

*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 2008.*

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# Abstracts de publicaciones internacionales ISI 2008

## ANESTESIOLOGÍA

EUR J ANAESTHESIOL. 2008 FEB;25(2):135-43.

### **TRANSOESOPHAGEAL ECHOCARDIOGRAPHY ACCURATELY DETECTS CARDIAC OUTPUT VARIATION: A PROSPECTIVE COMPARISON WITH THERMODILUTION IN CARDIAC SURGERY.**

Parra V, Fita G, Rovira I, Matute P, Gomar C, Paré C.

**BACKGROUND AND OBJECTIVE:** Intraoperative Doppler ultrasound can be used to measure cardiac output by transoesophageal echocardiography. Recently, its reliability, when compared to the thermodilution technique, has been questioned. The purpose of this study was to compare intraoperative changes in cardiac output measured by echo-Doppler and by thermodilution in cardiac surgery. We also assessed the agreement between the techniques. **METHODS:** Fifty cardiac surgical patients (38 male, 12 female, mean age of 63.4 +/- 14.3 yr) were prospectively included after approval by the Ethics Committee of the Institution. Cardiac output was assessed by thermodilution, with 10 mL saline at 12 degrees C, and simultaneously and blindly by echo-Doppler in deep transgastric view with pulsed wave Doppler at the level of the left ventricular outflow tract. Matched thermodilution cardiac output and echo-Doppler cardiac output measurements were taken three times at the end of expiration, both pre- and post-cardiopulmonary bypass. **RESULTS:** Echo-Doppler measurements were obtained in 44 patients (88%). In three patients, Doppler recordings could not be obtained adequately, and three developed left ventricular outflow tract obstruction after bypass. Bland-Altman analysis revealed a bias of 0.015 L min<sup>-1</sup>, with narrow limits of agreement (-1.21 to 1.22 L min<sup>-1</sup>) and 29.1% error. Echo-Doppler was accurate (92% sensitivity and 71% specificity, P = 0.008 by receiver operating characteristic curves) for detecting more than 10% of change in thermodilution cardiac output. There were no complications related to the study. **CONCLUSIONS:** The agreement between cardiac output by echo-Doppler and by thermodilution is clinically acceptable and transoesophageal echocardiography is a reliable tool to assess significant cardiac output changes in a population of selected patients.

## CARDIOLOGÍA

HYPERTENS RES. 2007 DEC;30(12):1159-67 (APARECE EN PUBMED EN MAYO 08)

### **RELATIONSHIP BETWEEN OXIDATIVE STRESS AND ESSENTIAL HYPERTENSION.**

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

This study investigated the association of blood pressure with blood oxidative stress-related parameters in normotensive and hypertensive subjects. A cross-sectional design was applied to 31 hypertensive patients and 35 healthy normotensive subjects. All subjects were men between the ages of 35 and 60 years. Exclusion criteria were obesity, dyslipidemia, diabetes mellitus, smoking and current use of any medication. All patients underwent 24-h ambulatory blood pressure monitoring and sampling of blood and urine. Antioxidant enzymes activity, reduced/oxidized glutathione ratio (GSH/GSSG), and lipid peroxidation (malondialdehyde) were determined in erythrocytes. Parameters measured in the plasma of test subjects were plasma antioxidant status, lipid peroxidation (8-isoprostane), plasma vitamin C and E, and the blood pressure modulators renin, aldosterone, endothelin-1 and homocysteine. Daytime systolic and diastolic blood pressures of hypertensives were negatively correlated with plasma antioxidant capacity ( $r=-0.46$ ,  $p<0.009$  and  $r=-0.48$ ,  $p<0.007$ ), plasma vitamin C levels ( $r=-0.53$ ,  $p<0.003$  and  $r=-0.44$ ,  $p<0.02$ ), erythrocyte activity of antioxidant enzymes, and erythrocyte GSH/GSSG ratio, with hypertensives showing higher levels of oxidative stress. Blood pressures showed a positive correlation with both plasma and urine 8-isoprostane. Neither plasma vitamin E nor the assessed blood pressure modulator levels showed significant differences between the groups or correlation with blood pressures. These findings demonstrate a strong association between blood pressure and some oxidative stress-related parameters and suggest a possible role of oxidative stress in the pathophysiology

CLIN SCI (LOND). 2008 MAY;114(10):625-34.

### **DECREASE IN OXIDATIVE STRESS THROUGH SUPPLEMENTATION OF VITAMINS C AND E IS ASSOCIATED WITH A REDUCTION IN BLOOD PRESSURE IN PATIENTS WITH ESSENTIAL HYPERTENSION.**

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

Oxidative stress has been associated with mechanisms of EH (essential hypertension). The aim of the present study was to test the hypothesis that the antioxidant properties of vitamins C and E are associated with a decrease in BP (blood pressure) in patients with EH. A randomized double-blind placebo-controlled clinical trial was conducted in 110 men with grade 1 EH (35-60 years of age without obesity, dyslipidaemia and diabetes mellitus, non-smokers, not undergoing vigorous physical exercise, without the use of any medication and/or high consumption of fruit and vegetables). Participants were randomly assigned to receive either vitamins C+E [vitamin C (1 g/day) plus vitamin E (400 international units/day)] or placebo for 8 weeks. Measurements included 24 h ambulatory BP and blood analysis of oxidative-stress-related parameters in erythrocytes (GSH/GSSH ratio, antioxidant enzymes and malondialdehyde) and plasma [FRAP (ferric reducing ability of plasma)], and levels of 8-isoprostane, vitamins C and E were measured at baseline and after treatment. Following administration of vitamins C+E, patients with EH had significantly lower systolic BP, diastolic BP and mean arterial BP and higher erythrocyte and serum antioxidant capacity compared with either placebo-treated patients with EH or the patients with EH at baseline prior to treatment. BP correlated positively with plasma 8-isoprostane levels and negatively with plasma FRAP levels in the vitamins C+E- and placebo-treated groups. In conclusion, the present study supports the view that oxidative stress is involved in the pathogenesis of EH, and that enhancement of antioxidant status by supplementation with vitamins C and E in patients with EH is associated with lower BP. This suggests intervention with antioxidants as an adjunct therapy for hypertension.

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

**(TTA)<sub>n</sub> 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)<sub>n</sub> 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)<sub>n</sub> 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)<sub>n</sub> 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)<sub>n</sub>.

PHARMACOL THER. 2008 APR;118(1):104-27.

**PREVENTION OF ATRIAL FIBRILLATION FOLLOWING CARDIAC SURGERY: BASIS FOR A NOVEL THERAPEUTIC STRATEGY BASED ON NON-HYPOXIC MYOCARDIAL PRECONDITIONING.**

Rodrigo R, Cereceda M, Castillo R, Asenjo R, Zamorano J, Araya J, Castillo-Koch R, Espinoza J, Larraín E.

Atrial fibrillation is the most common complication of cardiac surgical procedures performed with cardiopulmonary bypass. It contributes to increased hospital length of stay and treatment costs. At present, preventive strategies offer only suboptimal benefits, despite improvements in anesthesia, surgical technique, and medical therapy. The pathogenesis of postoperative atrial fibrillation is considered to be multifactorial. However oxidative stress is a major contributory factor representing the unavoidable consequences of ischemia/reperfusion cycle occurring in this setting. Considerable evidence suggests the involvement of reactive oxygen species (ROS) in the pathogenic mechanism of this arrhythmia. Interestingly, the deleterious consequences of high ROS exposure, such as inflammation, cell death (apoptosis/necrosis) or fibrosis, may be abrogated by a myocardial preconditioning process caused by previous exposure to moderate ROS concentration known to trigger survival response mechanisms. The latter condition may be created by n-3 PUFA supplementation that could give rise to an adaptive response characterized by increased expression of myocardial antioxidant enzymes and/or anti-apoptotic pathways. In addition, a further reinforcement of myocardial antioxidant defenses could be obtained through vitamins C and E supplementation, an intervention also known to diminish enzymatic ROS production. Based on this paradigm, this review presents clinical and experimental evidence supporting the pathophysiological and molecular basis for a novel therapeutic approach aimed to diminish the incidence of postoperative atrial fibrillation through a non-hypoxic preconditioning plus a reinforcement of the antioxidant defense system in the myocardial tissue.

PHARMACOL BIOCHEM BEHAV. 2008 FEB;88(4):481-6.

**ISOBOLOGRAPHIC ANALYSIS OF MULTIMODAL ANALGESIA IN AN ANIMAL MODEL OF VISCERAL ACUTE PAIN.**

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

Multiple analgesic-drug combinations are commonly used in the management of acute and chronic pain in humans during multimodal or balanced analgesia. At present, these combinations are used empirically in clinical practice and are considered to be beneficial for the patient. Interactions between two antinociceptive drugs have been thoroughly examined, but the nature of interactions between three analgesics has not been studied. The antinociceptive interaction of ketoprofen (K) with a

mixture of morphine (M) and paracetamol (P) was evaluated using a model of visceral acute tonic pain, the acetic-acid writhing test in mice. The i.p. administration of the combination M/P+K resulted in a significant potentiation of the antinociception induced either by K or by the synergic two-drug mixtures M/K, P/K and M/P. The effect of opioid, cholinergic, adrenergic and serotonergic antagonists on the analgesic interaction was assessed. The pretreatment of mice with atropine (1 mg/kg) did not produce any change in the synergistic interaction of the triple combination. The pretreatment with naltrexone (1 mg/kg) or tropisetron (1 mg/kg) reduced the intensity of M/P+K synergic interaction, while prazosin (0.1 mg/kg) significantly potentiated the synergy. The findings of this work suggest that the two major pathways of descending inhibitory systems, noradrenergic and serotonergic are significantly involved in the mechanism of the antinociceptive synergy induced by the triple combination. On the other hand, opioid pathways also seem to participate, since pretreatment with naltrexone reduced the synergy. In conclusion, the triple combination M/P+K induced a strong synergistic antinociceptive effect, which could be of interest for optimal multimodal clinical analgesia.

## CIRUGÍA

EUR SURG 2008;40:245–52

### **BARRETT'S ESOPHAGUS CAN DEVELOP AFTER ANTIREFLUX SURGERY.**

Csendes, G. Smok, P. Burdiles, I. Braghetto, A. Henriquez

Background: Surgical treatment in patients with gastroesophageal reflux disease (GERD) without Barrett's esophagus (BE) is an excellent alternative therapy to medical treatment, preventing the development of complications and the appearance of BE. Purpose: To determine the newly developed BE in a group of patients without BE prior to surgery, the patients were submitted to a late subjective and objective follow-up. Methods: From 115 non-BE patients submitted to surgery and followed up for a long period, 12 (10.4%) developed intestinal metaplasia after operation. They were submitted to endoscopic, histologic, manometric and functional studies (24-h pH and Bilitec). Results: The 12 patients had an average of 5 endoscopies after surgery with several biopsy samples. Symptoms of recurrent reflux were present in only 10 patients (83%) at a mean of 80 months after surgery. The mean follow-up was 135 months. Four patients showed the absence of pathologic reflux measured by 24-h pH and Bilitec monitoring, while 8 had the presence of abnormal acid reflux. There were no significant differences between endoscopic, histologic and functional studies comparing patients with the presence or absence of pathologic reflux. The time of appearance to intestinal metaplasia from cardiac or oxynto-Cardiac mucosa was 58–90 months. Four patients showed regression of intestinal metaplasia to cardiac mucosa after intensive medical treatment. Conclusions: Antireflux surgery in patients without BE does not prevent the late appearance of BE in near 10% of the cases, provided that a long-term follow-up is performed and several endoscopic and histologic evaluations are repeated. Near 2=3 of these patients showed the presence of acid reflux, while 1=3 showed no abnormal reflux. With this method of follow-up, metaplastic changes from cardiac to intestinal metaplasia and from intestinal metaplasia to low-grade dysplasia can be documented, as well as regression from intestinal metaplasia to cardiac mucosa.

