS: Based on these results, omentectomy is not justified as part of bariatric surgery. Its theoretical advantages are not reflected in this prospective random trial.

OBES SURG. 2009 MAR;19(3):269-73.

INCIDENCE OF ANASTOMOTIC STRICTURES AFTER GASTRIC BYPASS: A PROSPECTIVE CONSECUTIVE ROUTINE ENDOSCOPIC STUDY 1 MONTH AND 17 MONTHS AFTER SURGERY IN 441 PATIENTS WITH MORBID OBESITY.

Csendes A, Burgos AM, Burdiles P.

BACKGROUND: Anastomotic stricture after gastric bypass for morbid obesity has been reported as the most frequent complication after surgery. The objective of this study is to determine in a prospective and consecutive endoscopic evaluation the true incidence of this complication early and late after gastric bypass. METHODS: A total of 441 morbidly obese patients were included in this prospective study. They were 358 women and 97 men, with a mean age of 41 years and a mean body mass index of 43 kg/m2. In all an endoscopic evaluation was performed 1 month after surgery, which was repeated in 315 patients (71.6%) 17 months after surgery, independent of the presence or not of symptoms. Anastomotic diameter was measured and strictures were classified as: (a) mild, with a diameter of 7 to 9 mm, (b) moderate with a diameter of 5 to 6 mm, and (c) difficult or critical with a diameter equal or less to 4 mm. Two methods of dilatation were employed: the endoscope itself or Savary-Gilliard dilators. Patients were submitted to laparotomic resectional gastric bypass in whom a circular stapler 25 was employed for gastrojejunal anastomosis or to laparoscopic gastric bypass, in whom hand-sewn one layer continuous suture was employed. RESULTS: One month after surgery, 23% of patients after open gastric bypass employing circular stapler 25 presented anastomotic stricture, being 22% of them critical. After laparoscopic gastric bypass employing hand-sewn anastomosis, 36% of the patients presented strictures, being critical 10% (p>0.17). Patients with mild or moderate strictures needed one or two dilatations. Patients with critical strictures needed three to five dilatations. There were no complications associated to dilatation. Moderate and severe strictures were symptomatic; however 29% of patients with mild strictures were asymptomatic. Endoscopy was repeated in 71% of the whole group 17 months after surgery, demonstrating normal anastomosis in all. CONCLUSIONS: Stricture at the gastrojejunal anastomosis after gastric bypass is the commonest complication early after surgery. Near 60% present a mild stricture (with a diameter between 7 and 9 mm), being 28% asymptomatic. This complication is easily treated by endoscopic procedure if it is diagnosed early (3 to 4 weeks) after surgery. Routine endoscopy 1 month after surgery is the only objective scientific way to determine the real true incidence of this complication.

OBES SURG. 2009 JAN;19(1):41-6.

CHANGES IN BONE MINERAL DENSITY, BODY COMPOSITION AND ADIPONECTIN LEVELS IN MORBIDLY OBESE PATIENTS AFTER BARIATRIC SURGERY.

Carrasco F, Ruz M, Rojas P, **Csendes A**, Rebolledo A, Codoceo J, Inostroza J, Basfi-Fer K, **Papapietro K**, Rojas J, Pizarro F, Olivares M.

BACKGROUND: Gastric bypass surgery (GBP) is increasingly used as a treatment option in morbid obesity. Little is known about the effects of this surgery on bone mineral density (BMD) and the underlying mechanisms. To evaluate changes on BMD after GBP and its relation with changes in body composition and serum adiponectin, a longitudinal study in morbid obese subjects was conducted. METHODS: Forty-two women (BMI 45.0 +/- 4.3 kg/m(2); 37.7 +/- 9.6 years) were studied before surgery and 6 and 12 months after GBP. Percentage of body fat (%BF), fat-free mass (FFM), and BMD were measured by dual-energy X-ray absorptiometry and serum adiponectin levels by RIA. RESULTS: Twelve months after, GBP weight was decreased by 34.4 +/- 6.5% and excess weight loss was 68.2 +/- 12.8%. Significant reduction ($p < 0.001$) in total BMD (-3.0 +/- 2.1%), spine BMD (-7.4 +/- 6.8%) and hip BMD (-10.5 +/- 5.6%) were observed. Adiponectin concentration increased from 11.4 +/- 0.7 mg/L before surgery to 15.7 +/- 0.7 and 19.8 +/- 1.0 at the sixth and twelfth month after GBP, respectively ($p < 0.001$). Thirty-seven percent of the variation in total BMD could be explained by baseline weight, initial BMD, BF reduction, and adiponectin at the twelfth month ($r (2) = 0.373$; $p < 0.001$). Adiponectin at the twelfth month had a significant and positive correlation with the reduction of BMD, unrelated to baseline and variation in body composition parameters (adjusted correlation coefficient: $r = 0.36$). CONCLUSION: GBP induces a significant BMD loss related with changes in body composition, although some metabolic mediators, such as adiponectin increase, may have an independent action on BMD which deserves further study.

OBES SURG. 2009 FEB;19(2):135-8.

INCIDENCE OF MARGINAL ULCER 1 MONTH AND 1 TO 2 YEARS AFTER GASTRIC BYPASS: A PROSPECTIVE CONSECUTIVE ENDOSCOPIC EVALUATION OF 442 PATIENTS WITH MORBID OBESITY.

Csendes A, Burgos AM, Altuve J, Bonacic S.

BACKGROUND: Marginal ulcer (MU) is an occasional complication after gastric bypass. We studied the incidence of this complication by a prospective routine endoscopic evaluation. METHODS: 441 morbidly obese patients were studied prospectively. There were 358 women and 97 men, with mean age 41 years and mean BMI 43 kg/m(2). An endoscopic evaluation was performed in all 1 month after surgery, which was repeated in 315 patients (71%) 17 months after surgery, independent of the presence or absence of symptoms. Patients were submitted either to laparotomic resectional gastric bypass (360 patients), employing a circularstapler-25 or to laparoscopic gastric bypass (81 patients), in whom a hand-sewn anastomosis was performed. RESULTS: One month after surgery, 15 patients (4.1%) of the 360 laparotomic gastric bypass and 10 (12.3%) of the 81 laparoscopic gastric bypass presented an “early”

marginal ulcer (p < 0.02). Seven patients among the 25 with MU were asymptomatic (28%). Endoscopy was repeated 17 months after surgery. Among 290 patients with no early MU, one patient (0.3%) presented a "late" MU 13 months after surgery. From the 25 patients with "early" MU, one patient (4%) presented a "late" MU. All these patients were treated with PPIs. CONCLUSION: By performing prospective routine endoscopic study 1 month and 17 months after gastric bypass, two different behaviors were seen regarding the appearance MU: (a) "early" MU, 1 month after surgery in mean 6% and (b) "late" MU, in a very small proportion of patients (0.6%). Among patients with "early" MU, those who had undergone resectional gastric bypass showed significantly less ulcers compared to those patients in whom the excluded distal gastric segment had been left in situ. The operative method may play a significant role in the pathogenesis of MU after gastric bypass.

TOXICON. 2009 FEB;53(2):206-13.

EVIDENCE OF IN VITRO GLUCURONIDATION AND ENZYMATIC TRANSFORMATION OF PARALYTIC SHELLFISH TOXINS BY HEALTHY HUMAN LIVER MICROSOMES FRACTION.

García C, Rodríguez-Navarro A, **Díaz JC**, Torres R, Lagos N.

Paralytic Shellfish Toxins (PST) are endemic components found in filter bivalves in Southern Chile. Post-mortems analysis of fluid and tissue samples has shown biotransformation of PST in humans. The Gonyautoxin 3 (GTX3) and Gonyautoxin 2 (GTX2) are the major PST components in the toxin profile found in Chilean shellfish extracts, being as much as 65% of the total content of PST in filter bivalves. Therefore, they are the major accountable components of the human intoxication by shellfish consumption. The aim of this study is to show in vitro glucuronidation and biotransformation of GTX3 and GTX2 when they are incubated with microsomal fraction isolated from healthy human livers. Microsomes fractions isolated from human livers were incubated with GTX3 and GTX2 purified from contaminated mussels. After different incubation times, incubated samples were extracted and analyzed by HPLC with fluorescent on line detection and HPLC-MS analysis. The results revealed that GTX3 and GTX2, only when they were incubated with microsomal fraction and appropriated cofactors, showed to be enzymatic transformed in vitro. The glucuronidation of GTX3 and GTX2 followed typical Michaelis-Menten kinetics, resulting in apparent kinetic parameters of Km=39.4+/-0.24 microM and Vmax=6.0x10(-3) pmol/min/mg protein. In addition, the microsomes fraction also oxidized GTX3 and GTX2 into Gonyautoxin 4 (GTX 4) and Gonyautoxin 1 (GTX 1) resulting in 0.339x10(-3) pmol/min/mg protein. In conclusion, this study reports oxidation and glucuronidation of GTX3 and GTX2 when they are incubated with human liver microsomal fraction. The metabolism occurs via a glucuronidation reaction, the basis first step of biotransformation in human liver. Also it is showed that GTX4 and GTX1 came by biotransformation from GTX3 and GTX2 in humans. This data confirm human biotransformation found in human post-mortem fluid and tissue samples described previously. This data is the first evidence of in vitro glucuronidation of PST, given a metabolic pathway of detoxification and excretion of PST in human.

J PLAST RECONSTR AESTHET SURG. 2009 AUG 8.

RECENT DEVELOPMENTS IN THE ABILITY TO PREDICT AND MODIFY BREAST CANCER RISK.

Prado A, Andrades P, Parada F.

The identification of women at higher risk for breast cancer is a matter of public health and anyone who participates in any treatment modality of this condition (this includes the plastic surgeon) should be aware of the tools and predictive models of breast cancer. Screening for breast cancer in the community, and probably during the daily plastic surgery consultation, until recently, was limited to decisions about when to initiate a mammography study. New developments that predict and modify breast cancer risk must be clearly understood by our specialty through identification of women at higher risk for breast cancer and be familiar with the current issues related to screening and risk-reduction measures. In this review, we discuss current knowledge regarding the recent data of breast cancer risk, screening strategies for high-risk women and medical and surgical approaches to reduce breast cancer risk. Patients with breast cancer belong to one of three groups: Tools for breast cancer risk assessment include the Gail and Claus model, genetic screening,BRCAPRO and others that are evaluated in this review.

J PLAST RECONSTR AESTHET SURG. 2009 NOV;62(11):1453-8.

PERIOPERATIVE THROMBOELASTOGRAPHY ANALYSIS DURING SUCTION-ASSISTED LIPECTOMY: A PROSPECTIVE COHORT STUDY.

Prado A, Andrades P, Danilla S, Parada F.

OBJECTIVE: The purpose of this study was to prospectively investigate coagulation during suction-assisted lipoplasty (SAL) and to compare it to other plastic surgery where no SAL was used, with the aid of a computerised thromboelastograph coagulation analyser (TEG). METHODS: A prospective cohort study enrolled 50 pure SAL patients and 50 patients presenting for other aesthetic plastic surgery operations, without the need of liposuction. TEG evaluates in real time the competency of the blood clot in samples that are studied under a low shear environment resembling venous flow. Six thromboelastographic measurements were performed in each patient: one preoperative, two intraoperative at the middle and end of the surgery and three postoperative at 60, 90

minutes and 24 hours. All the patients also had standard pre- and postoperative coagulation studies. RESULTS: R (time of clot to form) and K (time or speed the clot takes to be firm) were shorter in the SAL group vs control (P<0.001). Angle (growth and stranding process of fibrin) and MA (dynamic properties of the platelets and the final strength and elasticity of the fibrin clot) were greater in SAL vs control (P<0.001). None of the cases had pre- or postoperative coagulation study abnormalities. CONCLUSIONS: TEG analysis demonstrates that SAL patients have decreased initial clotting time, decreased time to full clot formation, increased pro-coagulability state, and increased clot rigidity. The clot lysis time was not different between the studied groups.