EUR SURG 2008;40:154–64

### **RESULTS OF ANTIREFLUX SURGERY IN PATIENTS WITH BARRETT'S ESOPHAGUS**

A. Csendes

Background: Barrett's esophagus (BE) is defined as the presence of intestinal metaplasia with goblet cells, which replace the normal squamous epithelium of the distal esophagus. Purpose: To review the results of surgical treatment in patients with short- and long-segment BE. Methods: Between 1980 and 2006, a total of 35 articles published in English literature dealing with surgical treatment of patients with BE were reviewed. Clinical success, stop of acid and duodenal reflux into the distal esophagus, endoscopic and histologic evaluations and development of adenocarcinoma were the main issues included. Results: The majority of publications include very few patients (less than 50), the follow-up is less than 5 years in 80% and classic antireflux surgery obtains clinical success before 5 years of follow-up in 81% of the patients, but this success

deteriorates with the length of follow-up. Acid reflux before and after surgery was evaluated in few publications and duodeno-esophageal reflux in only 3 papers. The majority of reports include only 1 endoscopic evaluation after surgery while histologic analysis of Barrett's mucosa has shown regression of intestinal metaplasia in only 5%. Progression of adenocarcinoma has been reported in 3.8%, even in asymptomatic patients. On the contrary, the acid suppression and duodena diversion procedure obtained 91% of clinical success at a late follow-up (8 to 10 years), permanent control of acid and duodenal reflux, regression of intestinal metaplasia to cardiac mucosa in 55% of the patients and no progression to high grade dysplasia or adenocarcinoma has been documented. Patients with short-segment BE have shown very good results after laparoscopic fundoplication. Conclusions: Antireflux surgery in patients with long-segment BE does not prevent the development of adenocarcinoma. Acid suppression and duodenal diversion procedure is an alternative procedure, specially in patients below 60 years of age.

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<sup>2</sup>. 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 circular stapler-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.

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<sup>2</sup>; 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 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/m<sup>2</sup>. 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 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.

WORLD J SURG. 2008 OCT;32(10):2237-43.

**THE RELATIONSHIP OF MIRIZZI SYNDROME AND CHOLECYSTOENTERIC FISTULA: VALIDATION OF A MODIFIED CLASSIFICATION.**

Beltran MA, Csendes A, Cruces KS.

**BACKGROUND:** Mirizzi syndrome and cholecystoenteric fistula with or without gallstone ileus are late complications of gallstone disease. We previously suggested that the natural history of Mirizzi syndrome may not end with just a cholecystobiliary fistula and that the continuous inflammation in the triangle of Calot area may result in a complex fistula involving the biliary tract and the adjacent viscera. The purpose of this study was to establish the relationship of Mirizzi syndrome with cholecystoenteric fistulas. **METHODS:** We retrospectively reviewed the records of all patients older than aged 18 years submitted to emergency or elective cholecystectomy from 1995 to 2006. Of 5,673 cholecystectomies performed during that period, we found 327 (5.7%) patients with Mirizzi syndrome and 105 (1.8%) patients with cholecystoenteric fistula. Ninety-four (89.5%) patients with cholecystoenteric fistula also had an associated Mirizzi syndrome. **RESULTS:** Cholecystoenteric fistula was associated with Mirizzi syndrome ( $p < 0.0001$ ), increased age was associated with Mirizzi syndrome and cholecystoenteric fistula ( $p < 0.0001$ ), and female gender was associated with Mirizzi syndrome ( $p < 0.0001$ ). **CONCLUSION:** When during surgery for gallstone disease a cholecystoenteric fistula is encountered, the possibility of an associated Mirizzi syndrome must be considered. The findings of this study confirm the association of Mirizzi syndrome with cholecystoenteric fistula.

J GASTROINTEST SURG. 2008 SEP;12(9):1508-11.

**BEHAVIOR OF THE INFECTION BY HELICOBACTER PYLORI OF THE GASTRIC REMNANT AFTER SUBTOTAL GASTRECTOMY AND ROUX-EN-Y ANASTOMOSIS FOR BENIGN DISEASES**

Csendes A, Smok G, Burgos AM.

**INTRODUCTION:** Reinfection by *Helicobacter pylori* of the gastric remnant after partial gastrectomy has been implicated in the development of gastric cancer at the gastric stump. **OBJECTIVE:** The aim of this study is to determine the rate of infection by *H. pylori* after partial gastrectomy and Roux-en-Y anastomosis for benign disease. **MATERIALS AND METHODS:** A total of 79 patients with long segment Barrett's esophagus were submitted to vagotomy, anti-reflux surgery, two thirds distal gastrectomy, and Roux-en-Y anastomosis 70 cm long. In all preoperative biopsy samples were taken from the antrum. After surgery, four endoscopic studies were performed in different periods of time. Mean follow-up was 98 months after operation (60-240). **RESULTS:** Three groups of patients were identified: (a) group 1, 43 patients (54%) who had no preoperative infection by *H. pylori* and remained so late after surgery; (b) group 2, 21 patients (27%) who had no preoperative infection by *H. pylori* but presented infection of the gastric remnant that increased parallel to the length of follow-up; (c) group 3, 15 patients (19%) who presented infection by *H. pylori* before surgery. From them, 11 showed reinfection of the gastric remnant, while four patients had no reinfection. **CONCLUSION:** After partial gastrectomy and Roux-en-Y anastomosis for benign disease, there are three different patterns of behavior regarding reinfection or not by *H. pylori*. A total of 41% of patients presented *H. pylori* reinfection at the gastric remnant after Roux-en-Y anastomosis, which increased parallel to the length of follow-up.

PLAST RECONSTR SURG. 2008 JUN;121(6):2136-41.

**CORTICAL AND PARTIALLY CANCELLOUS BONE SPREADER GRAFTS: AN ALTERNATIVE FOR THE TREATMENT OF CARTILAGE-DEPLETED NOSES.**

Prado A, Andrades P, Guerra C, Wisnia P.

No abstract available

J PLAST RECONSTR AESTHET SURG. 2008 NOV;61(11):1284-93.

**UNDERSTANDING MODERN BREAST REDUCTION TECHNIQUES WITH A SIMPLIFIED APPROACH.**

Andrades P, Prado A.

**OBJECTIVE:** The purpose of this study was to analyse the geometrical principles of breast reduction, to propose a classification of reduction mammoplasty techniques and to show a simplified approach based on the authors experience. **METHODS:** A thorough analysis of the geometrical differences between the normal and enlarged breast was performed. As a result of this analysis, the concept of separate management of the skin and gland for breast reduction was used as a method to classify the different techniques. Some aspects of technique selection and the authors' preferences are also discussed. **RESULTS:** The four geometric differences between the normal and enlarged breast are: vertical excess, broadened base, horizontal excess and a descended nipple-areola complex. All breast reduction techniques use a specific pedicle and a separate skin incision pattern, so they should be named after the scar and pedicle used. Technique selection must consider the degree of hypertrophy and ptosis, the skin and gland quality, the patient's requirements, and the surgeon's experience and preferences. Some clinical examples are provided. **CONCLUSION:** The comprehension of basic breast geometry, a universal language for communication and a simple algorithm to approach the breast reduction patient are valuable tools, particularly for the surgeon who is becoming acquainted with reduction mammoplasty procedures.

J RECONSTR MICROSURG. 2008 APR;24(3):177-81.

**VASCULAR DIAMETER DETERMINING THE MAGNIFICATION FOR A MICROVASCULAR ANASTOMOSIS.**

Andrades P, Benítez S, Danilla S, Erazo C, Hasbun A, Fix J.

The purpose of this study was to determine the association between vascular diameters and amount of magnification and to assess the influence of the magnification media on the microanastomosis quality and permeability. Sixty arterial microanastomoses were distributed into three groups: group I (diameter 1.5 mm), group II (1.5 to 2.5 mm), and group III (> 2.5 mm). The models used were carotid artery of Sprague-Dawley rats and carotid and abdominal artery of wild rabbits. In each group, 10 anastomoses were performed with 2.5 x loupes and 10 with 10 x microscope. The total time of anastomosis, the quality of the anastomosis (Gorman scale), and 24-hour permeability rate were measured. The total anastomotic time and quality had statistical differences for the microscope by analyzing the total sample and group I only. The global permeability was 83% for the microscope and 40% for the loupe. The same result was observed in group I but no differences were observed in the other groups. The histology and the survey showed similar results. Microanastomoses performed under a microscope (10 x) were performed in less time, were of better quality, and had higher permeability rates when compared with those performed under a loupe (2.5 x). In vessels < 1.5 mm, these differences were statistically significant but in vessels > 1.5 mm no differences were observed.

LARYNGOSCOPE. 2008 JUL;118(7):1157-63.

**FISTULA ANALYSIS AFTER RADIAL FOREARM FREE FLAP RECONSTRUCTION OF HYPOPHARYNGEAL DEFECTS.**

Andrades P, Pehler SF, Baranano CF, Magnuson JS, Carroll WR, Rosenthal EL.

**OBJECTIVE/HYPOTHESIS:** To evaluate risk factors and management options for fistula formation after hypopharyngeal reconstruction using the radial forearm free flap reconstruction. **STUDY DESIGN:** Retrospective cohort study. **METHODS:** Patients undergoing radial forearm free flap for hypopharyngeal reconstruction were retrospectively reviewed. A total of 104 patients underwent this procedure between 2001 and 2007. Fistulas were classified as mild or severe depending on the response to conservative management. Demographics, operative details, pathology, and postoperative course were recorded as the prognostic variables. Univariate analysis and a logistic regression model were used to identify associated factors. **RESULTS:** Pharyngocutaneous fistula developed in 30 (28.8%) patients. Recurrence, cancer stage, cancer location, type of ablative surgery, and the addition of other oncologic procedures were identified as significant predictors of fistula formation. Fistula significantly increases hospital stay and recipient site complications such as flap survival, infection, and bleeding. Functional results such as diet, deformity, and socialization were also negatively affected by fistula development. One third of the cases responded to conservative management, and 20 cases required a surgical procedure to definitively close the fistulous track. **CONCLUSIONS:** Fistula formation remains a significant cause of morbidity associated with hypopharyngeal reconstruction. Postoperative course and successful preventive strategies are discussed.



CELL TRANSPLANT. 2008;17(6):713-20.

### **IL-10 AND IL-4 IN SKIN ALLOGRAFT SURVIVAL INDUCED BY T-CELL DEPLETION PLUS DEOXYSPERGUALIN.**

Asiedu C, Andrades P, Ray PD, George JF, Thomas JM.

The mechanisms mediating T-cell depletion plus 15-deoxyspergualin (DSG)-induced prolonged allograft survival or tolerance are uncertain. The purpose of this study is to evaluate the role of IL-4 and IL-10 in prolonged allograft survival induced by T-cell depletion plus DSG. MHC mismatched skin allograft transplantation was performed, using wild-type and three separate knockout (i.e., IL-4<sup>-/-</sup>, Stat6<sup>-/-</sup>, or IL-1<sup>-/-</sup>) mice as recipients. Induction therapy consisted of T-cell depletion and or brief course of DSG. The data demonstrate that monotherapy with T-cell-depleting mAbs or DSG prolonged skin allograft survival, compared to controls, in wild-type Balb/c recipients [median survival time (MST) = 25 and 21 vs. 10 days,  $p < 0.007$ ]. T-cell depletion plus DSG further augmented skin allograft survival in wild-type animals relative to monotherapy (MST = 35 days vs. 25 and 21 days,  $p < 0.006$  vs. mAbs or DSG only), and was equally effective in IL-4<sup>-/-</sup> and Stat6<sup>-/-</sup> recipients. In contrast, combined therapy was no better than monotherapy in IL-10<sup>-/-</sup> animals ( $p > 0.05$ ). Furthermore, skin allograft survival after combined therapy was shorter in IL-10<sup>-/-</sup> versus wild-type recipients (MST 20 and 41 days, respectively,  $p < 0.001$ ). IL-4-mediated signaling through Stat6 is dispensable for prolonged allograft survival induced by T-cell depletion plus DSG. In contrast, IL-10 appears to be important for prolonged allograft survival induced by combined therapy in this model.

HEAD NECK. 2008 OCT;30(10):1295-302. LINKS

### **ZYGOMATIC-MAXILLARY BUTTRESS RECONSTRUCTION OF MIDFACE DEFECTS WITH THE OSTEOCUTANEOUS RADIAL FOREARM FREE FLAP.**

Andrades P, Rosenthal EL, Carroll WR, Baranano CF, Peters GE.

**BACKGROUND:** The purpose of this study was to evaluate morbidity, functional, and aesthetic outcomes in midface zygomatic-maxillary buttress reconstruction using the osteocutaneous radial forearm free flap (OCRFFF). **METHODS:** A retrospective review of 24 consecutive patients that underwent midface reconstruction using the OCRFFF was performed. All patients had variable extension of maxillectomy defects that requires restoration of the zygomatic-maxillary buttress. After harvest, the OCRFFF was fixed transversely with miniplates connecting the remaining zygoma to the anterior maxilla. The orbital support was given by titanium mesh when needed that was fixed to the radial forearm bone anteriorly and placed on the remaining orbital floor posteriorly. The skin paddle was used for intraoral lining, external skin coverage, or both. The main outcome measures were flap success, donor-site morbidity, orbital, and oral complications. Facial contour, speech understandability, swallowing, oronasal separation, and socialization were also analyzed. **RESULTS:** There were 6 women and 18 men, with an average age of 66 years old (range, 34-87). The resulting defects after maxillectomy were (according to the Cordeiro classification; Disa et al, *Ann Plast Surg* 2001;47:612-619; Santamaria and Cordeiro, *J Surg Oncol* 2006;94:522-531): type I (8.3%), type II (33.3%), type III (45.8%), and type IV (12.5%). There were no flap losses. Donor-site complications included partial loss of the split thickness skin graft (25%) and 1 radial bone fracture. The most significant recipient-site complications were severe ectropion (24%), dystopia (8%), and oronasal fistula (12%). All the complications occurred in patients with defects that required orbital floor reconstruction and/or cheek skin coverage. The average follow-up was 11.5 months, and over 80% of the patients had adequate swallowing, speech, and reincorporation to normal daily activities. **CONCLUSIONS:** The OCRFFF is an excellent alternative for midface reconstruction of the zygomatic-maxillary buttress. Complications were more common in patients who underwent resection of the orbital rim and floor (type III and IV defects) or external cheek skin. Copyright (c) 2008 Wiley Periodicals, Inc. *Head Neck* 2008.

PLAST RECONSTR SURG. 2008 OCT;122(4):1121-30.

### **THE IMPORTANCE OF RADICAL INTRAVELAR VELOPLASTY DURING TWO-FLAP PALATOPLASTY.**

Andrades P, Espinosa-de-los-Monteros A, Shell DH 4th, Thurston TE, Fowler JS, Xavier ST, Ray PD, Grant JH 3rd.

**BACKGROUND:** The purpose of this study was to compare the two-flap palatoplasty technique for cleft palate repair, with and without radical intravelar veloplasty, with special emphasis on the fistula rate and speech outcome. **METHODS:** A retrospective, time-series cohort of 213 consecutive patients with primary two-flap palatoplasty before and after the introduction of a radical intravelar veloplasty was studied. The main outcome measures were immediate postoperative complications, oronasal fistula

rate, and speech. A perceptual speech evaluation was performed by two speech pathologists and included hypernasality, nasal emission, articulation, intelligibility, and overall velopharyngeal competence. The need for secondary palate surgery for velopharyngeal insufficiency was also analyzed. RESULTS: There were no differences in postoperative complications between the two study groups. Postoperative morbidity occurred in six patients (2.8 percent) and consisted of two patients with respiratory compromise, two patients who required reoperation for bleeding, and two patients with oronasal fistula. Perceptual speech evaluation demonstrated significantly better speech outcomes (81.9 percent versus 49.5 percent,  $p < 0.001$ ) and a significantly lower rate of secondary palate surgery for velopharyngeal insufficiency (29 percent versus 6.7 percent,  $p = 0.008$ ) in the radical intravelar veloplasty group. The most important predictive factor of speech outcome was the addition of a radical intravelar veloplasty (odds ratio, 0.175; 95 percent confidence interval, 0.039 to 0.785). CONCLUSIONS: Despite study design limitations, such as experience bias and follow-up differences, this study demonstrates that radical intravelar veloplasty may enhance the functional results of the two-flap palatoplasty without increasing postoperative morbidity. A novel classification of the muscle repair is proposed based on the amount of muscle dissection and repositioning.

DIABETOLOGIA. 2008 JUL;51(7):1236-44. EPUB 2008 MAY 9.

#### **PANCREATIC ISLET ISOLATION VARIABLES IN NON-HUMAN PRIMATES (RHESUS MACAQUES).**

Andrades P, Asiedu CK, Gansuud B, Inusah S, Goodwin KJ, Deckard LA, Jargal U, Thomas JM.

BACKGROUND: Non-human primates (NHPs) are important preclinical models for pancreatic islet transplantation (PIT) because of their close phylogenetic and immunological relationship with humans. However, low availability of NHP tissue, long learning curves and prohibitive expenses constrain the consistency of isolated NHP islets for PIT studies. To advance preclinical studies, we attempted to identify key variables that consistently influence the quantity and quality of NHP islets. METHODS: Seventy-two consecutive pancreatic islet isolations from rhesus macaques were reviewed retrospectively. A scaled down, semi-automated islet isolation method was used, and monkeys with streptozotocin-induced diabetes, weighing 3-7 kg, served as recipients for allotransplantation. We analysed the effects of 22 independent variables grouped as donor factors, surgical factors and isolation technique factors. Islet yields, success of isolation and transplantation results were used as quantitative and qualitative outcomes. RESULTS: In the multivariate analysis, variables that significantly affected islet yield were the type of monkey, pancreas preservation, enzyme lot and volume of enzyme delivered. The variables associated with successful isolation were the enzyme lot and volume delivered. The transplant result was correlated with pancreas preservation, enzyme lot, endotoxin levels and COBE collection method. CONCLUSIONS: Islet quantity and quality are highly variable between isolations. The data reviewed suggest that future NHP isolations should use bilayer preservation, infuse more than 80 ml of Liberase into the pancreas, collect non-fractionated tissue from the COBE, and strictly monitor for infection.

SURG CLIN NORTH AM. 2008 FEB;88(1):61-83, VIII.

#### **OPEN REPAIR OF VENTRAL INCISIONAL HERNIAS.**

Shell DH 4th, de la Torre J, Andrades P, Vasconez LO.

Despite advances in many fields of surgery, incisional hernias still remain a significant problem. There is a lack of general consensus among surgeons regarding optimal treatment. A surgeon's approach is often based on tradition rather than clinical evidence. The surgeon's treatment plan should be comprehensive, with attention focused not merely on restoration of structural continuity. An understanding of the structural and functional anatomy of the abdominal wall and an appreciation of the importance of restoring dynamic function are necessary for the successful reconstruction of the abdominal wall.

J MED PRIMATOL. 2008 FEB;37(1):1-11.

#### **INVARIANT NATURAL KILLER T CELLS FROM RHESUS MACAQUE SPLEEN AND PERIPHERAL BLOOD ARE PHENOTYPICALLY AND FUNCTIONALLY DISTINCT POPULATIONS.**

Gansuud B, Goodwin J, Asiedu CK, Jiang XL, Jargal U, Andrades P, Exley MA, Thomas JM.

BACKGROUND: Natural killer T cells (NKT) possess dual functions of innate and adaptive immune systems, controlling viral infections and regulating autoimmune diseases. Non-human primates (NHP) are penultimate models for advancing therapeutic immunoregulatory strategies for translational application in humans, though, little is known about NHP NKT cells. Here we

characterized rhesus macaque NKT cells ex vivo. METHODS: The frequency, phenotype and intracellular cytokine production of V alpha 24+ 6B11+ invariant NKT (iNKT) cells were analyzed by multi-color flow cytometry. V alpha 24J alpha Q mRNA expression was analyzed by real-time RT-PCR. RESULTS: The frequencies of peripheral blood (PB) and spleen V alpha 24+ 6B11+ iNKT cells were not significantly different. The iNKT cell subset in spleen was significantly increased for CD4+ CD8+ and CD3+ CD56+ co-expression as well as intracellular interleukin-4 production, which was rarely observed in circulating PB. CONCLUSION: Spleen iNKT cells in rhesus macaques are Th2 biased and display phenotypically and functionally distinct profiles from their PB counterpart.

ANN PLAST SURG. 2008 MAY;60(5):562-7.

### **ISCHEMIC COMPLICATIONS IN PEDICLE, FREE, AND MUSCLE SPARING TRANSVERSE RECTUS ABDOMINIS MYOCUTANEOUS FLAPS FOR BREAST RECONSTRUCTION.**

Andrades P, Fix RJ, Danilla S, Howell RE 3rd, Campbell WJ, De la Torre J, Vasconez LO.

Muscle sparing and perforator flaps techniques for breast reconstruction have focused in reducing the donor site morbidity. Theoretically this may result in a less robust blood supply to the flap. The purpose of this study was to assess flap ischemic complications with the pedicle, free, and the different muscle sparing transverse rectus abdominis myocutaneous (TRAMs) flaps for breast reconstruction and determine the factors associated with these complications. A total of 301 consecutive patients that underwent 399 breast reconstructions were retrospectively reviewed. Patient, oncologic, and reconstruction data were recorded. A flap ischemic complication scale was design including: wound healing problems, skin flap necrosis, fat necrosis, partial flap loss, and total flap loss. Analysis of donor site complications, bilateral and unilateral reconstructions were also performed. There were 147 pedicle TRAM and 154 free TRAM with the following subgroup distribution: MS-0 = 102; MS-1 = 37; and MS-2 = 15 patients. The groups were comparable in relation to age, comorbidities, cancer stage, and treatment. The overall complication rate after reconstruction had no statistical differences between the groups. The variables related to flap ischemia were statistically lower in the free TRAM. Mild and severe fat necrosis were the indicators with a statistical difference. The MS-0 group had lower ischemic complications and fat necrosis than the pedicled group, but no differences were observed for the MS-1 and MS-2 groups. The same results were seen in the unilateral reconstructions but not in the bilateral ones. No differences in donor site bulging or hernia were observed between the groups. In our study, the free TRAM flap demonstrated lower ischemic complications than the pedicle TRAM. A trend for decreased flap blood supply when more muscle is preserved and less number of perforators are used with a constant tissue volume was observed.

J MED PRIMATOL. 2008 FEB;37(1):1-11.

### **INVARIANT NATURAL KILLER T CELLS FROM RHESUS MACAQUE SPLEEN AND PERIPHERAL BLOOD ARE PHENOTYPICALLY AND FUNCTIONALLY DISTINCT POPULATIONS.**

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J RECONSTR MICROSURG. 2008 JUL;24(5):315-22

**DISTALLY BASED SUPERFICIAL SURAL FASCIOMUSCULOCUTANEOUS FLAP: A RELIABLE SOLUTION FOR DISTAL LOWER EXTREMITY RECONSTRUCTION.**

Reyes S, Andrades P, Fix RJ, Vasconez LO.

The objective of this study is to present a simple and rapid approach to elevate a consistent superficial sural fasciomusculocutaneous flap and show its clinical applications. All the patients with lower limb defects who underwent reconstruction using the distally based fasciomusculocutaneous sural flap were included in the study. The flap was elevated with a cuff of gastrocnemius muscle under the skin paddle, and the distal pedicle was dissected until 5 cm over the lateral malleolus. The donor site is primarily closed or skin-grafted. From March 2004 to August 2006, this distally based superficial sural fasciomusculocutaneous flap was applied to nine patients. All the defects resulted from traumatic injuries of the distal third of the leg, ankle, or foot, combined with bone or tendon exposure. Two flaps developed minor distal skin necrosis that recovered uneventfully with conservative therapy. The other flaps had an adequate postoperative evolution with good blood supply, contour, and function. The superficial sural fasciomusculocutaneous flap is a simple and consistent alternative for distal lower limb reconstruction, particularly when microsurgery is not available.

J PLAST RECONSTR AESTHET SURG. 2008 DEC 31.

**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.

J PLAST RECONSTR AESTHET SURG. 2008 DEC 31.

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J PLAST RECONSTR AESTHET SURG. 2008 SEP 3.

**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. 2008 MAR;121(3):983-93.

**FULL-FACE CARBON DIOXIDE LASER RESURFACING: A 10-YEAR FOLLOW-UP DESCRIPTIVE STUDY.**

Prado A, Andrades P, Danilla S, Benitez S, Reyes S, Valenzuela G, Guridi R, Fuentes P.