PLAST RECONSTR SURG. 2009 OCT;124(4):1285-93.

LATERAL ORBICULARIS OCULI MUSCLE PLASTY IN CONJUNCTION WITH FACE LIFTING FOR PERIORBITAL REJUVENATION.

Cabbabe SW, **Andrades P**, Vasconez LO.

BACKGROUND: The purpose of this study was to evaluate the lateral orbicularis oculi muscle plasty as an alternative periorbital rejuvenation technique during face lift. METHODS: The authors conducted a retrospective review of patients who underwent face lifts between 2004 and 2007. Postoperative follow-up, complications, aesthetic outcome, and patient satisfaction were recorded. The patients were further divided into four groups for the analysis: lateral orbicularis oculi muscle plasty with lower blepharoplasty (group 1), lower blepharoplasty without lateral orbicularis oculi muscle plasty (group 2), lateral orbicularis oculi muscle plasty without lower blepharoplasty (group 3), and neither lateral orbicularis oculi muscle plasty nor lower blepharoplasty (group 4). RESULTS: A total of 76 patients were identified as having had a midface lift with or without lateral orbicularis oculi muscle plasty in the study period. Sixty-eight percent of the patients had a lateral orbicularis oculi muscle plasty procedure. Group 3 showed the lowest complication rate followed by group 4, but there were no statistical differences in complication rates among the study groups. The higher aesthetic result and patient satisfaction were obtained by groups 3 and 4 ($p < 0.01$). Group 2 had the highest complication rate and lowest overall outcomes. CONCLUSION: The authors have been able to demonstrate that lateral orbicularis oculi muscle plasty is a safe technique that may be considered a good alternative for periorbital rejuvenation and may help in avoiding lower lid incisions or extensive dissections during face lifting in some cases.

J ORAL MAXILLOFAC SURG. 2009 NOV;67(11):2404-11.

DEGREES OF TOLERANCE IN POST-TRAUMATIC ORBITAL VOLUME CORRECTION: THE ROLE OF PREFABRICATED MESH.

Andrades P, Hernández D, Falguera MI, Millán JM, Heredero S, Gutiérrez R, Sánchez-Aniceto G.

PURPOSE: To identify factors influencing the volumetric correction of orbital fractures, and evaluate the use of prefabricated titanium mesh in their repair. MATERIALS AND METHODS: We included patients with unilateral orbital fractures and floor or medial-wall defects, subsequently reconstructed with titanium mesh, and subject to adequate follow-up with multislice, digitalized computed tomography (CT) images. Medical records were reviewed, and demographics, operative details, and postoperative course were recorded as prognostic variables. Moreover, orbital volume, apex-to-globe distance, and orbital rim area were measured using postoperative CT. Univariate analysis and a multiple-regression model were used to identify associated factors. RESULTS: A total of 32 patients fulfilled the inclusion criteria. Postoperative clinical evaluation and CT images were obtained in a mean +/- SD of 12.3 +/- 7.2 months after surgery. Clinically, 20 patients were considered normal (63%), and 12 manifested some ocular dystopia (37%). On postoperative CT, the mesh was in good position in 44% of cases, and in an insufficient position in 56% of cases. There was a significant difference between fractured and normal orbits in relation to orbital volume and apex-globe distance. Clinical evaluation significantly correlated with CT mesh placement, but there was no correlation between clinical evaluation and any of the variables measured on CT. The most important factors influencing postoperative orbital volume correction were type of fracture, affected walls, and use of prefabricated mesh. CONCLUSION: Volumetric and lineal symmetry between fractured and normal orbits are very difficult to achieve. In this study, postoperative CT measurements did not correlate with subjective clinical assessment. The clinical-radiological disagreement may be explained by measurement accuracy problems, clinical bias, or normal differences between orbits. The most important identified modifiable factor was the use of prefabricated mesh.

PLAST RECONSTR SURG. 2009 JUL;124(1):134-43.

LIPOSUCTION AND LIPOINJECTION TREATMENT FOR CONGENITAL AND ACQUIRED LIPODYSTROPHIES IN CHILDREN.

Giugliano C, Benitez S, Wisnia P, Sorolla JP, Acosta S, **Andrades P.**

BACKGROUND: The purpose of this clinical study was to establish liposuction and lipoinjection as a noncosmetic procedure in children to correct lipodystrophies. METHODS: Liposuction, fat injection, or a combination of both was performed on 30 patients between 1994 and 2006 at Roberto del Rio Hospital or Clinica Alemana, Santiago, Chile. Liposuction was indicated in patients with excessive amounts of fatty tissue or tumor-like swelling. Combined liposuction and lipoinjection was performed on patients with deficit and excess in soft tissues. Lipoinjection was used for patients with soft-tissue insufficiencies. Samples of fat obtained

by liposuction were submitted to histopathologic examination. Traditional tumescent technique was used for liposuction. The supernatant obtained by simple filtration was used for fat injection. Short- and long-term postoperative follow-up included registration of complications and assessment of aesthetic and functional outcome. The kappa test was used for statistical analysis. RESULTS: Thirty patients, nine boys and 21 girls, were operated on, with an average age of 11 years (range, 4 to 17 years). A total of 43 procedures were performed: 27 liposuctions, 10 lipoinjections, and six combined procedures. Average hospital stay was 1.1 days. Of a total 20 patients who underwent liposuction, six required revision. Histopathologic study showed 19 lipomatoses and one lipoblastomatosis. Cosmetic outcomes based on Strasser scale were as follows: six excellent, 19 good, four mediocre, and one poor. CONCLUSIONS: Liposuction and lipoinjection as sole or combined procedures are safe methods for the pediatric population. They are well tolerated, with a low rate of complications and satisfactory aesthetic results.

J CRANIOFAC SURG. 2009 JUL;20(4):1154-8.

SAFETY PROFILE OF WIRE OSTEOSYNTHESIS IN CRANIOSYNOSTOSIS SURGERY.

Thurston TE, **Andrades P,** Phillips RA, Ray PD, Grant JH 3rd.

With the advent of resorbable systems, most surgeons have stopped using wires for craniofacial fixation. Although numerous large retrospective reports regarding craniofacial surgery have been published, no documentation exists regarding the disadvantages or complications associated with wires. We review our experience with 47 consecutive patients with bicoronal and unicoronal craniosynostosis where wire osteosynthesis alone was used. Nine patients (19.1%) developed wire-related complications, but only 5 patients (10.6%) required reoperations. No other complications were observed including growth restrictions, implant migration, or interference with radiographic imaging. These results are comparable to those reported in the literature for other fixation systems and demonstrate that wires are a safe means of fixation of the cranial vault in infancy.

J PLAST RECONSTR AESTHET SURG. 2009 JUL;62(7):E222-4.

DEEP DOPAMINE EXTRAVASATION INJURY: A CASE REPORT.

Phillips RA, **Andrades P**, Grant JH, Ray PD.

We report the case of a 3-month-old girl with Down's syndrome, who sustained a deep and massive extravasation of dopamine, resulting in segmented, full-thickness skin necrosis and transient brachial plexus palsy of her left upper extremity. The patient was managed conservatively, including wound care, de-bridement of necrotic tissue, secondary wound healing and intensive physical therapy. The patient showed a satisfactory outcome with complete secondary closure of her wounds and full brachial plexus recovery after 1 year of follow-up. The mechanism of action of dopamine in the deep soft tissue, the difficulties of an adequate diagnosis of a deep dopamine extravasation and alternative treatments are presented in this article.

MICROSURGERY. 2009;29(3):171-7.

INDICATIONS AND OUTCOMES OF DOUBLE FREE FLAPS IN HEAD AND NECK RECONSTRUCTION.

Andrades P, Bohannon IA, Baranano CF, Wax MK, Rosenthal E.

OBJECTIVE: This study describes the clinical setting and operative outcomes for simultaneous double free flap treatment of extensive composite head and neck cancers. METHODS: A retrospective review at two tertiary referral centers was performed. Patient demographics, cancer characteristics, reconstruction methods, and postoperative course were recorded. All patients were assessed for diet, speech, esthetics, socialization, and satisfaction using specific evaluation scales. RESULTS: A total of 30 patients underwent double free flap reconstruction between 2001 and 2007. There were 19 men and 11 women, mean age of 62 years (range, 42-79). Comorbidities were present in 67% of the cases and 70% smoked. Most frequently the cancer was a squamous cell carcinoma (90%), in advanced stage (87%), and recurrent (67%), affecting the oral cavity (43%), larynx (23%) or pharynx (20%). The fibula osteoseptocutaneous/radial forearm fasciocutaneous flap combination was most commonly used (n = 13), followed by the jejunum-radial forearm flap (n = 10). Three flaps required early anastomosis revision and only two partial flap losses were observed. In 11 cases, there was a severe recipient site complication: wound dehiscence (n = 3), oral incompetence (n = 4), fistula (n = 2), and stenosis (n = 2). Two patients died in the postoperative period due to medical problems (7%). The mean follow up was 15.3 months. Patient satisfaction was poor to moderate and the overall functional evaluation score was low. CONCLUSIONS: Double free flaps for one-stage reconstruction of extensive head and neck defects should be used in selected cases. Although a reliable procedure, immediate postoperative morbidity and mortality is high, and the long-term functional and esthetic results are modest. Realistic outcomes should be discussed with patients during planning and consent.

BURNS. 2009 NOV;35(7):956-61.

METHODOLOGICAL QUALITY OF RANDOMISED CONTROLLED TRIALS IN BURNS CARE. A SYSTEMATIC REVIEW.

Danilla S, Wasiak J, Searle S, Arriagada C, Pedreros C, Cleland H, Spinks A.

OBJECTIVE: To evaluate the methodological quality of published randomised controlled trials (RCTs) in burn care treatment and management. METHODS: Using a predetermined search strategy we searched Ovid MEDLINE (1950 to January 2008) database to identify all English RCTs related to burn care. Full text studies identified were reviewed for key demographic and methodological characteristics. Methodological trial quality was assessed using the Jadad scale. RESULTS: A total of 257 studies involving 14,535 patients met the inclusion criteria. The median Jadad score was 2 (out of a best possible score of 5). Information was given in the introduction and discussion sections of most RCTs, although insufficient detail was provided on randomisation, allocation concealment, and blinding. The number of RCTs increased between 1950 and 2008 (Spearman's rho=0.6129, P<0.001), although the reporting quality did not improve over the same time period (P=0.1896) and was better in RCTs with larger sample sizes (median Jadad score, 4 vs. 2 points, P<0.0001). Methodological quality did not correlate with journal impact factor (P=0.2371). CONCLUSIONS: The reporting standards of RCTs are highly variable and less than optimal in most cases. The advent of evidence-based medicine heralds a new approach to burns care and systematic steps are needed to improve the quality of RCTs in this field. Identifying and reviewing the existing number of RCTs not only highlights the need for burn clinicians to conduct more trials, but may also encourage burn health clinicians to consider the importance of conducting trials that follow appropriate, evidence-based standards.

ANN PLAST SURG. 2009 DEC;63(6):659-60.

DOUBLE NEGATIVE PRESSURE FOR SEROMA TREATMENT IN TROCANTERIC AREA.

Calderón WL, Llanos S, Leniz P, **Danilla S**, Vielma R, Calderón D.

We report the use of topic negative pressure for seromas resulting from mobilization of tensor fascia lata miocutaneous flap in the trochanteric areas for pressure sores. In 5 consecutive patients we successfully treated seroma with the use of external and internal topic subatmospheric pressure.

J SURG ONCOL. 2009 DEC 1;100(7):589-93.

EARLY GALLBLADDER CANCER: IS FURTHER TREATMENT NECESSARY?

De Aretxabala X, Roa I, Hepp J, **Maluenda F**, Mordojovich G, Leon J, Roa JC.