BACKGROUND: The purposes of this study were to retrospectively compare the 1-, 5-, and 10-year cosmetic outcomes of full-face carbon dioxide laser resurfacing using the SilkTouch technology, and analyze its advantages, disadvantages, and long-term results. METHODS: Photographic results of full-face carbon dioxide laser resurfacing were evaluated after 1, 5, and 10 years. Statistical analysis considered surgeon and patient satisfaction based on a predetermined cosmetic visual analogue scale. Patients and two plastic surgeons unfamiliar with the cases evaluated objective postresurfacing results using Beausang's grading system and a modified wrinkle assessment scale. RESULTS: One hundred fifty-nine patients were treated and 46 patients completed 1-, 5-, and 10-year follow-up. Combined aesthetic procedures to the full-face carbon dioxide resurfacing were transcutaneous upper lid/lower lid transconjunctival blepharoplasty and endoscopic brow lifts in 15 patients. After 1 year, some relapse occurred, but the overall aesthetic result remained very good. At 5 and 10 years, respectively, 32 and 20 percent of the sample maintained good-quality skin texture; 22 and 19 percent achieved correction of skin pigmentation without scars; and 88 and 98 percent needed correction of recurrent rhytides, jowling, and redundant skin. Permanent hypopigmentation was found in four cases (8.7 percent). CONCLUSIONS: The authors' early experience with the carbon dioxide laser was excellent, but after 1 year, they noticed lines of demarcation between treated and nontreated skin or persistent erythema. After 5 and 10 years, advantages were maintenance of good skin texture, ablation of fine wrinkles, and long-term correction of skin pigmentation. Disadvantages included permanent hypopigmentation of the mandible-neck junction, telangiectasia, and possible accentuation of skin redundancy.

AESTHETIC PLAST SURG. 2008 SEP;32(5):748-52.

**AREOLA-NIPPLE PERCEPTION THRESHOLD TO FARADIC ELECTRICITY: A NEW MEASURE OF SENSIBILITY OF THE BREASTS.**

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

BACKGROUND: We describe a new method to study the sensibility of the nipple-areola complex of the breast with faradic electricity delivered through an electromyographic device used to monitor peripheral nerve conduction. METHODS: The objective results of faradic pulses (2-50 mA per pulse) delivered to the nipple-areola complex of the breast through a Nihon-Kohden II machine (Evoked potential/Electromyographs, Nihon-Kohden Co., Japan) were evaluated in normal volunteers to get a basal measure that was defined by the patient as "a soft electric discharge." The measures were recorded and their output discharges averaged (at least 5 to each complex). RESULTS: Twenty-eight volunteers with normal breasts, 28 patients with breast hypertrophy before and after breast reduction, and 28 patients before and after breast augmentation were studied. The faradic pulses were perceived from 1.5 to 3.5 mA in the areola and from 3 to 5.5 mA in the nipple in the control group and from 4.5 to 7.0 mA in the areola and from 6.5 to 9.5 mA in the nipple in the breast hypertrophy group with no significant changes before and after surgery. In the breast augmentation group the faradic pulses were very similar to the volunteers that had normal breasts, but 13 months after breast augmentation with silicone gel prosthesis, a difference was found because all the patients had a higher threshold and three cases had lost sensibility of the nipple-areola complex. CONCLUSION: In normal breasts the areola had a lower threshold for faradic pulses compared to the nipple. Hypertrophic breasts had a higher threshold to the faradic stimulation than normal subjects in the pre- and postoperative period. Hypoplastic breasts before breast augmentation had a perception threshold similar to that of the normal volunteers but after breast augmentation this perception was much higher.

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  $K_m=39.4\pm 0.24$  microM and  $V_{max}=6.0\times 10^{-3}$  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  $0.339\times 10^{-3}$  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.

OBES SURG. 2008 OCT 2.

**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<sup>2</sup>. 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.

SURG TODAY. 2008;38(12):1124-8.

### **VIDEOTHORACOSCOPIC MANAGEMENT OF MIDDLE ESOPHAGEAL DIVERTICULUM WITH SECONDARY BRONCHESOPHAGEAL FISTULA: REPORT OF A CASE.**

Braghetto I, Cardemil G, Schwartz E, Valladares H, Rencoret G, Estay R, Rodriguez-Navarro AJ.

Middle esophageal diverticulum is rare, but can result in bronchoesophageal fistula. Previous reports have described open surgical techniques to treat esophageal diverticula, but few have evaluated the effectiveness of a videothoracoscopy approach. We report a case of middle esophageal diverticulum associated with bronchoesophageal fistula, managed successfully with videothoracoscopy. We also review the relevant literature.

## **DERMATOLOGÍA**

ARCH DERMATOL 2008; VOL 144 (NO. 6):724-6

### **LAMOTRIGINE-INDUCED TOXIC EPIDERMAL NECROLYSIS TREATED WITH INTRAVENOUS IMMUNOGLOBULIN AND AMNIOTIC MEMBRANES**

Rodrigo Schwartz, Esteban Avello, Francis Palisson.

No abstract available

## **ENDOCRINOLOGÍA**

ENDOCCR PRACT. 2008 MAR;14(2):168-74.

### **EXPRESSION OF CYTOKERATIN 19 IN THE DIAGNOSIS OF THYROID PAPILLARY CARCINOMA BY QUANTITATIVE POLYMERASE CHAIN REACTION.**

Flanagan JN, Pineda P, Knapp PE, De Las Morenas A, Lee SL, Braverman LE.

**OBJECTIVE:** To examine cytokeratin 19 (CK19) expression levels by immunostaining for protein and quantitative reverse-transcription polymerase chain reaction (qPCR) for messenger RNA in thyroid surgical specimens from patients with papillary carcinoma (PC) and other types of thyroid lesions. **METHODS:** A total of 54 randomly selected postoperative thyroid tissue samples were collected for formalin-fixed paraffin-embedded sectioning or flash-frozen total RNA extraction for complementary DNA synthesis (or both). Tissue sections were stained for CK19 expression with use of a specific monoclonal antibody. qPCR was performed on synthesized complementary DNA with sequence-specific primers for human CK19 in conjunction with ribonucleoprotein S18 for normalization. **RESULTS:** CK19 immunostaining was diffuse and intense in all PC lesions and considerably less in specimens that harbored both Hashimoto thyroiditis (HT) and PC. CK19 immunostaining was mostly absent in areas of multinodular goiter (MNG), with occasional focal staining. HT and Hürthle cell adenoma were essentially negative for CK19 immunostaining, except for weak staining in focal areas. Analysis of CK19 gene expression by qPCR revealed that the PC samples tested ( $n = 21$ ) had significantly higher levels in comparison with all other groups ( $P < 0.0001$ ). Furthermore, PC had a 32-fold mean level increase in CK19 expression in comparison with CK19 expression in MNG. Hürthle cell adenoma ( $n = 5$ ) and HT ( $n = 7$ ) lesions were similar to MNG in CK19 expression, with some overlap of CK19 between HT and PC. **CONCLUSION:** The data indicate that expression of CK19 by qPCR is a quantitative method for distinguishing PC lesions from other types of thyroid lesions, in contrast to the more qualitative immunohistochemistry. Moreover, qPCR of CK19 is a valid method that could be used as an ancillary tool in diagnosing thyroid cancer. The expression of CK19 by qPCR may be adopted, in combination with other markers, for molecular definition of the various subtypes of thyroid lesions assessed by fine-needle aspiration biopsy in the preoperative diagnosis of thyroid lesions.

ENDOCRINE. 2008 NOV 15.

**EVALUATION OF THE EFFECT OF CALORIC RESTRICTION ON SERUM BDNF IN OVERWEIGHT AND OBESE SUBJECTS: PRELIMINARY EVIDENCES.**

Araya AV, Orellana X, Espinoza J.

Brain-derived neurotrophic factor (BDNF) has emerged as a new element related with insulin resistance and obesity. Objective To evaluate the effect of a 3-month reduced-calorie diet (RCD) on serum BDNF concentrations in overweight and obese subjects. Subjects Seventeen healthy overweight and obese subjects of both sexes (24-48 years, BMI 34.6 +/- 1.1 kg/m<sup>2</sup>). Methods Anthropometry, oral glucose tolerance test (OGTT), lipid levels, and serum BDNF were measured at baseline and at the end of the third month. Reduced-calorie diet was defined as a 25% reduction in energy intake composed of: 55% carbohydrates, 20% proteins, and 25% fat (less than 10% saturated fat and over 10% nonsaturated fat). Refined sugar was not allowed. Results There was a significant decrease in BMI, waist circumference, body fat percentage, fasting glucose, post-OGTT glucose levels, area under the curve of glucose, and HOMA2-IR after 3 months of RCD. Serum BDNF showed a significant increase (3.97 +/- 0.87 to 6.75 +/- 1.62 ng/ml, P = 0.02). Final serum BDNF correlated negatively with weight (r = -0.51, P = 0.03), and basal post-OGTT insulin correlated positively with final serum BDNF (r = 0.48, P = 0.04). Conclusions Serum BDNF increases in insulin-resistant overweight and obese subjects after three months on a RCD. This observation could indicate that BDNF may be modulated in humans through diet composition.

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, Santibañez C, Araya AV, Smok G, Csendes A, Gutierrez 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. Obesity (2009) 17 5, 973-979. doi:10.1038/oby.2008.601.



## GASTROENTEROLOGÍA

GASTROENTEROL HEPATOL. 2008 FEB;31(2):59-74.

### **CONSENSO LATINOAMERICANO DE ESTREÑIMIENTO CRÓNICO.**

Schmulson W., Francisconi C., Olden K., Aguilar P., Bustos-Fernandez L., Cohen H., Passos M.C., Gonzalez-Martinez M.A., Iade B., Iantorno G., Ledesma G., Lopez-Colombo A., Perez C.L., Madrid-Silva A.M., Quilici F., Quintero S., Rodriguez V., Suazo J., Valenzuela J., Zolezzi A.,

The Latin-American Consensus on Chronic Constipation aimed to establish guidelines to improve the identification, diagnosis and treatment of this disorder in the region. Two coordinators and an honorary coordinator established the process and the topics to be discussed, based on a systematic review of the literature published in the previous 10 years, since 1995. Seventeen members participated with the support of their local gastroenterology societies. The members reviewed the different subjects based on the levels of evidence and grades of recommendation; the topics were then discussed in a plenary session. A written report was drafted and the coordinators prepared the final declarations to be submitted to a vote by all the members in October 2006. The consensus concluded that chronic constipation has an estimated prevalence of 5-21% in the region, with a female-to-male ratio of 3:1. Among individuals with constipation, 75% use some type of medication, with more than 50% using home remedies. A diagnosis based on Rome Criteria was recommended and diagnostic testing only in persons older than 50 years or with alarm symptoms. The use of barium enema as an initial investigation was recommended only in countries with a high prevalence of idiopathic megacolon or Chagas' disease. Recommendations on treatment included an increase in dietary fiber of up to 25-30 g/day (grade C). No evidence was found to recommend measures such as exercise, increased water intake, or frequent visits to the toilet. Fiber supplements such as Psyllium received a grade B and pharmacological treatments such as tegaserod and polyethylene glycol, both grade A. There was insufficient evidence to recommend lactulose, but the consensus did not dis advise its use when necessary. Complementary investigations such as colonic transit followed by anorectal manometry and defecography were only recommended to rule out colonic inertia and/or obstructive defecation in patients not responding to treatment. Biofeedback was recommended (grade B) for those with pelvic dyssynergia.

GASTROENTEROL HEPATOL. 2008 JAN;31(1):8-11.

### **[STUDY OF CELIAC DISEASE IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER AND AUTOIMMUNE HEPATIC DISEASES] [ARTICLE IN SPANISH]**

Valera JM, Hurtado C, Poniachik J, Abumohor P, Brahm J.

Celiac disease (CD) has been associated with non-alcoholic fatty liver disease (NAFLD) and other chronic liver diseases (CLD), such as primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH) and primary sclerosing cholangitis (PSC). AIM: To study the frequency of serological markers of CD in patients with NAFLD and CLD and their correlation with duodenal biopsy. PATIENTS AND METHODS: In patients with NAFLD, PBC, AIH and PSC, we studied anti-endomysium (AE) IgA by indirect immunofluorescence and anti-gliadin IgA-IgG (AG) and human anti-tissue transglutaminase (tTG) IgA antibodies by an ELISA technique. Patients with positive serology for at least one marker underwent endoscopy with duodenal biopsies. RESULTS: Positive CD markers were found in 9 of 101 patients (8.9%): 7 patients were positive for tTG alone, 1 for AE and AG, and 1 patient for 3 antibodies. Positivity was as follows: 3/38 (7.9%) in NAFLD, 3/44 (6.8%) in PBC, 2/16 (12.5%) in AIH and 1/3 in PSC. Endoscopy was performed in 8 patients, with normal duodenal biopsy in 7 and 1 patient with Marsh stage 1 CD with NAFLD, positive AE and AG. The only patient with 3 positive markers died during the study without undergoing endoscopy. None of the patients had symptoms suggestive of CD. CONCLUSION: A high prevalence of positive tTG was found in patients with CLD and NAFLD. However, duodenal biopsy should be performed in these patients, given that the results of this procedure were normal in most patients in this study.

GASTROENTEROL HEPATOL. 2008 FEB;31(2):79-81.

### **HEMOBILIA TRAUMÁTICA: CASO CLÍNICO Y REVISIÓN DE LA LITERATURA MÉDICA.**

Munoz C., Fernandez M., Brahm J.,

Traumatic hemobilia consists of hemorrhage into the biliary tract as a result of abdominal trauma. The classical triad of biliary colic, jaundice and upper gastrointestinal bleeding is not a constant finding, and clinically silent hemobilia has been reported. The treatment of choice is selective embolization, but spontaneous cessation of bleeding can occur, especially in mild forms. We report a case of occult traumatic hemobilia in which the diagnosis was suggested by transitory changes in ultrasonography and hepatic biochemistry.

ARCH VIROL. 2008;153(11):2129-32.

### **PREVALENCE OF HEPATITIS B VIRUS GENOTYPES IN CHRONIC CARRIERS IN SANTIAGO, CHILE.**

Venegas M, Muñoz G, Hurtado C, Alvarez L, Velasco M, Villanueva RA, Brahm J.

The eight genotypes (designated A-H) of hepatitis B virus (HBV) display distinctive geographical distribution worldwide, with genotypes A, D and F frequently detected in South America. To determine the prevalence of HBV genotypes in Santiago, Chile, 131 samples from chronic carriers were used for PCR amplification, and genotyping was performed by RFLP. The results indicated that genotype F was the most prevalent among HBV carriers (84% of the cases), whereas genotypes A, B, C and D were found at a prevalence of 3.8, 3.8, 6.1, and 2.3%, respectively. We discuss these data in the complex scenario of HBV epidemiology.

EUR CYTOKINE NETW. 2008 DEC;19(4):190-5.

### **IL-23R ARG381GLN POLYMORPHISM IN CHILEAN PATIENTS WITH INFLAMMATORY BOWEL DISEASE.**

Venegas M, Beltrán CJ, Alvarez L, Castro A, Torres T, Leal AD, Lahsen FM, Hermoso MA, Quera R.

Crohn's disease (CD) and ulcerative colitis (UC) are multifactorial diseases with a genetic background. Recent results have shown that a non-synonymous, single nucleotide polymorphism (rs11209026, c.1142G>A, p.Arg381Gln) located in the IL-23R gene is associated with inflammatory bowel disease (IBD). The prevalence of IBD is rapidly rising in Chile and there is no information about the frequency of this polymorphism in the Chilean population. AIM: To assess the distribution of DNA variants in the IL-23R gene in Chilean patients with IBD. METHODS: We studied 100 IBD patients (38 CD and 62 UC) and 59 healthy controls. IL-23R Arg381Gln (G1142A) was genotyped by the polymerase chain reaction and restriction fragment length polymorphism assay. Clinical and demographic features were characterized. RESULTS: The IL-23R genetic variant did not have an association with IBD in Chilean patients. This polymorphism was present in 5.2% of the control group and 5% of IBD patients (7.9% for CD and 3.2% for UC) ( $p > 0.05$ ). CONCLUSIONS: These results suggest that the IL-23R Arg381Gln seems not to be involved in the genetic predisposition to IBD in a Chilean population, and confirms that there are ethnic differences in the genetic background of IBD. Replication studies by independent groups are necessary to elucidate the contribution of susceptibility genes to IBD in different ethnic populations.

## **GERIATRÍA**

NEUROPSYCHIATR DIS TREAT. 2008 AUG;4(4):715-22.

### **COGNITIVE IMPAIRMENT AND ALZHEIMER'S DISEASE: LINKS WITH OXIDATIVE STRESS AND CHOLESTEROL METABOLISM.**

Sekler A, Jiménez JM, Rojo L, Pastene E, Fuentes P, Slachevsky A, Maccioni RB.

Oxidative stress has been implicated in the progression of a number of neurodegenerative diseases, including Alzheimer's disease (AD), Parkinson's disease and amyotrophic lateral sclerosis. We carried out an in-depth study of cognitive impairment and its relationships with oxidative stress markers such as ferric-reducing ability of plasma (FRAP), plasma malondialdehyde and total antioxidative capacity (TAC), as well as cholesterol parameters, in two subsets of subjects, AD patients ( $n = 59$ ) and a control group of neurologically normal subjects ( $n = 29$ ), attending the University Hospital Salvador in Santiago, Chile. Cognitive impairment was assessed by a set of neuropsychological tests (Mini-Mental State Examination, Boston Naming

Test, Ideomotor Praxia by imitation, Semantic Verbal Fluency of animals or words with initial A, Test of Memory Alteration, Frontal Assessment Battery), while the levels of those oxidative stress markers and cholesterol metabolism parameters were determined according with standard bioassays in fresh plasma samples of the two subgroups of patients. No significant differences were observed when the cholesterol parameters (low-, high-density lipoprotein, total cholesterol) of the AD group were compared with normal controls. Interestingly, a correlation was evidenced when the levels of cognitive impairment were analyzed with respect to the plasma antioxidant capacity (AOC) of patients. In this context, the subset of subjects exhibiting cognitive impairment were divided into two subgroups according with their Global Dementia Scale performance: a subgroup with mild AD and a subgroup with moderate to severe AD. Significant differences in AOC were found between subgroups. The different correlations between cognitive impairment of subgroups of subjects with the oxidative stress profile are discussed in the context of AD pathogenesis.

INTENSIVE CARE MED. 2008 OCT;34(10):1907-15.

### **UNDERSTANDING INTERNATIONAL DIFFERENCES IN TERMINOLOGY FOR DELIRIUM AND OTHER TYPES OF ACUTE BRAIN DYSFUNCTION IN CRITICALLY ILL PATIENTS.**

Morandi A, Pandharipande P, Trabucchi M, Rozzini R, Mistraretti G, Trompeo AC, Gregoret C, Gattinoni L, Ranieri MV, Brochard L, Annane D, Putensen C, Guenther U, Fuentes P, Tobar E, Anzueto AR, Esteban A, Skrobik Y, Salluh JI, Soares M, Granja C, Stubhaug A, de Rooij SE, Ely EW.

**BACKGROUND:** Delirium (acute brain dysfunction) is a potentially life threatening disturbance in brain function that frequently occurs in critically ill patients. While this area of brain dysfunction in critical care is rapidly advancing, striking limitations in use of terminology related to delirium internationally are hindering cross-talk and collaborative research. In the English literature, synonyms of delirium such as the Intensive Care Unit syndrome, acute brain dysfunction, acute brain failure, psychosis, confusion, and encephalopathy are widely used. This often leads to scientific “confusion” regarding published data and methodology within studies, which is further exacerbated by organizational, cultural and language barriers. **OBJECTIVE:** We undertook this multinational effort to identify conflicts in terminology and phenomenology of delirium to facilitate communication across medical disciplines and languages. **METHODS:** The evaluation of the terminology used for acute brain dysfunction was determined conducting communications with 24 authors from academic communities throughout countries/regions that speak the 13 variants of the Romanic languages included into this manuscript. **RESULTS:** In the 13 languages utilizing Romanic characters, included in this report, we identified the following terms used to define major types of acute brain dysfunction: coma, delirium, delirio, delirium tremens, délire, confusion mentale, delir, delier, Durchgangs-Syndrom, acute verwardheid, intensiv-psykose, IVA-psykos, IVA-syndrom, akutt konfusion/forvirring. Interestingly two terms are very consistent: 100 % of the selected languages use the term coma or koma to describe patients unresponsive to verbal and/or physical stimuli, and 100% use delirium tremens to define delirium due to alcohol withdrawal. Conversely, only 54% use the term delirium to indicate the disorder as defined by the DSM-IV as an acute change in mental status, inattention, disorganized thinking and altered level of consciousness. **CONCLUSIONS:** Attempts towards standardization in terminology, or at least awareness of differences across languages and specialties, will help cross-talk among clinicians and researchers.

J ALZHEIMERS DIS. 2008 MAR;13(2):225-32.

### **MILD COGNITIVE IMPAIRMENT AND ALZHEIMER PATIENTS DISPLAY DIFFERENT LEVELS OF REDOX-ACTIVE CSF IRON.**

Lavados M, Guillón M, Mujica MC, Rojo LE, Fuentes P, Maccioni RB.

Oxidative stress constitutes a hallmark of Alzheimer’s disease (AD). Recent studies also point to redox active metals such as iron, copper and zinc in mediating oxidative stress in AD pathogenesis. However, the reactivity of cerebrospinal fluid (CSF) iron and its possible correlation with the severity of cognitive decline in both Alzheimer’s patients and subjects with mild cognitive impairment (MCI) is still unknown. Here we show that different stages of cognitive and functional impairment are associated with changes in CSF reactive iron. In this work, we compared CSF samples from 56 elders, classified into 4 groups according to their scores on the Clinical Dementia Rating scale (CDR). Total CSF iron was analyzed by atomic absorption spectrometry. Redox-active iron was analyzed by a novel fluorimetric assay. One-way ANOVA was used to test differences in mean values, and Newman-Keuls Multiple Comparison Test was used for multi group comparisons. No difference in total CSF iron was

found between different groups. Significant amounts of redox-active iron were found in CSF and their levels correlated with the extent of cognitive impairment. Redox-active CSF iron levels increased with the degree of cognitive impairment from normal to MCI subjects, while AD patients showed an abrupt decrease to levels close to zero. Given the relevance of oxidative damage in neurodegeneration, it might be possible to associate the development of cognitive and functional decline with the presence of redox-active iron in the CSF. The decrease in redox-active iron found in AD patients may represent a terminal situation, whereby the central nervous system attempts to minimize iron-associated toxicity.

## IMAGENOLOGÍA

RADIOLOGY. 2008 APR;247(1):273-85.

### **RENAL ARTERY STENOSIS EVALUATION: DIAGNOSTIC PERFORMANCE OF GADOBENATE DIMEGLUMINE-ENHANCED MR ANGIOGRAPHY--COMPARISON WITH DSA.**

Soulez G, Pasowicz M, Benea G, Grazioli L, Niedmann JP, Konopka M, Douek PC, Morana G, Schaefer FK, Vanzulli A, Bluemke DA, Maki JH, Prince MR, Schneider G, Ballarati C, Coulden R, Wasser MN, McCauley TR, Kirchin MA, Pirovano G.