BACKGROUND AND OBJECTIVES: The goal of this study was to evaluate a series of patients with early gallbladder cancer, focusing on the selection of treatment and the role of Rokitansky Aschoff sinus infiltration. METHODS: We performed a retrospective analysis of a prospective series of 371 patients with gallbladder cancer. Specimens were reviewed by an independent pathologist to confirm the diagnosis and depth of infiltration and to evaluate the presence of Rokitansky Aschoff sinus involvement. RESULTS: Forty-nine and 45 patients with muscular (pT1b) and mucosal (pT1a) infiltration gallbladder cancer tumors were studied respectively. Simple cholecystectomy was the treatment in all patients, with the exception of 11 patients who underwent further surgery. Rokitansky Aschoff sinus invasion was seen in seven patients with mucosa (pT1a) and three with muscular (pT1b) compromise. The 5-year survival rates of patients with muscular (pT1b) and mucosal (pT1a) infiltration were 87.6% and 86.4%, respectively. Patients with Rokitansky Aschoff involvement had a lower survival rate than those with no involvement in both categories. CONCLUSIONS: Early gallbladder cancer is associated with a favorable prognosis and cholecystectomy should be the standard treatment. Despite some patients having a worse prognosis, there are no data to support more aggressive treatment.

TOXICON. 2009 FEB;53(2):206-13.

EVIDENCE OF IN VITRO GLUCURONIDATION AND ENZYMATIC TRANSFORMATION OF PARALYTIC SHELLFISH TOXINS BY HEALTHY HUMAN LIVER MICROSOMES FRACTION.

García C, Rodríguez-Navarro A, **Díaz JC,** Torres R, Lagos N.

Paralytic Shellfish Toxins (PST) are endemic components found in filter bivalves in Southern Chile. Post-mortems analysis of fluid and tissue samples has shown biotransformation of PST in humans. The Gonyautoxin 3 (GTX3) and Gonyautoxin 2 (GTX2) are the major PST components in the toxin profile found in Chilean shellfish extracts, being as much as 65% of the total content of PST in filter bivalves. Therefore, they are the major accountable components of the human intoxication by shellfish consumption. The aim of this study is to show in vitro glucuronidation and biotransformation of GTX3 and GTX2 when they are incubated with microsomal fraction isolated from healthy human livers. Microsomes fractions isolated from human livers were incubated with GTX3 and GTX2 purified from contaminated mussels. After different incubation times, incubated samples were extracted and analyzed by HPLC with fluorescent on line detection and HPLC-MS analysis. The results revealed that GTX3 and GTX2, only when they were incubated with microsomal fraction and appropriated cofactors, showed to be enzymatic transformed in vitro.

The glucuronidation of GTX3 and GTX2 followed typical Michaelis-Menten kinetics, resulting in apparent kinetic parameters of Km=39.4+/-0.24 microM and Vmax=6.0x10(-3) pmol/min/mg protein. In addition, the microsomes fraction also oxidized GTX3 and GTX2 into Gonyautoxin 4 (GTX 4) and Gonyautoxin 1 (GTX 1) resulting in 0.339x10(-3) pmol/min/mg protein. In conclusion, this study reports oxidation and glucuronidation of GTX3 and GTX2 when they are incubated with human liver microsomal fraction. The metabolism occurs via a glucuronidation reaction, the basis first step of biotransformation in human liver. Also it is showed that GTX4 and GTX1 came by biotransformation from GTX3 and GTX2 in humans. This data confirm human biotransformation found in human post-mortem fluid and tissue samples described previously. This data is the first evidence of in vitro glucuronidation of PST, given a metabolic pathway of detoxification and excretion of PST in human.

MOL BIOL CELL. 2009 APR;20(8):2297-310.
CAVEOLIN-1-MEDIATED SUPPRESSION OF CYCLOOXYGENASE-2 VIA A BETA-CATENIN-TCF/LEF-DEPENDENT TRANSCRIPTIONAL MECHANISM REDUCED PROSTAGLANDIN E2 PRODUCTION AND SURVIVIN EXPRESSION.
Rodríguez DA, Tapia JC, **Fernández JG**, Torres VA, Muñoz N, Galleguillos D, Leyton L, Quest AF.

Augmented expression of cyclooxygenase-2 (COX-2) and enhanced production of prostaglandin E(2) (PGE(2)) are associated with increased tumor cell survival and malignancy. Caveolin-1 is a scaffold protein that has been proposed to function as a tumor suppressor in human cancer cells, although mechanisms underlying this ability remain controversial. Intriguingly, the possibility that caveolin-1 regulates the expression of COX-2 has not been explored. Here we show that augmented caveolin-1 expression in cells with low basal levels of this protein, such as human colon cancer (HT29, DLD-1), breast cancer (ZR75), and embryonic kidney (HEK293T) cells reduced COX-2 mRNA and protein levels and beta-catenin-Tcf/Lef and COX-2 gene reporter activity, as well as the production of PGE(2) and cell proliferation. Moreover, COX-2 overexpression or PGE(2) supplementation increased levels of the inhibitor of apoptosis protein survivin by a transcriptional mechanism, as determined by PCR analysis, survivin gene reporter assays and Western blotting. Furthermore, addition of PGE(2) to the medium prevented effects attributed to caveolin-1-mediated inhibition of beta-catenin-Tcf/Lef-dependent transcription. Finally, PGE(2) reduced the coimmunoprecipitation of caveolin-1 with beta-catenin and their colocalization at the plasma membrane. Thus, by reducing COX-2 expression, caveolin-1 interrupts a feedback amplification loop involving PGE(2)-induced signaling events linked to beta-catenin/Tcf/Lef-dependent transcription of tumor survival genes including cox-2 itself and survivin.

TRANSPLANT PROC. 2009 NOV;41(9):3879-83.
ALLOTRANSPLANT OF MICROENCAPSULATED PARATHYROID TISSUE IN SEVERE POSTSURGICAL HYPOPARATHYROIDISM: A CASE REPORT.
Cabané P, Gac P, Amat J, Pineda P, Rossi R, Caviedes R, Caviedes P.

The last therapeutic alternative in severe postsurgical hypoparathyroidism is allotransplantation of microencapsulated parathyroid cells. With this technique, it is possible to implant cells or tissue of parathyroid origin to replace them in such patients, without immusupression. We report an allotransplant of parathyroid tissue in a patient with continous endovenous requirement of calcium to survive. The microencapsulation was carried out with a commercial sodium alginate. We implant 23 microspheres in the nondominant forearm and 40 microspheres in the leg in a second attempt. In this article, we show functionality of the graft for at least 20 months without requirement of endovenous calcium. We report this procedure as a therapeutical alternative in severe hypoparathyroidism.

DEPARTAMENTO DE DERMATOLOGÍA

J ULTRASOUND MED. 2009 JUN;28(6):787-93.
SONOGRAPHY OF PLANTAR WARTS: ROLE IN DIAGNOSIS AND TREATMENT.
Wortsman X, **Sazunic I**, Jemec GB.

OBJECTIVE: The purpose of this presentation is to show the sonographic morphologic characteristics of plantar warts and the scope of sonography in the treatment of these lesions. METHODS: We retrospectively reviewed 27 sonographic examinations of the plantar region; 17 corresponded to plantar warts diagnosed by dermatologists in which the diagnoses were medically derived from sonographic examinations after failure of their treatments. The remaining group consisted of 10 healthy individuals. Sonograms were compared with standard histologic findings. RESULTS: The sonographic features of normal plantar skin and plantar warts are described, including the shape, echogenicity, pattern of growth, involvement of skin layers, and blood flow in the lesions. CONCLUSIONS: Sonography may be considered as reliable support for plantar wart diagnosis and may have a role in the evaluation of plantar wart treatment modalities, allowing monitoring of therapeutic responses, especially in recurrent and difficult cases with persistent symptoms such as pain

J AM ACAD DERMATOL. 2009 SEP;61(3):512-5.
UNCOMBABLE HAIR SYNDROME.
Calderón P, Otberg N, Shapiro J.

Uncombable hair syndrome is a relatively rare anomaly of the hair shaft, with less than 100 cases reported to date, that results in a disorganized, unruly hair pattern that is impossible to comb flat. The characteristic longitudinal grooves along the hair shaft, along with the triangular or kidney-shaped cross section allows this condition to be diagnosed microscopically. The majority of cases are inherited in an autosomal-dominant manner with either complete or incomplete penetrance. There is no definitive treatment, and most cases improve with the onset of puberty.

INT J DERMATOL. 2009 AUG;48(8):830-3.
HIGH-RESOLUTION COLOR DOPPLER ULTRASOUND OF A CALIBER-PERSISTENT ARTERY OF THE LIP, A SIMULATOR VARIANT OF DERMATOLOGIC DISEASE: CASE REPORT AND SONOGRAPHIC FINDINGS.
Wortsman X, **Calderón P,** Arellano J, Orellana Y.

BACKGROUND: Caliber-persistent labial artery (CPLA) is a vascular anomaly in which a primary artery penetrates the submucosa without caliber loss. It presents as an asymptomatic papular lesion, usually on the lower lip, which may be misdiagnosed as a malignant skin tumor and can cause severe bleeding during biopsy or surgery. Development of new high-resolution ultrasound equipment has improved its observation. AIM: This study was undertaken to assess the scope of ultrasound for the diagnosis of CPLA. METHODS: We report a case of a 65-year-old woman with a nodule involving the lower lip, initially misdiagnosed as a malignant skin tumor. Diagnosis was confirmed by high-resolution color Doppler ultrasound using a compact linear probe that generates frequencies of 7-15 MHz. RESULTS: The clinical presentation of the lesion, ultrasound technique, and sonographic findings are described. A current literature review of CPLA diagnosis was performed. Clinical and sonographic images are given as examples. CONCLUSIONS: High-resolution color Doppler ultrasound is a reliable noninvasive technique for CPLA diagnosis. It allows direct visualization of this vascular variant in real time without the use of an intravenous contrast agent. It may avoid surgical complications and help in the differential diagnosis. Newer high-resolution equipment allows a clear definition of the cutaneous and muscular layers, as well as the vascularity of the lips

DEPARTAMENTO DE MEDICINA

ENDOCRINOLOGÍA

BIOCHIM BIOPHYS ACTA. 2009 NOV;1792(11):1080-6.
ENHANCEMENT IN LIVER SREBP-1C/PPAR-ALPHA RATIO AND STEATOSIS IN OBESE PATIENTS: CORRELATIONS WITH INSULIN RESISTANCE AND N-3 LONG-CHAIN POLYUNSATURATED FATTY ACID DEPLETION.
Pettinelli P, Del Pozo T, Araya J, Rodrigo R, **Araya AV, Smok G, Csendes A**, Gutierrez L, Rojas J, **Korn O, Maluenda F, Diaz JC**, Rencoret G, **Braghetto I, Castillo J, Poniachik J**, Videla LA.

Sterol receptor element-binding protein-1c (SREBP-1c) and peroxisome proliferator-activated receptor-alpha (PPAR-alpha) mRNA expression was assessed in liver as signaling mechanisms associated with steatosis in obese patients. Liver SREBP-1c and PPAR-alpha mRNA (RT-PCR), fatty acid synthase (FAS) and carnitine palmitoyltransferase-1a (CPT-1a) mRNA (real-time RT-PCR), and n-3 long-chain polyunsaturated fatty acid (LCPUFA)(GLC) contents, plasma adiponectin levels (RIA), and insulin resistance (IR) evolution (HOMA) were evaluated in 11 obese patients who underwent subtotal gastrectomy with gastro-jejunal anastomosis in Roux-en-Y and 8 non-obese subjects who underwent laparoscopic cholecystectomy (controls). Liver SREBP-1c and FAS mRNA levels were 33% and 70% higher than control values ($P<0.05$), respectively, whereas those of PPAR-alpha and CPT-1a were 16% and 65% lower ($P<0.05$), respectively, with a significant 62% enhancement in the SREBP-1c/PPAR-alpha ratio. Liver n-3 LCPUFA levels were 53% lower in obese patients who also showed IR and hipoadiponectinemia over controls ($P<0.05$). IR negatively correlated with both the hepatic content of n-3 LCPUFA ($r=-0.55$; $P<0.01$) and the plasma levels of adiponectin ($r=-0.62$; $P<0.005$). Liver SREBP-1c/PPAR-alpha ratio and n-3 LCPUFA showed a negative correlation ($r=-0.48$; $P<0.02$) and positive associations with either HOMA ($r=0.75$; $P<0.0001$) or serum insulin levels ($r=0.69$; $P<0.001$). In conclusion, liver up-regulation of SREBP-1c and down-regulation of PPAR-alpha occur in obese patients, with enhancement in the SREBP-1c/PPAR-alpha ratio associated with n-3 LCPUFA depletion and IR, a condition that may favor lipogenesis over FA oxidation thereby leading to steatosis.

GASTROENTEROLOGÍA

J MED VIROL. 2009 NOV;81(11):1887-94.

DIVERSITY OF HEPATITIS B AND C VIRUSES IN CHILE.

Di Lello FA, Piñeiro Y Leone FG, **Muñoz G**, Campos RH.

Although there is a low prevalence rate (around 1% of the population) of infection with hepatitis B virus (HBV) and hepatitis C virus (HCV) in Chile, little is known about the diversity and molecular characteristics of the circulating viruses. In the present study, 40 HBV and 57 HCV samples from Santiago City, Chile, were examined. The phylogenetic analysis of HBV samples showed the autochthonous genotype F as the most represented genotype in the study (67.5%), while genotypes A, B, C, and D were less frequent (7.5%, 5%, 7.5%, and 12.5%, respectively). The frequency of circulation of HBV genotypes observed is in accordance with the genetic background of the Chilean population. Most of the HCV samples tested belonged to subtype 1b (82%). The coalescent analysis conducted for both the NS5A and NS5B regions of the HCV strains showed similar population growth rates, with a most recent common ancestor estimated to date between 1893 and 1901. This result may indicate that genotype 1b strains circulating in Chile have epidemiological features similar to those described for HCV genotype 1b in Brazil and the United States. However, the most recent common ancestor for Chile is older than that reported recently for genotype 1b in Argentina.

BRAZ J MED BIOL RES. 2009 DEC;42(12):1203-9.

DETECTION OF PATIENTS WITH FUNCTIONAL DYSPEPSIA USING WAVELET TRANSFORM APPLIED TO THEIR ELECTROGASTROGRAM.

Chacón M, Curilem G, Acuña G, Defilippi C, **Madrid AM**, Jara S.

The aim of the present study was to develop a classifier able to discriminate between healthy controls and dyspeptic patients by analysis of their electrogastrograms. Fifty-six electrogastrograms were analyzed, corresponding to 42 dyspeptic patients and 14 healthy controls. The original signals were subsampled, filtered and divided into the pre-, post-, and prandial stages. A time-frequency transformation based on wavelets was used to extract the signal characteristics, and a special selection procedure based on correlation was used to reduce their number. The analysis was carried out by evaluating different neural network structures to classify the wavelet coefficients into two groups (healthy subjects and dyspeptic patients). The optimization process of the classifier led to a linear model. A dimension reduction that resulted in only 25% of uncorrelated electrogastrogram characteristics gave 24 inputs for the classifier. The prandial stage gave the most significant results. Under these conditions, the classifier achieved 78.6% sensitivity, 92.9% specificity, and an error of 17.9 +/- 6% (with a 95% confidence level). These data show that it is possible to establish significant differences between patients and normal controls when time-frequency characteristics are extracted from an electrogastrogram, with an adequate component reduction, outperforming the results obtained with classical Fourier analysis. These findings can contribute to increasing our understanding of the pathophysiological mechanisms involved in functional dyspepsia and perhaps to improving the pharmacological treatment of functional dyspeptic patients.

GENÉTICA

CLIN GENET. 2009 NOV;76(5):465-70.

CLINICAL FEATURES OF CHROMOSOME 22Q11.2 MICRODELETION SYNDROME IN 208 CHILEAN PATIENTS.

Repetto GM, Guzmán ML, Puga A, Calderón JF, Astete CP, Aracena M, Arriaza M, **Aravena T, Sanz P.**

Patients with chromosome 22q11 deletion syndrome exhibit significant phenotypic variability. Epidemiologic data suggest a higher incidence in Hispanics, but limited clinical information is available from Latin-American patients. We describe the clinical features of Chilean patients with 22q11 deletion syndrome and compare their findings with those reported in large European, Japanese and US series. Data were obtained from 208 patients from five medical centers. Mean age at diagnosis was 5.2 years, with a median of 2.3 years. Congenital heart defects were present in 59.6%, lower than other large series that averaged 75.8%. Palate abnormalities were present in 79%, higher than previous reports averaging 56%. Patients with congenital heart disease were diagnosed earlier (median 0.3 years of age) than those without heart defects (median 5.6 years) and had greater mortality attributable to the syndrome (9.8% vs 2.4%, respectively). The differences in frequencies of major anomalies may be due to growing awareness of more subtle manifestations of the syndrome, differences in clinical ascertainment or the presence of modifier factors. These observations provide additional data useful for patient counseling and for the proposal of health care guidelines.

GERIATRÍA

CURR MED RES OPIN. 2009 MAY;25(5):1171-8.

PHYSICIANS' ATTITUDES AND ADHERENCE TO USE OF RISK SCORES FOR PRIMARY PREVENTION OF CARDIOVASCULAR DISEASE: CROSS-SECTIONAL SURVEY IN THREE WORLD REGIONS.

Sposito AC, Ramires JA, Jukema JW, **Molina JC**, da Silva PM, Ghadanfar MM, Wilson PW.

OBJECTIVE: To evaluate physicians' attitudes and adherence to the use of risk scores in the primary prevention of cardiovascular disease (CVD). DESIGN AND METHODS: A cross-sectional survey of 2056 physicians involved in the primary prevention of CVD. Participants included cardiologists (47%), general practitioners (42%), and endocrinologists (11%) from several geographical regions: Brazil (n = 968), USA (n = 381), Greece (n = 275), Chile (n = 157), Venezuela (n = 128), Portugal (n = 42), The Netherlands (n = 41), and Central America (Costa Rica, Panama, El Salvador and Guatemala; n = 64). RESULTS: The main outcome measure was the percentage of responses on a multiple-choice questionnaire describing a hypothetical asymptomatic patient at intermediate risk for CVD according to the Framingham Risk Score. Only 48% of respondents reported regular use of CVD risk scores to tailor preventive treatment in the case scenario. Of non-users, nearly three-quarters indicated that 'It takes up too much of my time' (52%) or 'I don't believe they add value to the clinical evaluation' (21%). Only 56% of respondents indicated that they would prescribe lipid-lowering therapy for the hypothetical intermediate-risk patient. A significantly greater proportion of regular users than non-users of CVD risk scores identified the need for lipid-lowering therapy in the hypothetical patient (59 vs. 41%; $p < 0.0001$). CONCLUSIONS: Based on a survey conducted in a 'real-world' setting, risk scores are generally not used by a majority of physicians to guide primary prevention in asymptomatic persons at intermediate risk for CVD. Appropriate prescribing of lipid-lowering therapy in such patients is equally neglected. Changing physicians' attitudes towards the use of CVD risk scores is one of several challenges that need to be addressed to reduce the world-wide burden of CVD.

MEDICINA NUCLEAR

COMPUT MED IMAGING GRAPH. 2009 JUN;33(4):247-55.

SEMI-AUTOMATED ASSESSMENT OF LEFT VENTRICULAR MASS USING TRANSAXIAL TC-99M SESTAMIBI SPECT IMAGING.

Rojas G, Raff U, **González P**, Jaimovich R, Quintana JC.

The "left ventricular mass" (LVM) using Tc-99m Sestamibi SPECT imaging may be a useful parameter to quantitatively assess the left ventricle and hence its function. The LVM was determined without reorienting the images along the long axis of the left ventricle. A comparison with reoriented SPECT images was then performed. The LVM showed the expected variations among different pathological heart conditions and the control subjects. The left ventricular mass obtained from non-reoriented tomographic views of the myocardium can be a useful index to quantitatively assess various heart conditions where the myocardium lacks perfusion either between rest and stress studies or similar conditions in longitudinal studies.

J NUCL MED. 2009; 50 (SUPPLEMENT 2):1195

BRAIN PERFUSION DEFECTS ARE ASSOCIATED WITH ENDOTHELIAL DYSFUNCTION IN COCAINE USERS.

Teresa Massardo, Julio Pallavicini, Juan Carlos Quintana, Rodrigo Jaimovich, Claudia Sáez, Paulina Olivares, Diego Mezzano, **Rita Alay** and Jaime Pereira.

Objectives: Chronic cocaine consumption induces cortical brain perfusion defects. Vasospasm appears to play a role associated with haemostatic system activation. Endothelial dysfunction (ED), which is involved in vascular damage, is reliably assessed by circulating endothelial cells (CEC). Goal: Investigate ED evidence in patients with recent demonstrated cocaine consumption. Methods: We studied 15 DSM-IV cocaine dependent patientst; 12 male; mean age 31±9 y.o. Basal brain perfusion SPECT with 99mTc-ethylencistein-dimer performed a week after admittance; 13 of them controlled after 4 weeks of strict abstinence. Statistical Parametric Map and Neurostat were used to evaluate hypoperfusion (<66% maximal cortical activity). Whole blood CEC levels were also enumerated. Results: All patients presented focal bilateral perfusion baseline abnormalities, mainly in limbic and fronto temporal areas without significant change after abstinence. CEC were increased at baseline (636±208 cells/ml) and after abstinence (464±172 cells/ml), (p<0.0001 in both) with a significant reduction (p:0.0027). Initial brain hypoperfusion correlated better with CEC levels after a month of abstinence: Global Brain r=0.7694, Global Cortex r=0.7695, Prefrontal r=0.8427 and Cingulate r=0.6365. Conclusions: Cocaine dependent patients had persistant brain hypoperfusion associated to ED after abstinence. These findings support the notion that cocaine-induced endothelial damage may play a pathogenic role in the ischemic vascular damage observed in chronic cocaine users.

NEFROLOGÍA

PERIT DIAL INT. 2009 FEB;29 SUPPL 2:S222-6.

POLICIES AND HEALTH CARE FINANCING ISSUES FOR DIALYSIS IN LATIN AMERICA: EXTRACTS FROM THE ROUNDTABLE DISCUSSION ON THE ECONOMICS OF DIALYSIS AND CHRONIC KIDNEY DISEASE.

Pecoits-Filho R, Campos C, Cerdas-Calderón M, Fortes P, Jarpa C, Just P, Luconi P, Lugon JR, **Pacheco A**, Paniagua R, Rodríguez K, Sanabria M, Sciaraffia V, Velasco C, De Arteaga J.

During the 2008 Congress of the International Society for Peritoneal Dialysis, academic nephrologists, nephrology societies, and government officials from Colombia, Brazil, Argentina, Chile, Central America, Ecuador, and Mexico participated in a roundtable discussion on the Economics of Dialysis and Chronic Kidney Disease in Latin America. The main focus was policy and health care financing. The roundtable promoted open discussion between policymakers and clinicians on how to find viable solutions to contain spending on treatment for end-stage renal disease into the future. A number of options were proposed, including early medical intervention (disease management programs) to slow the progression of chronic kidney disease in high-risk patients, promotion of pre-emptive renal transplantation, and use of the most cost-effective dialysis therapy that can be offered to a patient without compromising outcome. It was concluded that the burden of treating more patients in the future could be alleviated by wider utilization of peritoneal dialysis (PD). However, important changes in health care reimbursement systems and realignment of incentives in the region are required to support wider PD penetration.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

MOV DISORD. 2009 OCT 30;24(14):2104-11.