**PURPOSE:** To prospectively determine diagnostic performance and safety of contrast material-enhanced (CE) magnetic resonance (MR) angiography with 0.1 mmol per kilogram of body weight gadobenate dimeglumine for depiction of significant steno-occlusive disease (> or =51% stenosis) of renal arteries, with digital subtraction angiography (DSA) as reference standard. **MATERIALS AND METHODS:** This multicenter study was approved by local institutional review boards; all patients provided written informed consent. Patient enrollment and examination at centers in the United States complied with HIPAA. Two hundred ninety-three patients (154 men, 139 women; mean age, 61.0 years) with severe hypertension (82.2%), progressive renal failure (11.3%), and suspected renal artery stenosis (6.5%) underwent CE MR angiography with three-dimensional spoiled gradient-echo sequences after administration of 0.1 mmol/kg gadobenate dimeglumine at 2 mL/sec. Anteroposterior and oblique DSA was performed in 268 (91.5%) patients. Three independent blinded reviewers evaluated CE MR angiographic images. Sensitivity, specificity, and accuracy of CE MR angiography for detection of significant steno-occlusive disease (> or =51% vessel lumen narrowing) were determined at segment (main renal artery) and patient levels. Positive and negative predictive values and positive and negative likelihood ratios were determined. Interobserver agreement was analyzed with generalized kappa statistics. A safety evaluation (clinical examination, electrocardiogram, blood and urine analysis, monitoring for adverse events) was performed. **RESULTS:** Of 268 patients, 178 who were evaluated with MR angiography and DSA had significant steno-occlusive disease of renal arteries at DSA. Sensitivity, specificity, and accuracy of CE MR angiography for detection of 51% or greater stenosis or occlusion were 60.1%-84.1%, 89.4%-94.7%, and 80.4%-86.9%, respectively, at segment level. Similar values were obtained for predictive values and for patient-level analyses. Few CE MR angiographic examinations (1.9%-2.8%) were technically inadequate. Interobserver agreement for detection of significant steno-occlusive disease was good (79.9% agreement; kappa = 0.69). No safety concerns were noted. **CONCLUSION:** CE MR angiography performed with 0.1 mmol/kg gadobenate dimeglumine, compared with DSA, is safe and provides good sensitivity, specificity, and accuracy for detection of significant renal artery steno-occlusive disease.

## INFECTOLOGÍA

SCAND J INFECT DIS. 2008;40(11-12):983-5.

### **SEIZURES ASSOCIATED WITH ERTAPENEM USE IN PATIENTS WITH CNS DISORDERS AND RENAL INSUFFICIENCY.**

Fica AE, Abusada NJ.

Three patients presented seizures during ertapenem therapy. They were classified as probably-related in 1 case and as possible-related in the others. Convulsions appeared after 1 week of therapy at usual doses with 1 or 2 events, and were observed only among patients with CNS disorders and renal insufficiency.

## LABORATORIO DE ENDOCRINOLOGÍA Y BIOLOGÍA DE LA REPRODUCCIÓN

J STEROID BIOCHEM MOL BIOL. 2008 MAY;110(1-2):163-9.

### **IN SITU ESTROGEN METABOLISM IN PROLIFERATIVE ENDOMETRIA FROM UNTREATED WOMEN WITH POLYCYSTIC OVARIAN SYNDROME WITH AND WITHOUT ENDOMETRIAL HYPERPLASIA.**

Bacallao K, Leon L, Gabler F, Soto E, Romero C, Valladares L, Vega M.

The aim of the present investigation was to study whether the endocrinological status of women bearing polycystic ovarian syndrome (PCOS) affects the endometrial in situ steroid metabolism. For this purpose, we evaluated the mRNA levels (RT-PCR), and the activity of steroid metabolic enzymes: P450 aromatase, steroid sulfatase (STS), estrogen sulfotransferase (EST) and 17beta-hydroxysteroid dehydrogenase (17beta-HSD) in 23 samples of normal endometria (CE), 18 PCOS endometria without treatment (PCOSE), 10 specimens from PCOS women with endometrial hyperplasia (HPCOSE), and 7 endometria from patients with endometrial hyperplasia not associated to PCOS (EH). The data showed lower levels of STS mRNA for PCOSE and HPCOSE ( $p < 0.05$ ,  $p < 0.01$ , respectively) and of EST for HPCOSE and EH compared to control ( $p < 0.05$ ). However, higher levels for EST mRNA were obtained in PCOSE ( $p < 0.05$ ) versus CE. The mRNA and protein levels for P450 aromatase were undetectable in all analyzed endometria. The relationship between the activities of STS and EST was lower in PCOSE and HPCOSE ( $p < 0.05$ ) versus CE. The ratio between the mRNA from 17beta-HSD type 1/type 2 was higher in PCOSE ( $p < 0.05$ ), whereas, a diminution in the 17beta-HSD type 2 activity was observed in PCOSE ( $p < 0.05$ ). These results indicate that the activity of enzymes related to the steroid metabolism in analyzed PCOSE differ from those found in the CE. Consequently, PCOSE may present an in situ deregulation of the steroid metabolism.

STEROIDS. 2008 JAN;73(1):88-95.

### **ACTIVITIES OF STEROID METABOLIC ENZYMES IN SECRETORY ENDOMETRIA FROM UNTREATED WOMEN WITH POLYCYSTIC OVARY SYNDROME.**

Leon L, Bacallao K, Gabler F, Romero C, Valladares L, Vega M.

Polycystic Ovary Syndrome (PCOS) is an endocrine-metabolic pathology related with infertility and recurrent miscarriage. We have previously shown that the endometrium of these patients can exhibit a potentially higher sensitivity to estrogen action, being estrogens important regulators of the cell cycle and tissue homeostasis. The effect of estrogens on tissues depends on their in situ availability, which is in part regulated by the activity of steroid metabolic enzymes within the tissues. Therefore, the objective of the present study was to analyze if the activity and/or expression of steroid metabolic enzymes in endometria from women with PCOS differ from controls. For this purpose, the activity of the enzymes was determined by using radiometric assays and the mRNA levels measured by semi-quantitative RT-PCR. Both assays were assessed in endometria obtained during mid secretory phase from control (CE,  $n=12$ ) and PCOS women (PCOSE,  $n=11$ ). For the statistical analyses, Mann-Whitney and Student's t-tests were used to compare CE and PCOSE, considering a  $p$  value  $< 0.05$  significantly different. The results showed an increase in the sulfatase activity in PCOS respect to control endometria ( $200 \pm 28$  pmol/mg vs.  $115 \pm 13$  pmol/mg;  $p < 0.05$ ), in agreement with the higher mRNA levels found for the enzyme in PCOSE. In addition, a PCOSE exhibited lower activity of sulfotransferase respect to the control group ( $50 \pm 21$  pmol/mg vs.  $124 \pm 10$  pmol/mg;  $p < 0.05$ ), whereas a higher level of 17beta-hydroxysteroid dehydrogenase type 1 mRNA was found in PCOSE compared with the control tissues ( $p < 0.05$ ). The activity of 17beta-hydroxysteroid dehydrogenase type 2 and the mRNA levels of sulfotransferase were similar in both groups; meanwhile, the expression of aromatase was undetectable. These data indicate that the sulfatase pathway could play an important role in the local production of estrogens in PCOSE from secretory phase. This potentially higher bioavailability of estrogens in endometria from PCOS women could influence the deregulation of tissue homeostasis that we have previously reported, and could partially explain the poor reproductive performance observed in this group of patients.

## MEDICINA NUCLEAR

REV ESP MED NUCL. 2008 MAR-APR;27(2):83-9.

### **[INTEROBSERVER CORRELATION IN THE INTERPRETATION OF 99MTC-SESTAMIBI SPECT IN REPERFUSED ACUTE MYOCARDIAL INFARCTION][ARTICLE IN SPANISH]**

Massardo T, Lavados H, Jaimovich R, Herrera E, Quevedo L, Alfaro L, Assef V, Coll C, Velásquez C, Pereira ME, Olea E, Quintana JC.

**INTRODUCTION AND OBJECTIVES:** The correct interpretation of myocardial perfusion single photon emission computed tomography (SPECT) requires knowledge of the technique reproducibility. The objective was analyze the interobserver correlation of different experience in the interpretation of myocardial perfusion SPECT in patients following acute myocardial infarction (AMI) in order to improve the quality of our site. **METHODS:** Sixty cases (56 +/- 11 years, 87 % men) with transmural AMI who had recently undergone successful thrombolysis were included. Resting perfusion with (99m)Tc-sestamibi was performed at one week post-AMI. **ANALYSIS:** Semiquantitative interpretation using 17 segment-model by 2 independent specialists and 5 observers, was performed blindly. Left ventricular ejection fraction (LVEF) was measured with isotopic ventriculography one month after AMI, with a mean of 38 %. **RESULTS:** Using independent and then agreed on perfusion analysis, average involved segments/patient was 9.3 +/- 4 and the sum of severity 25 +/- 13. Readings of other observers ranged from 7 +/- 3.7 to 9.4 +/- 3.9 and 16.7 +/- 9.7 to 24.6 +/- 13, respectively, consistent with the reading of the specialists of between 0.779-0.871 (kappa: 0.565-0.741). There was no significant difference when the number of segments were analyzed in 40 % of the cases and for intensity in 60 % of them in more experienced observers. Correlation with consensus reading for the number of segments ranged from 0.84 to 0.94 and for severity from 0.79 to 0.89. Identification of culprit arteries was acceptable, with r values between 0.612 and 0.683 and kappas between 0.629 and 0.656. Correlation of the number of involved segments and severity with LVEF performed one month after AMI was 0.73 and 0.74, respectively. **CONCLUSIONS:** There was good correlation in the interpretation of myocardial perfusion SPECT, with a significantly better fit in more experienced observers. This academic exercise was also helpful in improving our residents' skills in cardiology.

## NEUROLOGÍA Y NEUROCIRUGÍA

HYPERTENSION. 2008 AUG;52(2):295-300.

### **MINERALOCORTICOID RECEPTOR ANTAGONISM ATTENUATES CARDIAC HYPERTROPHY AND PREVENTS OXIDATIVE STRESS IN UREMIC RATS.**

Michea L, Villagrán A, Urzúa A, Kuntsmann S, Venegas P, Carrasco L, Gonzalez M, Marusic ET.

Chronic renal failure causes left ventricular hypertrophy, but the molecular mechanisms involved remain unknown. We, therefore, investigated whether the mineralocorticoid receptor is implicated in the cardiac hypertrophy observed in uremic rats and whether mineralocorticoid receptor blockade could be protective in chronic renal failure. Experimental groups were: control rats, uremic rats (NPX) with 5/6 nephrectomy (5 weeks), and NPX rats fed with spironolactone for 5 weeks. Systolic blood pressure was increased in both NPX rats and NPX rats fed with spironolactone for 5 weeks. Echocardiography revealed concentric left ventricular hypertrophy in uremia, which was attenuated by spironolactone. Enlarged cardiomyocyte size was observed in both left and right ventricles of NPX rats, an effect that was prevented by spironolactone. Mineralocorticoid receptor antagonism attenuated the increase of ventricular brain natriuretic peptide mRNA levels induced by nephrectomy. Left ventricular gene expressions of aldosterone synthase, mineralocorticoid receptor, and hydroxysteroid dehydrogenase type 2 were the same in the 3 groups, whereas gene expression of the glucocorticoid receptor was significantly diminished in chronic renal failure rats. No significant differences in cardiac aldosterone were observed between control rats and NPX rats, although NPX rats fed with spironolactone for 5 weeks showed increased plasma aldosterone levels. However, a significant increase in serum and glucocorticoid-inducible kinase-1 mRNA expression and protein was present in the NPX group; spironolactone treatment significantly reduced serum and glucocorticoid-inducible kinase-1 mRNA and protein in the left ventricle. Uremic rats exhibited a significant increase of superoxide production and reduced nicotinamide-adenine

dinucleotide phosphatase subunits expression (NOX-2, NOX-4, and p47(phox)) in the left ventricle, which was prevented by the mineralocorticoid receptor antagonist. Our findings provide evidence of the beneficial effects of spironolactone in cardiac hypertrophy and cardiac oxidative stress in chronic renal failure.

J NEUROSCI. 2008 SEP 17;28(38):9463-72.

### **ISCHEMIA ENHANCES ACTIVATION BY $Ca^{2+}$ AND REDOX MODIFICATION OF RYANODINE RECEPTOR CHANNELS FROM RAT BRAIN CORTEX.**

Bull R, Finkelstein JP, Gálvez J, Sánchez G, Donoso P, Behrens MI, Hidalgo C.

Cerebral ischemia stimulates  $Ca^{2+}$  influx and thus increases neuronal intracellular free  $[Ca^{2+}]$ . Using a rat model of cerebral ischemia without recirculation, we tested whether ischemia enhances the activation by  $Ca^{2+}$  of ryanodine receptor (RyR) channels, a requisite feature of RyR-mediated  $Ca^{2+}$ -induced  $Ca^{2+}$  release (CICR). To this aim, we evaluated how single RyR channels from endoplasmic reticulum vesicles, fused into planar lipid bilayers, responded to cytoplasmic  $[Ca^{2+}]$  changes. Endoplasmic reticulum vesicles were isolated from the cortex of rat brains incubated without blood flow for 5 min at 37 degrees C (ischemic) or at 4 degrees C (control). Ischemic brains displayed increased oxidative intracellular conditions, as evidenced by a lower ratio (approximately 130:1) of reduced/oxidized glutathione than controls (approximately 200:1). Single RyR channels from ischemic or control brains displayed the same three responses to  $Ca^{2+}$  reported previously, characterized by low, moderate, or high maximal activity. Relative to controls, RyR channels from ischemic brains displayed with increased frequency the high activity response and with lower frequency the low activity response. Both control and ischemic cortical vesicles contained the RyR2 and RyR3 isoforms in a 3:1 proportion, with undetectable amounts of RyR1. Ischemia reduced  $[^3H]$ ryanodine binding and total RyR protein content by 35%, and increased at least twofold endogenous RyR2 S-nitrosylation and S-glutathionylation without affecting the corresponding RyR3 endogenous levels. In vitro RyR S-glutathionylation but not S-nitrosylation favored the emergence of high activity channels. We propose that ischemia, by enhancing RyR2 S-glutathionylation, allows RyR2 to sustain CICR; the resulting amplification of  $Ca^{2+}$  entry signals may contribute to cortical neuronal death.

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, Rodriguez-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.

## OFTALMOLOGÍA

MOL VIS. 2008 MAY 7;14:829-35.

### **ANTICIPATION IN FAMILIAL LATTICE CORNEAL DYSTROPHY TYPE I WITH R124C MUTATION IN THE TGFBI (BIGH3) GENE.**

Romero P, Vogel M, Diaz JM, Romero MP, Herrera L.

**PURPOSE:** To report the clinical, ophthalmic, and genetic characteristics for lattice corneal dystrophy type I (LCDI) in a Chilean family. **METHODS:** Six affected family members were examined clinically including visual acuity, color cornea photography, applanation tonography, and funduscopy. Genomic DNA was extracted from peripheral leukocytes from six affected and three unaffected members of a family with lattice corneal dystrophy type I. Exon 4 of the transforming growth factor-induced gene (TGFBI) was screened for the most frequent mutation, R124C, in the proband by sequencing. We also designed a rapid polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) method to analyze the same mutation, amplifying exon 4 and digesting with PstI restriction enzyme. Using this strategy, we analyzed the mutation in six affected and three healthy family members. **RESULTS:** Three generations of family members were positively diagnosed with lattice corneal dystrophy. Six participants demonstrated LCDI in both eyes, most of whom were symmetric. Age at onset of symptoms was variable (3-42 years old). Moreover, in this family, the age of onset of the disease decreased in succeeding generations, which could be interpreted as anticipation. Visual acuity varied from 1.0 to 0.13. Two patients, ages 69 and 44 years old, demonstrated a degree of severity "Bad" according to best-corrected vision and corneal commitment. The exon 4 sequence of TGFBI of the proband exhibits the heterozygous single-nucleotide mutation, C417T, leading to amino acid substitution (R124C) in the encoded TGF-induced protein. Using PCR-RFLP, we confirmed the heterozygous mutation in six affected family members and excluded it in three healthy members. **CONCLUSIONS:** The R124C mutation in TGFBI cosegregated with LCD type I in the investigated family. This is the first report of a molecular analysis of LCD type I in Chilean patients. The early onset affected persons in the fourth generation raises the possibility of anticipation.

## ONCOLOGÍA

BMC CANCER. 2008 APR 23;8:117.

### **ASSOCIATION OF COMMON ATM VARIANTS WITH FAMILIAL BREAST CANCER IN A SOUTH AMERICAN POPULATION.**

González-Hormazábal P, Bravo T, Blanco R, Valenzuela CY, Gómez F, Waugh E, Peralta O, Ortuzar W, Reyes JM, Jara L.

**BACKGROUND:** The ATM gene has been frequently involved in hereditary breast cancer as a low-penetrance susceptibility gene but evidence regarding the role of ATM as a breast cancer susceptibility gene has been contradictory. **METHODS:** In this study, a full mutation analysis of the ATM gene was carried out in patients from 137 Chilean breast cancer families, of which 126 were BRCA1/2 negatives and 11 BRCA1/2 positives. We further perform a case-control study between the subgroup of 126 cases BRCA1/2 negatives and 200 controls for the 5557G>A missense variant and the IVS38-8T>C and the IVS24-9delT polymorphisms. **RESULTS:** In the full mutation analysis we detected two missense variants and eight intronic polymorphisms. Carriers of the variant IVS24-9delT, or IVS38-8T>C, or 5557G>A showed an increase in breast cancer risk. The higher significance was observed in the carriers of IVS38-8T>C (OR = 3.09 [95%CI 1.11-8.59], p = 0.024). The IVS24-9 T/(-T), IVS38-8 T/C, 5557 G/A composite genotype conferred a 3.19 fold increase in breast cancer risk (OR = 3.19 [95%CI 1.16-8.89], p = 0.021). The haplotype estimation suggested a strong linkage disequilibrium between the three markers (D' = 1). We detected only three haplotypes in the cases and control samples, some of these may be founder haplotypes in the Chilean population. **CONCLUSION:** The IVS24-9 T/(-T), IVS38-8 T/C, 5557 G/A composite genotype alone or in combination with certain genetic background and/or environmental factors, could modify the cancer risk by increasing genetic instability or by altering the effect of the normal DNA damage response.



## OTORRINOLARINGOLOGÍA

OTOLARYNGOL HEAD NECK SURG. 2008 MAY;138(5):633-6.

### **URINARY LEUKOTRIENES IN PATIENTS WITH NASAL POLYPOSIS.**

Royer M, Guzmán MA, Gormaz JP, Nazar G.

**OBJECTIVES:** To compare urinary leukotriene E4 (ULT) level in patients with nasal polyposis (NP) with and without aspirin intolerance and allergic rhinitis (AR), and correlate it with disease severity. **STUDY DESIGN AND SETTING:** Prospective study from November 2005 to November 2006. Patients with NP (n = 30) and AR (n = 35) were included. The concentration of ULT was measured in both groups. Oral provocation test with aspirin was performed to patients with NP. ULT level between both groups was compared and correlated with NP disease severity. **RESULTS:** ULT concentration was elevated on NP and AR. The patients with NP and aspirin intolerance (n = 4) presented higher levels of ULT compared to aspirin-tolerant patients. Leukotriene concentration was not correlated with NP severity. **CONCLUSIONS:** Patients with NP and aspirin intolerance have increased ULT excretion; thus their measurement can be used as an indicator of arachidonic acid metabolism alteration.

J COMP PHYSIOL A NEUROETHOL SENS NEURAL BEHAV PHYSIOL. 2008 AUG;194(8):693-700.

### **STIMULUS-DEPENDENT OSCILLATIONS AND EVOKED POTENTIALS IN CHINCHILLA AUDITORY CORTEX.**

Delano PH, Pavez E, Robles L, Maldonado PE.

Besides the intensity and frequency of an auditory stimulus, the length of time that precedes the stimulation is an important factor that determines the magnitude of early evoked neural responses in the auditory cortex. Here we used chinchillas to demonstrate that the length of the silent period before the presentation of an auditory stimulus is a critical factor that modifies late oscillatory responses in the auditory cortex. We used tetrodes to record local-field potential (LFP) signals from the left auditory cortex of ten animals while they were stimulated with clicks, tones or noise bursts delivered at different rates and intensity levels. We found that the incidence of oscillatory activity in the auditory cortex of anesthetized chinchillas is dependent on the period of silence before stimulation and on the intensity of the auditory stimulus. In 62.5% of the recordings sites we found stimulus-related oscillations at around 8-20 Hz. Stimulus-induced oscillations were largest and consistent when stimuli were preceded by 5 s of silence and they were absent when preceded by less than 500 ms of silence. These results demonstrate that the period of silence preceding the stimulus presentation and the stimulus intensity are critical factors for the presence of these oscillations.

## 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.

## NEFROLOGÍA

MED CLIN (BARC). 2008 APR 5;130(12):441-5.

### **[STUDY OF AEROBIC CAPACITY IN CHRONIC HEMODIALYZED PATIENTS: EFFECT OF L-CARNITINE SUPPLEMENTATION][ARTICLE IN SPANISH]**

Pacheco A, Torres R, Sanhueza ME, Elgueta L, Segovia E, Cano M.

BACKGROUND AND OBJECTIVE: Chronic hemodialyzed patients have a low level of aerobic capacity, caused by the pathologies concomitant to renal insufficiency, according with a low level of physical activity. One of the factors that would contribute to this level of aerobic capacity is the L-carnitine deficit on skeletal muscle. However, the value of the supplementation of L-carnitine to improve the physical fitness has been controversial. The objective of this work was to evaluate the effect of the administration of L-carnitine on VO<sub>2</sub> max in hemodialyzed patients. PATIENTS AND METHODS: A group of 21 patients (20-50 years old) on a program of chronic hemodialysis was studied. During 12 weeks, 13 of them received L-carnitine, 7 men and 6 women, 38.8 (9.5) years old; BMI 24.2 (2.1) Kg/m<sup>2</sup>; 8 of them received placebo, 4 men and 4 women, 35.8 (11.4) years old; BMI 24.5 (5.8) Kg/m<sup>2</sup>. RESULTS: There was an increase in VO<sub>2</sub> peak on L-carnitine group from 16.3 (2.8) mL x Kg(-1) x min(-1) to 19.5 (3.3) mL x Kg(-1) x min(-1), and the same was seen in the placebo group (increase in VO<sub>2</sub> peak from 14.8 (3.8) mL x Kg(-1) x min(-1) to 18.9 (4.8) mL x Kg(-1) x min(-1)). The L-carnitine and placebo groups did not show statistical differences at the end of this study (all values above p > 0.05). CONCLUSION. In this group of patients, the intravenous supplementation of L-carnitine during 12 weeks did not have an impact on the improvement of the VO<sub>2</sub> peak.

## NEUROLOGÍA

REV NEUROL. 2008 JAN 1-15;46(1):24-9.

### **[COGNITIVE PERFORMANCE IN PATIENTS WITH CORONARY HEART DISEASE AND CARDIOVASCULAR RISK FACTORS IN CHILE]**

Delgado-Derío C, Vasquez-Vivar C, Orellana-Pineda P, Reccius-Meza A, Donoso-Sepúlveda A, Behrens-Pellegrino Ml.

INTRODUCTION: Cardiovascular risk factors (CRF) are related to long-term cognitive impairment. Coronary heart disease (CHD) has been associated with bad cognitive performance in an inconsistent way. AIM. To measure the cognitive performance in Chilean patients with diverse CRF, with and without CHD. SUBJECTS AND METHODS: Cross-sectional study of the cognitive performance of three groups of patients older than sixty years, without history of stroke: with CHD and high CRF (CHD-hCRF) (n = 62), with high CRF but without CHD (hCRF) (n = 57), and non hypertensive non diabetic (NHND) (n = 25). RESULTS: Higher age, lower education and been men were significantly associated with cognitive impairment in the total sample. There were no differences in the proportion of cognitive impairment and age between the groups. The CHD group had a predominance of men and a higher proportion of high cholesterol and periphery vascular disease than the other groups. The NHND group was more educated than the other groups. After adjusting for years of education and sex there were no significant differences in the neuropsychological performance and depression scales between the groups, been the coronary group significantly more functionally impaired. CONCLUSIONS: Isolated CHD is not associated with worse cognitive performance in patients, but it is related with greater systemic vascular damage and functional impairment in patients without history of stroke.

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.

## **RESPIRATORIO**

J MED MICROBIOL. 2008 DEC;57(P12):1491-5.

**DETECTION OF MYCOPLASMA PNEUMONIAE IN ADULT COMMUNITY-ACQUIRED PNEUMONIA BY PCR AND SEROLOGY.**

Martínez MA, Ruiz M, Zunino E, Luchsinger V, Avendaño LF.