ATP13A2 VARIANTS IN EARLY-ONSET PARKINSON'S DISEASE PATIENTS AND CONTROLS.

Djarmati A, Hagenah J, Reetz K, Winkler S, **Behrens MI**, Pawlack H, Lohmann K, Ramirez A, Tadić V, Brüggemann N, Berg D, Siebner HR, Lang AE, Pramstaller PP, Binkofski F, Kostić VS, Volkmann J, Gasser T, Klein C.

Four genes responsible for recessively inherited forms of Parkinson's disease (PD) have been identified, including the recently discovered ATP13A2 (PARK9) gene. Our objective was to investigate the role of this gene in a large cohort of PD patients and controls. We extensively screened all 29 exons of the ATP13A2 coding region in 112 patients with early-onset PD (EOPD; <40 years) of mostly European ethnic origin and of 55 controls. We identified four carriers (3.6%) of novel single heterozygous ATP13A2 missense changes that were absent in controls. Interestingly, the carrier of one of these variants also harbored two mutations in the Parkin gene. None of the carriers had atypical features previously described in patients with two mutated ATP13A2 alleles (Kufor-Rakeb syndrome). Our data suggest that two mutated ATP13A2 alleles are not a common cause of PD. Although heterozygous variants are present in a considerable number of patients, they are-based on this relatively small sample-not significantly more frequent in patients compared to controls. (c) 2009 Movement Disorder Society.

CURR ALZHEIMER RES. 2009 JUN;6(3):196-204.

A COMMON BIOLOGICAL MECHANISM IN CANCER AND ALZHEIMER'S DISEASE?

Behrens MI, Lendon C, Roe CM.

Cancer and Alzheimer's disease (AD) are two common disorders for which the final pathophysiological mechanism is not yet clearly defined. In a prospective longitudinal study we have previously shown an inverse association between AD and cancer, such that the rate of developing cancer in general with time was significantly slower in participants with AD, while participants with a history of cancer had a slower rate of developing AD. In cancer, cell regulation mechanisms are disrupted with augmentation of cell survival and/or proliferation, whereas conversely, AD is associated with increased neuronal death, either caused by, or concomitant with, beta amyloid (Abeta) and tau deposition. The possibility that perturbations of mechanisms involved in cell survival/death regulation could be involved in both disorders is discussed. Genetic polymorphisms, DNA methylation or other mechanisms that induce changes in activity of molecules with key roles in determining the decision to "repair and live"- or "die" could be involved in the pathogenesis of the two disorders. As examples, the role of p53, Pin1 and the Wnt signaling pathway are discussed as potential candidates that, speculatively, may explain inverse associations between AD and cancer.

GENET TEST MOL BIOMARKERS. 2009 FEB;13(1):105-8.

DYSFERLINOPATHY IN CHILE: EVIDENCE OF TWO NOVEL MUTATIONS IN THE FIRST REPORTED CASES.

Bevilacqua JA, Krahn M, Pedraza L, Gejman R, González S, Lévy N.

We describe two Chilean patients with dysferlinopathy, a 32-year-old man with Miyoshi's distal myopathy and a 29-year-old woman with a proximodistal phenotype. Absence of dysferlin in frozen muscle biopsy allowed diagnostic confirmation. In these two patients, two mutations not previously identified in other populations were found: a homozygous c.1948delC (p.Leu650TyrfsX6) was found in the male patient; the heterozygous mutation c.1276G > A (p.Gly426Arg) was found in the female patient in association with the previously reported c.2858dupT (p.Phe954ValfsX2). To our knowledge, this is the first time that mutations in DYSF are identified in native Chileans. Our findings suggest the possibility that mutations in the DYSF gene were present in the Native American population before colonization.

ACTA NEUROPATHOL. 2009 MAR;117(3):283-91.

"NECKLACE" FIBERS, A NEW HISTOLOGICAL MARKER OF LATE-ONSET MTM1-RELATED CENTRONUCLEAR MYOPATHY.

Bevilacqua JA, Bitoun M, Biancalana V, Oldfors A, Stoltenburg G, Claeys KG, Lacène E, Brochier G, Manéré L, Laforêt P, Eymard B, Guicheney P, Fardeau M, Romero NB.

Mutations in the gene encoding the phosphoinositide phosphatase myotubularin 1 protein (MTM1) are usually associated with severe neonatal X-linked myotubular myopathy (XLMTM). However, mutations in MTM1 have also been recognized as the underlying cause of "atypical" forms of XLMTM in newborn boys, female infants, female manifesting carriers and adult men. We reviewed systematically the biopsies of a cohort of patients with an unclassified form of centronuclear myopathy (CNM) and identified four patients presenting a peculiar histological alteration in some muscle fibers that resembled a necklace ("necklace fibers"). We analyzed further the clinical and morphological features and performed a screening of the genes involved in CNM. Muscle biopsies in all four patients demonstrated 4-20% of fibers with internalized nuclei aligned in a basophilic ring (necklace) at 3 microm beneath the sarcolemma. Ultrastructurally, such necklaces consisted of myofibrils of smaller diameter, in oblique orientation, surrounded by mitochondria, sarcoplasmic reticulum and glycogen granules. In the four patients (three women and one man), myopathy developed in early childhood but was slowly progressive. All had mutations in the MTM1 gene. Two mutations have previously been reported (p.E404K and p.R241Q), while two are novel; a c.205_206delinsAACT frameshift change in exon 4 and a c.1234A>G mutation in exon 11 leading to an abnormal splicing and the deletion of nine amino acids in the catalytic domain of MTM1. Necklace fibers were seen neither in DNM2- or BIN1-related CNM nor in males with classical XLMTM. The presence of necklace fibers is useful as a marker to direct genetic analysis to MTM1 in CNM.

NEUROL RES. 2009 APR;31(3):228-33.

LOCAL INFILTRATION OF GONYAUTOXIN IS SAFE AND EFFECTIVE IN TREATMENT OF CHRONIC TENSION-TYPE HEADACHE.

Lattes K, **Venegas P**, Lagos N, Lagos M, Pedraza L, Rodríguez-Navarro AJ, García C.

BACKGROUND: Gonyautoxin are phycotoxins, whose molecular mechanism of action is a reversible block of the voltage-gated sodium channels at axonal level, impeding nerve impulse propagation. OBJECTIVE: To evaluate clinical efficacy of gonyautoxin in the treatment of patients with chronic tensional-type headache. METHODS: Open trial from September 2004 to 2005 in Hospital Clínico Universidad de Chile. Twenty-seven patients with chronic tension-type headache were locally infiltrated with gonyautoxins (50 micrograms) in ten sites considered as pain trigger points in a fixed infiltration protocol. In each site, a volume of 200 microlitres was injected. EMG recording was performed before and immediately after infiltrations. Main outcome measures are where a significantly drop-off in acute headache pain score occurs and number of days without headache pain. RESULTS: No side effects were detected in the follow-up period. From base line of 2 weeks, 19 patients of 27 (70%) are the successfully responders to the treatment. They showed the remarkable immediate effect after infiltration demonstrated by trapezium EMG recording. Patients reported a fall in pain score 5 minutes post-injection from 5.0 +/- 2.8 to 1.6 +/- 1.6 (mean +/- SD). The responder showed an average of 8.1 +/- 9.9 weeks of headache pain-free, all of them without a second infiltration or use of any additional analgesic medication. DISCUSSION: The therapeutic properties of gonyautoxin local infiltration in chronic tension-type headache patients are shown to be safe and effective. This report describes a new therapy for chronic tension-type headache involving local infiltrations of gonyautoxins. The immediate headache pain relief effect shown only minutes after toxin infiltrations were the most remarkable feature of this protocol. This is the first gonyautoxins testing report in the treatment of chronic tension-type headache.

STROKE. 2009 MAY;40(5):1721-8.

PLACEBO-CONTROLLED TRIAL OF HIGH-DOSE ATORVASTATIN IN PATIENTS WITH SEVERE CEREBRAL SMALL VESSEL DISEASE.

Lavallée PC, Labreuche J, Gongora-Rivera F, **Jaramillo A**, Brenner D, Klein IF, Touboul PJ, Vicaut E, Amarenco P; Lacunar-BICHAT Investigators.

BACKGROUND AND PURPOSE: Uncontrolled studies have shown that statins can improve cerebral vasoreactivity (CVR) in patients with mild small vessel disease. We sought to determine whether high-dose atorvastatin increases CVR compared with placebo in patients with severe small vessel disease. METHODS: Ninety-four adults with recent lacunar stroke were randomly allocated in a

double-blind manner to 80 mg of atorvastatin daily or matching placebo after stratification for hypertensive and diabetic status. The primary end point was change in CVR after 3 months of treatment. Secondary outcomes were changes in brachial and carotid artery endothelial-dependent vasodilations. RESULTS: At baseline, all patients had a severely impaired CVR (mean, 12.1%; 95% CI, 9.5-14.7) and carotid (mean, -0.25%; 95% CI, -1.17-0.67) and brachial artery (mean, 2.72%; 95% CI, 1.39-4.05) endothelial function. Despite reductions of 55% in low-density lipoprotein cholesterol and of 30% in high-sensitivity C-reactive protein in the active arm compared to placebo, atorvastatin 80 mg per day did not improve CVR or endothelial dysfunction of carotid and brachial arteries. CONCLUSIONS: We found no positive effect of 3-month treatment with atorvastatin on severe cerebral microvasculature endothelial dysfunction in patients with lacunar stroke.

J STROKE CEREBROVASC DIS. 2009 MAR-APR;18(2):164-6.

ACUTE PONTINE INFARCT IN A 16-YEAR-OLD MAN WITH ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT EPITHELIOPATHY. A CASE REPORT.

Jaramillo A, Gaete G, Romero P, **Orellana P, Illanes S.**

A 16-year-old boy recently diagnosed with acute posterior multifocal placoid pigment epitheliopathy (APMPPE) developed an acute infarct in the left pontine region. No relevant abnormalities were found in the brain and cervical angiography, echocardiography, cerebrospinal fluid, and blood samples. Funduscopically, lesions were multiple circumscribed, creamy yellow patches, flat lesions at the level of the retinal pigment epithelium, and the fluorescence angiography confirmed an APMPPE. All visual and neurological symptoms reverted completely after use of steroid. Our patient is the youngest patient with APMPPE and stroke described so far, being the common age presentation between 20 to 40 years.

HUM MUTAT. 2009 OCT;30(10):1419-27.

DYNAMIN 2 MUTATIONS ASSOCIATED WITH HUMAN DISEASES IMPAIR CLATHRIN-MEDIATED RECEPTOR ENDOCYTOSIS.

Bitoun M, Durieux AC, Prudhon B, **Bevilacqua JA**, Herledan A, Sakanyan V, Urtizberea A, Cartier L, Romero NB, Guicheney P.

Dynamin 2 (DNM2) is a large GTPase involved in the release of nascent vesicles during endocytosis and intracellular membrane trafficking. Distinct DNM2 mutations, affecting the middle domain (MD) and the Pleckstrin homology domain (PH), have been identified in autosomal dominant centronuclear myopathy (CNM) and in the intermediate and axonal forms of the Charcot-Marie-Tooth peripheral neuropathy (CMT). We report here the first CNM mutation (c.1948G>A, p.E650 K) in the DNM2 GTPase effector domain (GED), leading to a slowly progressive moderate myopathy. COS7 cells transfected with DNM2 constructs harboring a disease-associated mutation in MD, PH, or GED show a reduced uptake of transferrin and low-density lipoprotein (LDL) complex, two markers of clathrin-mediated receptor endocytosis. A decrease in clathrin-mediated endocytosis was also identified in skin fibroblasts from one CNM patient. We studied the impact of DNM2 mutant overexpression on epidermal growth factor (EGF)-induced extracellular signal-regulated kinase 1 (ERK1) and ERK2 activation, known to be an endocytosis- and DNM2-dependent process. Activation of ERK1/2 was impaired for all the transfected mutants in COS7 cells, but not in CNM fibroblasts. Our results indicate that impairment of clathrin-mediated endocytosis may play a role in the pathophysiological mechanisms leading to DNM2-related diseases, but the tissue-specific impact of DNM2 mutations in both diseases remains unclear.