Diagnosis of pneumonia caused by *Mycoplasma pneumoniae* in adults is hampered by a lack of rapid and standardized tests for detection. This prospective study was conducted to compare the diagnostic values of an indirect immunofluorescence assay and a 16S rRNA gene PCR for the diagnosis of *M. pneumoniae* pneumonia in adults. From February 2005 to January 2008, 357 patients (53.8 % males, median age 63 years, range 18-94) admitted for community-acquired pneumonia (CAP) to two hospitals in Santiago, Chile, were enrolled in the study. Thirty-two patients (9.0 %) met the criteria of current or recent *M. pneumoniae* infection, and laboratory diagnosis was definitive in 26 cases (81.2 %) and presumptive in six cases (18.8 %). Among the 32 *M. pneumoniae* infections, the PCR assay was positive in 23 (71.9 %) and the serology in 27 (84.4 %) of the cases. IgM was positive in acute-phase serum specimens in 13 cases (40.6 %) of *M. pneumoniae* infections. Using serology as the gold standard, the sensitivity, specificity, and positive and negative predictive values of the PCR were 66.7, 98.5, 78.3 and 97.3 %, respectively, whereas the global agreement of the methods was 343/357 (96.1 %). The frequency of *M. pneumoniae* CAP cases declined significantly during the second year of study, suggesting the end of an epidemic period. In conclusion, although good global agreement was found between PCR and serology, the lower sensitivity of the PCR leads us to recommend the use of both procedures in parallel to confirm *M. pneumoniae* in CAP in adults.

J CRIT CARE. 2008 SEP 10.

**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<sup>2</sup>. **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<sup>2</sup> vs 22 +/- 3 kg/m<sup>2</sup> 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.

## REUMATOLOGÍA

OCUL IMMUNOL INFLAMM. 2008 JUL-AUG;16(4):161-5.

**AZATHIOPRINE IN THE MANAGEMENT OF AUTOIMMUNE UVEITIS.**

Pacheco PA, Taylor SR, Cuchacovich MT, Diaz GV.

**PURPOSE:** To evaluate the role of azathioprine as an immunosuppressive for steroid-resistant autoimmune uveitis (AIU). **METHODS:** Patients using oral prednisolone for active AIU without clinical response were recruited. A standard protocol of oral prednisolone and azathioprine was used. **RESULTS:** Twenty-seven patients participated in the study: 3 with anterior uveitis, 1 pars planitis, 4 idiopathic panuveitis, 8 Vogt-Koyonagi-Harada syndrome, 3 Behcet disease, and 8 choroidoretinopathies. Complete response was observed in 92%. Eleven patients had well-tolerated minor side effects. **CONCLUSION:** Azathioprine is safe and effective in controlling steroid-resistant AIU.

CLIN RHEUMATOL. 2008 APR;27(4):533-5.

**INFLIXIMAB CAN INDUCE A PROLONGED CLINICAL REMISSION AND A DECREASE IN THYROID HORMONAL REQUIREMENTS IN A PATIENT WITH SAPHO SYNDROME AND HYPOTHYROIDISM.**

Sabugo F, Liberman C, Niedmann JP, Soto L, Cuchacovich M.

SAPHO syndrome is a rare entity that compromises the skeletal system (arthritis-osteitis) and is associated with various dermatological conditions such as palmoplantar pustulosis (PPP) and acne. We present the case of a 39-year-old man with invalidating arthritis derived from a SAPHO syndrome and hypothyroidism (after radioiodine treatment for a Graves' disease). Due to the severity and refractoriness of his disease, we decided to use infliximab. He showed a prompt and prolonged response of his joint and cutaneous manifestations after three doses of a tumor necrosis factor alpha (TNF-alpha) blocker. Interestingly, he also decreased his levothyroxine requirements after TNF-alpha blockade therapy.

CLIN EXP RHEUMATOL. 2008 NOV-DEC;26(6):1067-73.

**BASAL ANTI-CYCLIC CITRULLINATED PEPTIDE (ANTI-CCP) ANTIBODY LEVELS AND A DECREASE IN ANTI-CCP TITRES ARE ASSOCIATED WITH CLINICAL RESPONSE TO ADALIMUMAB IN RHEUMATOID ARTHRITIS.**

Cuchacovich M, Catalan D, Wainstein E, Gatica H, Soto L, Aravena O, Pesce B, Sabugo F, Aguillón JC.

**OBJECTIVE:** To investigate the effect of adalimumab treatment on anti-cyclic citrullinated peptide antibodies (anti-CCP) in patients with rheumatoid arthritis (RA). **METHODS:** 70 RA patients who failed treatment with disease modifying antirheumatic drugs (DMARDs) received 40 mg adalimumab subcutaneously every other week during 24 weeks. Serum samples were collected at baseline and at weeks 8, 16 and 24 before the corresponding adalimumab dose. The serum anti-CCP levels were tested by enzyme linked immunosorbent assay. **RESULTS:** At baseline, 52 of the 70 patients (74.3%) were positive for anti-CCP antibodies. 60 % of the anti CCP positive patients and 44.4% of the anti CCP negative patients were ACR 20 responders at week 24 ( $p < 0.049$ ). The serum levels of anti-CCP antibodies decreased significantly after 24 weeks of adalimumab treatment only in those patients who met ACR 20 response criteria at week 24 ( $p < 0.00044$ ). Differences between baseline anti-CCP titers and those at 8, 16 and 24 weeks were all statistically significant ( $p < 0.014$ , 0.003 and 0.019 respectively). No statistically significant changes in the anti-CCP levels were observed in patients who did not meet the ACR 20 response criteria. **CONCLUSION:** Basal anti-CCP antibodies levels correlate with clinical response to adalimumab. A decrease in anti-CCP levels on time was observed in patients showing also clinical improvement, suggesting that serum anti-CCP antibodies determination may be useful in assessing treatment efficacy in RA patients.

ANN RHEUM DIS. 2008 SEP;67(9):1235-41.

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

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

**BACKGROUND:** The use of regulatory or immature dendritic cells (DCs) as tools for modulating experimental rheumatoid arthritis is very recent. Tumour necrosis factor (TNF)-stimulated DCs have been shown to restore tolerance in experimental autoimmune encephalomyelitis and collagen-induced arthritis (CIA). **OBJECTIVE:** We investigated the capacity of short-term lipopolysaccharide (LPS)-stimulated DCs pulsed with type II collagen (CII) to induce tolerance against established CIA. **METHODS:** Bone marrow-derived DCs were generated in the presence of granulocyte monocyte colony-stimulating factor (GM-CSF). After CIA induction, mice were injected at day 35 with a single dose of 4- or 24-h LPS-stimulated DCs that had been loaded with CII (4hLPS/CII/DCs or 24hLPS/CII/DCs). Arthritis progression was monitored by clinical and histological evaluations. **RESULTS:** Flow cytometry of 4hLPS/CII/DCs showed intermediate CD40 and CD86 expression, lower than that of 24hLPS/CII/DCs (fully mature) and higher than that of CII/DCs (immature). A functional assay showed that 4hLPS/CII/DCs display increased endocytosis ability with respect to 24hLPS/CII/DCs, indicating a semimature state. The single inoculation of 4hLPS/CII/DCs in mice with established CIA reduced disease severity significantly over time. Histological evaluation of mice treated with 4hLPS/CII/DCs revealed diminished inflammatory synovitis, cartilage damage and fibrosis. Co-cultures of DCs with splenocytes from CIA mice showed that collagen-specific interferon (IFN)gamma production was dramatically inhibited by 4hLPS/CII/DCs. 4hLPS/CII/DCs were high IL10 producers, which could explain the inhibition of arthritis progression in mice receiving this treatment because neither antibodies nor regulatory CD4+CD25+Foxp3+ T lymphocytes were demonstrated to be involved. **CONCLUSION:** Short-term LPS-modulated DCs inoculation interferes with CIA progression when loaded with CII.

## UNIDAD PACIENTES CRÍTICOS

NEUROCRIT CARE. 2008 JAN 18.

### **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.

J CRIT CARE. 2008 SEP 10.

### **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<sup>2</sup>. **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<sup>2</sup> vs 22 +/- 3 kg/m<sup>2</sup> 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.

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<sub>2</sub>/Fio<sub>2</sub> (92 +/- 12 vs 227 +/- 43, P < .0001) and oxygenation index (22 +/- 5 vs 8 +/- 2, P < .0001), reduction of PaCo<sub>2</sub> (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.

J CRIT CARE. 2008 DEC;23(4):461-7.

### **INTRA-ABDOMINAL HYPERTENSION: INCIDENCE AND ASSOCIATION WITH ORGAN DYSFUNCTION DURING EARLY SEPTIC SHOCK.**

Regueira T, Bruhn A, Hasbun P, Aguirre M, Romero C, Llanos O, Castro R, Bugedo G, Hernandez G.

**PURPOSE:** The objective of this article is to study the cumulative incidence of intra-abdominal hypertension (IAH) in septic shock (SS) patients during the first 72 hours of intensive care unit (ICU) admission and to determine if the presence and severity of IAH are associated with sepsis morbidity and mortality. **MATERIALS AND METHODS:** Eighty-one consecutive SS patients admitted to a surgical-medical ICU of an academic university hospital (January 2005 to January 2006) were included. Intra-abdominal pressure (IAP) and abdominal perfusion pressure (APP) were measured every 6 h (intermittently) for 72 h. Intra-abdominal pressure was registered as minimal, mean, and maximal values per day, during shock and throughout the study period. Intra-abdominal hypertension was diagnosed if IAP remained 12 mm Hg or higher on 2 consecutive measurements and stratified according to the most recent consensus definition ([www.wsacs.org](http://www.wsacs.org)). **RESULTS:** According to maximal and mean IAP values, 67 (82.7%) and 62 (76.5%) of the patients developed IAH during the study period, respectively. Mean IAP values remained stable throughout the study period. Surgical patients had a higher incidence of IAH than medical patients (93% vs 73%, P < .009). Maximal IAPs were normally distributed, with nonsurvivors exhibiting significantly higher IAP levels during shock (survivors, 17.2 +/- 5.3; nonsurvivors, 19.9 +/- 5.6 mm Hg; P < .04). Patients with IAH exhibited significantly lower values of APP and diuresis, higher values of lactate and creatinine, and higher maximal norepinephrine doses, and were more frequently mechanically ventilated (P < .05 for all). Increasing degrees of IAH and the development of the abdominal compartment syndrome were associated with lower APP and higher maximal serum creatinine levels (P < .03 for both). **CONCLUSIONS:** Septic shock patients have a very high incidence of IAH, which seems to be associated with the severity of shock and could be related to the development of organ dysfunctions, particularly renal dysfunction. Intra-abdominal pressure should be routinely monitored during the course of SS.

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### **EVALUATION OF MENT ON PRIMARY CELL CULTURES FROM BENIGN PROSTATIC HYPERPLASIA AND PROSTATE CARCINOMA.**

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7-alpha-Methyl-19-Nortestosterone (MENT) is a synthetic androgen more potent than testosterone (T) and cannot be reduced at 5-alpha position. No important effects of MENT on prostate growth have been reported. However, little is known about the effect of MENT on benign prostatic hyperplasia (BPH) or prostate carcinoma (CaP). We evaluate the effect of MENT, T and dihydrotestosterone (DHT) on secretion, proliferation and gene expression of primary cell cultures from human BPH and CaP. Moreover, the effect of these androgens was examined in the presence of finasteride to determine the influence of the 5-alpha reductase (5-AR) activity on the androgenic potency. BPH and CaP primary cultures were treated with 0, 1, 10 and 100 nm of T, MENT or DHT during 24 and 48 h. Prostate-specific antigen (PSA) was measured by micro particles immunoassay and proliferation rate by spectrophotometric assay (MTT) and by the immunochemical detection of the proliferation marker Ki-67. Gene expression of FGF8b (androgen sensitive gene) was evaluated by semi-quantitative RT-PCR. Results showed that MENT treatments increased PSA secretion and proliferation rate with a potency ranged between T and DHT. Similar effects of MENT were observed in both BPH and CaP cultures. The studies with finasteride showed that in BPH and CaP cells, the conversion of T into DHT significantly contributes to its effect on the proliferation and PSA secretion, and corroborated the resistance of MENT to the 5-AR. The effect of MENT on the gene expression of FGF8b in CaP cells was similar to T and lower than DHT. It is concluded that MENT increases proliferative and secretory activities and gene expression on pathological prostate cells although in less extent than the active metabolite DHT. Furthermore, the fall of endogenous concentration of T during MENT treatment anticipates that this androgen will be of low impact for the prostate.