HUM MUTAT. 2009 FEB;30(2):E345-75.

ANALYSIS OF THE DYSF MUTATIONAL SPECTRUM IN A LARGE COHORT OF PATIENTS.

Krahn M, Béroud C, Labelle V, Nguyen K, Bernard R, Bassez G, Figarella-Branger D, Fernandez C, Bouvenot J, Richard I, Ollagnon-Roman E, **Bevilacqua JA**, Salvo E, Attarian S, Chapon F, Pellissier JF, Pouget J, Hammouda el H, Laforêt P, Urtizberea JA, Eymard B, Leturcq F, Lévy N.

Dysferlinopathies belong to the heterogeneous group of autosomal recessive muscular dystrophies. Mutations in the gene encoding dysferlin (DYSF) lead to distinct phenotypes, mainly Limb Girdle Muscular Dystrophy type 2B (LGMD2B) and Miyoshi myopathy (MM). Here, we analysed the mutational data from the largest cohort described to date, a cohort of 134 patients, included based on clinical suspicion of primary dysferlinopathy and/or dysferlin protein deficiency identified on muscle biopsy samples. Data were compiled from 38 patients previously screened for mutations in our laboratory (Nguyen, *et al*., 2005; Nguyen, *et al*., 2007), and 96 supplementary patients screened for DYSF mutations using genomic DHPLC analysis, and subsequent sequencing of detected variants, in a routine diagnostic setting. In 89 (66%) out of 134 patients, molecular analysis identified two disease causing mutations, confirming the diagnosis of primary Dysferlinopathy on a genetic basis. Furthermore, one mutation was identified in 30 patients, without identification of a second deleterious allele. We are currently developing complementary analysis for patients in whom only one or no disease-causing allele could be identified using the genomic screening procedure. Altogether, 64 novel mutations have been identified in this cohort, which corresponds to approximately 25% of all DYSF mutations reported to date. The mutational spectrum of this cohort significantly shows a higher proportion of nonsense mutations, but a lower proportion of deleterious missense changes as compared to previous series.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

J THROMB HAEMOST. 2009 JUN;7(6):955-61.

PREGNANCY OUTCOME AND FIBRINOLYTIC, ENDOTHELIAL AND COAGULATION MARKERS IN WOMEN UNDERGOING UTERINE ARTERY DOPPLER SCREENING AT 23 WEEKS.

Hunt BJ, Missfelder-Lobos H, **Parra-Cordero M**, Fletcher O, Parmar K, Lefkou E, Lees CC.

BACKGROUND: Pre-eclampsia (PET) and/or fetal growth restriction (FGR) remain a major cause of maternal and fetal morbidity and mortality. In pregnancy, fibrinolysis is controlled by the maternal endothelium and placenta, both of which are central to the pathogenesis of PET/FGR. Clinically, uterine artery Doppler screening at 23 weeks is used to predict PET/FGR. An abnormal uterine artery Doppler finding is defined as early diastolic bilateral uterine artery notching (BN) in the waveform. However, about 50% of mothers with BN do not develop PET/FGR. OBJECTIVES: We investigated fibrinolytic changes and uterine artery Doppler findings in the second trimester, and related them to pregnancy outcome; in particular assessing whether fibrinolytic markers could discriminate between normal and abnormal outcome in mothers with BN. PATIENTS/METHODS: Plasma levels of tissue-type plasminogen activator (t-PA), plasminogen activator inhibitor-1 (PAI-1), plasminogen activator inhibitor-2 (PAI-2), plasmin-alpha(2) antiplasmin (PAP), D-dimers and markers of endothelial dysfunction were measured with Doppler ultrasound at 23 weeks. RESULTS: Those with BN had decreased PAP and D-dimer levels, and raised PAI-1 and thrombomodulin levels. Mothers with BN and PET/FGR had significantly increased t-PA levels and reduced PAI-2 levels. CONCLUSIONS: BN at 23 weeks of gestation is associated with increased PAI-1 levels. Within the BN group, mothers who developed PET/FGR had increased t-PA levels and decreased PAI-2 levels, although there was no net change in fibrinolysis as measured by D-dimer levels. No single fibrinolytic marker is helpful in determining pregnancy outcome in those with BN, but t-PA and PAI-2 are worthy of study in a multifactorial algorithm.

PRENAT DIAGN. 2009 DEC;29(12):1118-22.

INCREASED FREE FETAL DNA LEVELS IN EARLY PREGNANCY PLASMA OF WOMEN WHO SUBSEQUENTLY DEVELOP PREECLAMPSIA AND INTRAUTERINE GROWTH RESTRICTION.

Illanes S, **Parra M**, Serra R, Pino K, Figueroa-Diesel H, **Romero C**, Arraztoa JA, Michea L, Soothill PW.

OBJECTIVE: To determine if maternal plasma ffDNA is increased early in pregnancies which subsequently develop preeclampsia (PE) and intrauterine growth restriction (IUGR). METHODS: Blood was obtained at 11-14 weeks and plasma stored. Among those who delivered a male infant and had a birth weight under the tenth centile and/or PE, we divided them into those who delivered before 35 weeks (9) and those who delivered after this gestation (15). A third group with uncomplicated pregnancies was used as controls (24). Real time-polymerase chain reaction (RT-PCR) was carried out to detect the multi-copy Y chromosome associated DSY14 gene. RESULTS: There were no differences between the ffDNA levels in the group delivered after 35 weeks and the control group (2.23ge/mL-1.61ge/mL p = 0.39). However, the levels of ffDNA at 11-14 weeks were statistically, significantly higher in patients that delivered before 35 weeks (4.34ge/mL-1.61ge/mL p = 0.0018). A logistic regression analysis shows that for every unit (1ge/mL) in which ffDNA increases, the likelihood of having PE or a fetus growing under the tenth centile delivered before 35 weeks increases by 1.67 times (CI 1.13-2.47). CONCLUSION: The concentration of ffDNA is significantly higher even during early pregnancy, in patients who subsequently develop PE and/or IUGR and are delivered before 35 weeks.

LABORATORIO DE ENDOCRINOLOGÍA

GYNECOL ONCOL. 2009 OCT;115(1):102-7.

INVOLVEMENT OF AKT, RAS AND CELL CYCLE REGULATORS IN THE POTENTIAL DEVELOPMENT OF ENDOMETRIAL HYPERPLASIA IN WOMEN WITH POLYCYSTIC OVARIAN SYNDROME.

Villavicencio A, Goyeneche A, Telleria C, Bacallao K, Gabler F, Fuentes A, **Vega M.**

OBJECTIVE: To examine whether the abundance, localization, and/or activity of cell cycle regulators CDK2, Cyclin E, p27, and survival proteins AKT and Ras in PCOS-associated endometria (with and without hyperplasia) differ from non-PCOS endometria. METHODS: The expression of CDK2, Cyclin E, p27, AKT and Ras was measured by immunohistochemistry and/or Western blot in 9 normal endometria (NE), 12 endometria from PCOS patients without endometrial hyperplasia (PCOSE), 7 endometria from PCOS women with endometrial hyperplasia (HPCOSE), and 9 endometria from patients with endometrial hyperplasia (HE). The activity of CDK2 was assessed by an in vitro kinase assay. RESULTS: CDK2, Cyclin E and p27 proteins were expressed mainly in the endometrial epithelial cells of the studied groups. No change in the activity of CDK2 was observed in total extracts obtained from the tissue samples. However, the nuclear expression of CDK2 in epithelial cells was slightly elevated in PCOSE and significantly increased in HPCOSE when compared to NE. Higher expression of p27 was detected in the cytoplasm of epithelial cells of PCOSE and HPCOSE when compared to NE. Also, we found an increment in Ser473-AKT phosphorylation and an over-expression of the Ras oncogene in endometria of patients with PCOS. CONCLUSION: The PCOS condition is associated with increased Ser473-AKT phosphorylation,

elevated expression of Ras, increased cytoplasmic abundance of p27, and increased nuclear abundance of CDK2 in the endometrial epithelial cells. These biological events could potentially provide a chance for endometrial cells from PCOS patients to exit the controlled cell cycle and become hyperplastic at a later stage.

J CLIN ENDOCRINOL METAB. 2009 AUG;94(8):3065-71.

NERVE GROWTH FACTOR INDUCES VASCULAR ENDOTHELIAL GROWTH FACTOR EXPRESSION IN GRANULOSA CELLS VIA A TRKA RECEPTOR/MITOGEN-ACTIVATED PROTEIN KINASE-EXTRACELLULARLY REGULATED KINASE 2-DEPENDENT PATHWAY.

Julio-Pieper M, Lozada P, **Tapia V, Vega M, Miranda C, Vantman D**, Ojeda SR, **Romero C.**

CONTEXT: Acquisition of ovulatory competence by antral follicles requires development of an adequate vascular supply. Although it is well established that ovarian angiogenesis is cyclically regulated by vascular endothelial growth factor (VEGF), the factors controlling VEGF production by ovarian follicles remain largely unknown. Nerve growth factor (NGF) may be one of these factors, because NGF promotes angiogenesis and synthesis of angiogenic factors in other tissues and is produced by human granulosa cells (hGCs). OBJECTIVE: The aim of the study was to determine whether NGF influences the production of VEGF by hGCs and to identify a potential signaling pathway underlying this effect. DESIGN: We conducted a prospective experimental study. PATIENTS: hGCs were obtained from 41 women participating in the in vitro fertilization program of our institution. METHODS: Changes in VEGF mRNA after exposure to NGF were evaluated in cultured hGCs by PCR and real-time PCR. The effect of NGF on VEGF secretion was determined by ELISA. The involvement of trkA, the high affinity NGF receptor, was examined by inhibiting the receptor's tyrosine kinase activity with K252a. The contribution of an ERK1/ERK2-mediated signaling pathway was identified by detecting NGF-dependent phosphorylation of these proteins and by blocking their activity with the inhibitor U0126. Results: NGF promotes VEGF production in cultured hGCs. Blockade of trkA receptor tyrosine kinase activity blocks this effect. NGF induces MAPK-ERK2 phosphorylation, and blockade of this signaling pathway prevents the NGF-induced increase in VEGF production. CONCLUSIONS: NGF promotes ovarian angiogenesis by enhancing the synthesis and secretion of VEGF from hGCs via a trkA- and ERK2-dependent mechanism.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

WORLD J BIOL PSYCHIATRY. 2009;10(4 PT 2):512-7.

PLANNING IN BORDERLINE PERSONALITY DISORDER: EVIDENCE FOR DISTINCT SUBPOPULATIONS.

Bustamante ML, Villarroel J, Francesetti V, Ríos M, Arcos-Burgos M, Jerez S, Iturra P, Solari A, **Silva H.**

OBJECTIVE: Borderline personality disorder is a severe mental disorder, whereas previous studies suggest executive functions may be impaired. The aim of this study was to evaluate executive planning in a sample of 85 individuals. METHODS: Planning was assessed by means of the Tower of London (Drexel University version) task. Latent class cluster analysis models were adjusted to the data. RESULTS: We identified two different subpopulations of borderline personality disorder patients, one of them with significantly reduced performance. CONCLUSION;. Neuropsychological mechanisms may be involved in borderline personality disorder, at least in a subgroup of patients.

J NEUROCHEM. 2009 NOV;111(4):891-900.

MOLECULAR MECHANISMS UNDERLYING GLUTAMATERGIC DYSFUNCTION IN SCHIZOPHRENIA: THERAPEUTIC IMPLICATIONS.

Gaspar PA, Bustamante ML, **Silva H**, Aboitiz F.

Early models for the etiology of schizophrenia focused on dopamine neurotransmission because of the powerful anti-psychotic action of dopamine antagonists. Nevertheless, recent evidence increasingly supports a primarily glutamatergic dysfunction in this condition, where dopaminergic disbalance is a secondary effect. A current model for the pathophysiology of schizophrenia involves a dysfunctional mechanism by which the NMDA receptor (NMDAR) hypofunction leads to a dysregulation of GABA fast- spiking interneurons, consequently disinhibiting pyramidal glutamatergic output and disturbing the signal-to-noise ratio. This mechanism might explain better than other models some cognitive deficits observed in this disease, as well as the dopaminergic alterations and therapeutic effect of anti-psychotics. Although the modulation of glutamate activity has, in principle, great therapeutic potential, a side effect of NMDAR overactivation is neurotoxicity, which accelerates neuropathological alterations in this illness. We propose that metabotropic glutamate receptors can have a modulatory effect over the NMDAR and regulate excitotoxity mechanisms. Therefore, in our view metabotropic glutamate receptors constitute a highly promising target for future drug treatment in this disease.

ACTAS ESP PSIQUIATR. 2009 JAN-FEB;37(1):21-6.

[MENTAL RETARDATION AS A RISK FACTOR TO DEVELOP A PSYCHOTIC DISEASE]

López MN, Domínguez AC, Quintero J, Rodríguez MM, Fernández Del Moral A, Arriero MA, Vigo MM, Villamor IB, Vicente MJ, Castromán JL, Jiménez RN, Zambrano-Enríquez D, González de Rivera JL, García EB.

INTRODUCTION: One of the main aims of research on schizophrenia has been to pinpoint the early symptoms and signals of the disease before its appearance. OBJECTIVES: We have examined the diagnoses previously given to patients before they were diagnosed of schizophrenia. METHOD: This is a case-control study in which we used a data register including the fields of minimum basic data set (MBDS) whose time period included 1999 to 2005. RESULTS: In our study, there was a 3.6% frequency of mental retardation and 2.1% one of behavioral and emotional disorders with onset usually occurring in childhood and adolescence, both diagnosed previously. The estimated odds ratio for a mentally retarded patient to suffer adult onset psychosis is 4.6 (95%CI [3.43-6.26]), schizophrenia 5.8 (95% CI [4.20-7.88]), paranoid schizophrenia 4.8 (95% CI [3.39 -6.93]), residual schizophrenia 7.0 (95% CI [4.81 -10.09]) and persistent delusional disorder 2.7 (95% CI [1.57 -4.73]). CONCLUSIONS: It can be concluded from our study that there is an increased frequency of mental retardation among the pathological records of subjects who will be diagnosed with paranoid schizophrenia and residual schizophrenia in the future. This fact supports the etiological thesis of schizophrenia involving neurodevelopment disorders.

COMPUT MED IMAGING GRAPH. 2009 JUN;33(4):247-55.

SEMI-AUTOMATED ASSESSMENT OF LEFT VENTRICULAR MASS USING TRANSAXIAL TC-99M SESTAMIBI SPECT IMAGING.

Rojas G, Raff U, Gonzalez P, Jaimovich R, Quintana JC.

The “left ventricular mass” (LVM) using Tc-99m Sestamibi SPECT imaging may be a useful parameter to quantitatively assess the left ventricle and hence its function. The LVM was determined without reorienting the images along the long axis of the left ventricle. A comparison with reoriented SPECT images was then performed. The LVM showed the expected variations among different pathological heart conditions and the control subjects. The left ventricular mass obtained from non-reoriented tomographic views of the myocardium can be a useful index to quantitatively assess various heart conditions where the myocardium lacks perfusion either between rest and stress studies or similar conditions in longitudinal studies.

SERVICIO DE PEDIATRÍA

PEDIATR INFECT DIS J. 2009 APR;28(4):267-72.

SAFETY, TOLERABILITY, PHARMACOKINETICS, AND IMMUNOGENICITY OF MOTAVIZUMAB, A HUMANIZED, ENHANCED-POTENCY MONOCLONAL ANTIBODY FOR THE PREVENTION OF RESPIRATORY SYNCYTIAL VIRUS INFECTION IN AT-RISK CHILDREN.

Abarca K, Jung E, **Fernández P**, Zhao L, Harris B, Connor EM, Losonsky GA; Motavizumab Study Group.

BACKGROUND:: Respiratory syncytial virus (RSV) is a major cause of lower respiratory tract infection in young children. Motavizumab is an investigational humanized monoclonal antibody for RSV prophylaxis. METHODS:: A dose-escalation study was conducted followed by assessment of safety, tolerability, serum concentrations, and immunogenicity during a second consecutive RSV season. In season 1, premature infants aged < or =6 months or children < or =24 months with chronic lung disease of prematurity received monthly motavizumab (3 or 15 mg/kg). In season 2, children who received > or =3 motavizumab doses in season 1 were randomized to receive monthly motavizumab or palivizumab 15 mg/kg. RESULTS:: Of 217 children enrolled in season 1, 211 (97.2%) received motavizumab 15 mg/kg and 205 (94.5%) patients completed the study through 90 days after the final dose. In season 2, 136 children were randomized to receive motavizumab (n = 66) or palivizumab (n = 70). The most commonly reported related adverse event was transient injection site erythema. In season 1, mean trough motavizumab concentrations were 7.9 and 50.2 microg/mL after the 3- and 15-mg/kg doses, respectively. Trough concentrations increased with repeated motavizumab dosing; a similar pattern was seen in season 2. Antimotavizumab reactivity occurred infrequently (3.3%) in season 1. In season 2, no treatment group-specific antidrug antibody was detected through 90 to 120 days after dosing with either product. CONCLUSIONS:: The pharmacokinetic profile of motavizumab was similar to that of other IgG1 antibodies. Increased adverse reactions or immunogenicity were not observed during and after a second season of treatment with motavizumab. Safety findings from these studies supported the continued development of motavizumab.

UPC

J CRIT CARE. 2009 DEC;24(4):494-500.

FIBEROPTIC BRONCHOSCOPY-ASSISTED PERCUTANEOUS TRACHEOSTOMY IS SAFE IN OBESE CRITICALLY ILL PATIENTS: A PROSPECTIVE AND COMPARATIVE STUDY.

Romero CM, Cornejo RA, Ruiz MH, Gálvez LR, Llanos OP, Tobar EA, Larrondo JF, Castro JS.

BACKGROUND: Obesity has reached epidemic proportions worldwide. In Latin America, 10% to 35% of the population is obese. Obese critically ill patients are at greater risk for requiring intubation and prolonged mechanical ventilation; and in some cases, it is necessary to perform a tracheostomy. OBJECTIVE: The objective of the study was to compare the incidence of perioperative complications associated with percutaneous tracheostomy (PT) using the fiberoptic bronchoscopy-assisted Ciaglia Blue Rhino technique (Cook Critical Care, Bloomington, IN) in obese vs nonobese critically ill patients. PATIENTS AND METHOD: A prospective evaluation was made of 120 patients who underwent PT because of prolonged mechanical ventilation. An analysis of the incidence of operative and early postoperative complications was performed comparing an obese patient group (n = 25) with a nonobese patient group (n = 80). Obesity was defined by a body mass index of at least 30 kg/m(2). RESULTS: The 2 groups had no significant differences in their demographic characteristics. The average body mass index for the obese patient group was 38 +/- 9 kg/m(2) vs 22 +/- 3 kg/m(2) for the nonobese patient group (P < .001). The obese patients required 18 +/- 7 days of mechanical ventilation, on average, before PT vs 16 +/- 7 days for the nonobese patients (P = .15). The incidence of operative complications for the obese patients vs nonobese patients was 8% and 7.5%, respectively (P = 1). The incidence of early postoperative complications was 8% for the obese patients vs 2.5% for the nonobese patients (P = .2). CONCLUSION: Percutaneous tracheostomy using the fiberoptic bronchoscopy-assisted Ciaglia Blue Rhino technique is safe for obese critically ill patients when performed by an experienced intensivist.

CRIT CARE. 2009;13(3):R63.

IMPACT OF EMERGENCY INTUBATION ON CENTRAL VENOUS OXYGEN SATURATION IN CRITICALLY ILL PATIENTS: A MULTICENTER OBSERVATIONAL STUDY.

Hernández G, Peña H, **Cornejo R**, Rovegno M, Retamal J, **Navarro JL**, Aranguiz I, Castro R, Bruhn A.

INTRODUCTION: Central venous oxygen saturation (ScvO2) has emerged as an important resuscitation goal for critically ill patients. Nevertheless, growing concerns about its limitations as a perfusion parameter have been expressed recently, including the uncommon finding of low ScvO2 values in patients in the intensive care unit (ICU). Emergency intubation may induce strong and eventually divergent effects on the physiologic determinants of oxygen transport (DO2) and oxygen consumption (VO2) and, thus, on ScvO2. Therefore, we conducted a study to determine the impact of emergency intubation on ScvO2. METHODS: In this prospective multicenter observational study, we included 103 septic and non-septic patients with a central venous catheter in place and in whom emergency intubation was required. A common intubation protocol was used and we evaluated several parameters including ScvO2 before and 15 minutes after emergency intubation. Statistical analysis included chi-square test and t test. RESULTS: ScvO2 increased from 61.8 +/- 12.6% to 68.9 +/- 12.2%, with no difference between septic and non-septic patients. ScvO2 increased in 84 patients (81.6%) without correlation to changes in arterial oxygen saturation (SaO2). Seventy eight (75.7%) patients were intubated with ScvO2 less than 70% and 21 (26.9%) normalized the parameter after the intervention. Only patients with pre-intubation ScvO2 more than 70% failed to increase the parameter after intubation. CONCLUSIONS: ScvO2 increases significantly in response to emergency intubation in the majority of septic and non-septic patients. When interpreting ScvO2 during early resuscitation, it is crucial to consider whether the patient has been recently intubated or is spontaneously breathing.

J CRIT CARE. 2009 MAR;24(1):81-8.

EXTENDED PRONE POSITION VENTILATION IN SEVERE ACUTE RESPIRATORY DISTRESS SYNDROME: A PILOT FEASIBILITY STUDY.

Romero CM, Cornejo RA, Gálvez LR, Llanos OP, Tobar EA, Berasaín MA, Arellano DH, Larrondo JF, Castro JS.

OBJECTIVES: The aim of the study was to evaluate the safety of extended prone position ventilation (PPV) and its impact on respiratory function in patients with severe acute respiratory distress syndrome (ARDS). DESIGN: This was a prospective interventional study. SETTING: Patients were recruited from a mixed medical-surgical intensive care unit in a university hospital. PATIENTS: Fifteen consecutive patients with severe ARDS, previously unresponsive to positive end-expiratory pressure adjustment, were treated with PPV. INTERVENTION: Prone position ventilation for 48 hours or until the oxygenation index was 10 or less (extended PPV). RESULTS: The elapsed time from the initiation of mechanical ventilation to pronation was 35 +/- 11 hours. Prone position ventilation was continuously maintained for 55 +/- 7 hours. Two patients developed grade II pressure ulcers of small extent. None of the patients experienced life-threatening complications or hemodynamic instability during the

procedure. The patients showed a statistically significant improvement in Pao(2)/Fio(2) (92 +/- 12 vs 227 +/- 43, P < .0001) and oxygenation index (22 +/- 5 vs 8 +/- 2, P < .0001), reduction of PaCo(2) (54 +/- 9 vs 39 +/- 4, P < .0001) and plateau pressure (32 +/- 2 vs 27 +/- 3, P < .0001), and increment of the static compliance (21 +/- 3 vs 37 +/- 6, P < .0001) with extended PPV. All the parameters continued to improve significantly while they remained in prone position and did not change upon returning the patients to the supine position. CONCLUSIONS: The results obtained suggest that extended PPV is safe and effective in patients with severe ARDS when it is carried out by a trained staff and within an established protocol. Extended PPV is emerging as an effective therapy in the rescue of patients from severe ARDS.

NEUROCRIT CARE. 2009;11(2):165-71.

MILRINONE AS A RESCUE THERAPY FOR SYMPTOMATIC REFRACTORY CEREBRAL VASOSPASM IN ANEURYSMAL SUBARACHNOID HEMORRHAGE.

Romero CM, Morales D, Reccius A, Mena F, Prieto J, **Bustos P**, Larrondo J, Castro J.

INTRODUCTION: Delayed ischemic neurological deficit associated to cerebral vasospasm is the most common cause of sequelae and death that follows the rupture of an aneurysm. The objective of this study was to evaluate the safety and efficacy of intra-arterial Milrinone in patients with symptomatic refractory cerebral vasospasm. PATIENTS AND METHOD: Eight patients diagnosed with aneurysmal subarachnoid hemorrhage who developed symptomatic cerebral vasospasm refractory to conventional medical therapy were enrolled. They received an intra-arterial infusion of Milrinone at a rate of 0.25 mg/min, with a total dose of 10-15 mg. Qualitative evaluation of angiographic response, neurological and systemic complications as well as functional outcome at 3 months were documented. RESULTS: All patients had a significant angiographic response. This was evidenced by a pre-treatment vessel stenosis greater than 70%, that improved to less than 50% after the intra-arterial Milrinone infusion. Three patients developed recurrent vasospasm that improved after a second intra-arterial Milrinone infusion. None of the patients developed neurologic or systemic complications attributed to the intervention. At 3 months follow-up all patients were alive and had a mean modified Rankin scale of 2 +/- 1 and a Barthel index of 83 +/- 10. CONCLUSION: Intra-arterial Milrinone infusion seems to be a safe and effective treatment for patients who develop refractory symptomatic cerebral vasospasm following aneurysmal subarachnoid hemorrhage.

DEPARTAMENTO DE UROLOGÍA

PROSTATE. 2009 JUL 1;69(10):1025-33.

GONADOTROPIN RELEASING HORMONE ANALOGS INDUCE APOPTOSIS BY EXTRINSIC PATHWAY INVOLVING P53 PHOSPHORYLATION IN PRIMARY CELL CULTURES OF HUMAN PROSTATIC ADENOCARCINOMAS.

Clementi M, Sánchez C, Benítez DA, Contreras HR, **Huidobro C**, Cabezas J, **Acevedo C**, Castellón EA.

BACKGROUND: Gonadotropin-releasing-hormone (GnRH) analogs are widely used to block hypothalamic-pituitary-gonadal axis and inhibit blood androgen levels in patients with prostate cancer (PCa). In addition, GnRH analogs induce proliferation arrest and apoptosis through GnRH receptors expressed on the membrane of PCa cells. Possible molecular mechanisms involved in GnRH-mediated apoptosis on prostate cancer cells were studied. METHODS: Primary cultures from PCa and benign prostatic hyperplasia (BPH) (non-malignant control) were derived from samples provided by our Institutional Hospital. Cell cultures were incubated for 24 hr with 20 ng/ml of GnRH agonist Leuprolide (Lp) or antagonist Cetrorelix (Cx). Apoptosis was evaluated by studying the expression of Bax and Bcl-2 and the activation of caspase-9 (intrinsic pathway), caspase-8 (extrinsic pathway), and caspase-3. Also, mRNA level, protein expression and phosphorylation of p53 were studied. RESULTS: Cleaved caspase-8 and -3, but not -9, increased in presence of Lp and Cx in PCa cell cultures. Bax and Bcl-2 mRNA levels showed no changes after GnRH-analog treatments. Only Bax protein showed an increase after Cx treatment in PCa cell cultures. p53 mRNA level was higher in PCa than in BPH cell cultures. Lp and Cx increased p53 expression and phosphorylation in PCa cell cultures. CONCLUSIONS: Apoptosis induced by GnRH analogs seems to be mediated by extrinsic pathway involving p53 phosphorylation. Phosphorylated-p53 might be associated with the increase in apoptotic NGF receptor, p75, previously reported by our laboratory. These findings reinforce the concept of clinical use of GnRH analogs for PCa suggesting that intraprostatic treatment may be more effective.

PROSTATE. 2009 SEP 15;69(13):1448-59.

EXPRESSION OF MULTIDRUG RESISTANCE PROTEINS IN PROSTATE CANCER IS RELATED WITH CELL SENSITIVITY TO CHEMOTHERAPEUTIC DRUGS.

Sánchez C, Mendoza P, Contreras HR, Vergara J, McCubrey JA, **Huidobro C**, Castellón EA.

BACKGROUND: Multidrug resistance (MDR) proteins have been associated with the lack of chemotherapy response. Expression of these proteins has been described in the prostate, but there is no information about their role in the chemotherapy response

of prostate cancer (PC). We studied the gene and protein expression of MDR proteins in primary cell cultures from PC tumors and PC cell lines, their relationship with chemotherapy and their effects on cell survival. METHODS: Primary cell cultures from PC were obtained from samples provided by our Institutional Hospital. Cell lines LNCaP, PC3, and DU145 were also examined. Cells were treated during 72 hr with several chemotherapeutic drugs. Protein and mRNA expressions of P-glycoprotein (P-Gp), MRP1 and LRP, before and after drug treatment, were evaluated by RT-PCR and Western blot analyses. The effect on cell survival was evaluated by proliferation assays (MTT), and cell cycle and apoptosis by flow cytometry. RESULTS: Primary PC cultures exhibited higher MDR protein expression and lower drug sensitivity than cell lines, in which P-Gp was not detected. Docetaxel and mitoxantrone displayed the highest apoptotic effect. Exposure to chemotherapeutic drugs increased apoptosis, cell cycle arrest, and MDR expression. Long-term treatment with doxorubicin diminished apoptosis elicited by all drugs examined in this study, suggesting a cross-resistance phenomenon. CONCLUSIONS: Low chemotherapy response observed in PC primary cultures could be explained, in part, by the high levels of MDR proteins (intrinsic MDR phenotype), and also, by their over-expression induced after long-term exposure to drugs (acquired MDR phenotype), which increase treatment resistance.

UROL ONCOL. 2009 MAY 16.

THE EXPRESSION OF SYNDECAN-1 AND -2 IS ASSOCIATED WITH GLEASON SCORE AND EPITHELIAL-MESENCHYMAL TRANSITION MARKERS, E-CADHERIN AND BETA-CATENIN, IN PROSTATE CANCER.

Contreras HR, Ledezma RA, Vergara J, Cifuentes F, Barra C, Cabello P, Gallegos I, Morales B, **Huidobro C**, Castellón EA.

The epithelial-mesenchymal transition (EMT) is considered a key step in tumor progression, where the invasive cancer cells change from epithelial to mesenchymal phenotype. During this process, a decrease or loss in adhesion molecules expression and an increase in migration molecules expression are observed. The aim of this work was to determine the expression and cellular distribution of syndecan-1 and -2 (migration molecules) and E-cadherin and beta-catenin (adhesion molecules) in different stages of prostate cancer progression. A quantitative immunohistochemical study of these molecules was carried out in tissue samples from benign prostatic hyperplasia and prostate carcinoma, with low and high Gleason score, obtained from biopsies archives of the Clinic Hospital of the University of Chile and Dipreca Hospital. Polyclonal specific antibodies and amplification system of estreptavidin-biotin peroxidase and diaminobenzidine were used. Syndecan-1 was uniformly expressed in basolateral membranes of normal epithelium, changing to a granular cytoplasmatic expression pattern in carcinomas. Syndecan-2 was observed mainly in a cytoplasmatic granular pattern, with high immunostaining intensity in areas of low Gleason score. E-cadherin was detected in basolateral membrane of normal epithelia showing decreased expression in high Gleason score samples. beta-Catenin was found in cell membranes of normal epithelia changing its distribution toward the nucleus and cytoplasm in carcinoma samples. We concluded that changes in expression and cell distribution of E-cadherin and beta-catenin correlated with the progression degree of prostate adenocarcinoma, suggesting a role of these molecules as markers of progression and prognosis. Furthermore, changes in the pattern expression of syndecan-1 and -2 indicate that both molecules may be involved in the EMT and tumor progression of prostate cancer.

INT J ANDROL. 2009 NOV 10.

P450-AROMATASE ACTIVITY AND EXPRESSION IN HUMAN TESTICULAR TISSUES WITH SEVERE SPERMATOGENIC FAILURE.

Lardone MC, Castillo P, **Valdevenito R**, Ebensperger M, Ronco AM, Pommer R, Piottante A, Castro A.

There is evidence that impaired spermatogenesis is associated with an imbalance in the oestradiol/testosterone ratio and with Leydig cell (LC) dysfunction. In testis, P450-aromatase, encoded by CYP19, is responsible for the conversion of testosterone to oestradiol. The aims of this study were to quantify CYP19 mRNA expression, aromatase activity and protein localization, and to measure the oestradiol to testosterone ratio in testicular tissues of men with spermatogenic impairment. Twenty-four men with complete Sertoli cell-only syndrome (SCOS), 14 with focal SCOS, 14 with maturation arrest (MA), 8 with mixed atrophy and 30 controls with normal spermatogenesis were subjected to testicular biopsy. All subjects underwent a physical examination, cytogenetic and serum hormonal studies. Testicular CYP19 mRNA was quantified using real time RT-PCR. Testicular aromatase activity was measured using the (3)H(2)0 assay and protein expression was evaluated using immunohistochemistry. In cases, serum testosterone and oestradiol were normal, but the testosterone/LH ratio was lower compared with controls ($p < 0.05$). Aromatase was localized in the Leydig, Sertoli and germ cells of all tissues, although stronger intensity was observed in LC. Aromatase mRNA and activity were not altered in cases and correlated positively with LC number ($r = 0.516$ and $r = 0.369$; $p < 0.008$). The intratesticular oestradiol/testosterone ratio was elevated ($p = 0.005$) in complete SCOS patients compared with controls. In conclusion, testicular aromatase seems to be normal in most subjects with impaired spermatogenesis. However, an altered intratesticular oestradiol/testosterone ratio in some patients with complete SCOS suggests that aromatase is increased, which might contribute to Leydig cell dysfunction.

SCIENTIFIC WORLD JOURNAL. 2009 JAN 18;9:10-6.

CHARACTERIZING PROSTIVA RF TREATMENTS OF THE PROSTATE FOR BPH WITH GADOLINIUM-ENHANCED MRI.

Huidobro C, Larson B, Mynderse S, Myers JJ, Busel D, **Acevedo C,** Larson TR, Mynderse LA.

Transurethral needle ablation (TUNA) is an accepted and effective therapy for the treatment of lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH). Prostiva (Medtronic, Shoreview, MN) is the newest-generation device, which includes a new needle design and radio frequency (RF) generator. This device creates temperatures of 120 degrees C and necrotic lesions in less than 2.5 min. Using previously described techniques, we analyzed dynamic, gadolinium-enhanced MRIs to characterize the ablative properties of the new Prostiva RF device. Ten men with LUTS due to BPH were treated with the standard Prostiva manufacturer-recommended protocol. The bladder neck and lateral lobes received treatment based on prostate volume and prostatic urethral length. Gadolinium-enhanced MRI sequences were obtained prior to and 1 week post-treatment. Analyze software (Mayo Clinic Biomedical Imaging Resource, Rochester, MN) was used to evaluate MRIs. New gadolinium defects were seen in all patients following Prostiva treatments. All lesions coalesced within the prostate. No defects were seen beyond the prostate, and the urethra was spared in all patients. The mean volume of necrosis was 7.56 cc, representing a mean of 11.28% of total prostate volume. Dynamic, gadolinium-enhanced MRIs demonstrate new vascular defects representing necrosis caused by Prostiva RF therapy of the prostate. The standard Prostiva RF protocol produces lesions that coalesce to create larger lesions in the bladder neck and lateral lobes. Compared to the TUNA Precision Plus device, the ablative lesions appear comparable while produced with a shorter burn time.