

Abstracts de publicaciones internacionales ISI 2013

DEPARTAMENTO DE CIRUGÍA

CIR ESP. 2013 AUG-SEP;91(7):438-43.

[HIATAL HERNIAS: WHY AND HOW SHOULD THEY BE SURGICALLY TREATED].

Braghetto I, Csendes A, Korn O, Musleh M, Lanzarini E, Saure A, Hananias B, Valladares H.

INTRODUCTION: There is controversy in the literature about the choice of expectant medical treatment versus surgical treatment of hiatal hernias, depending on the presence or absence of symptoms. This study presents the results obtained by our group, considering disease duration and postoperative results. **PATIENTS AND METHOD:** A total of 121 patients were included and divided by age, disease duration, type of hiatal hernia and postoperative outcome. **RESULTS:** In 32% of the patients younger than 70 years, symptom duration was longer than 11 years and 68% of those aged more than 71 years had long-term symptoms ($p < .05$). Type iv hernias (complex) and those with diameters measuring more than 16 cm were observed in the group with longer symptom duration. Complications were more frequent in the older age group, in those with longer symptom duration and in those with type iv complex hernias. There was no postoperative mortality and only one patient (0.8%) with a type iii hernia and severe oesophagitis required reoperation. **CONCLUSION:** We recommend that patients with hiatal hernia undergo surgery at diagnosis to avoid complications and risks. Older patients should not be excluded from surgical indication but should undergo a complete multidisciplinary evaluation to avoid complications and postoperative mortality.

OBES SURG. 2013 FEB;23(2):234-40.

TYPE 2 DIABETES MELLITUS IN PATIENTS WITH MILD OBESITY: PRELIMINARY RESULTS OF SURGICAL TREATMENT.

Lanzarini E, Csendes A, Gutierrez L, Cuevas P, Lembach H, Molina JC, Musleh M, Braghetto I, Papapietro K, Araya V, Lahsen R, Olguin P, Riffo A, Diaz E, Montt D, Marin L.

In the last years, type 2 diabetes mellitus (T2DM) and obesity have become a serious public health problem, behaving as epidemic diseases. There is great interest in exploring different options for the treatment of T2DM in nonmorbidly obese patients. The purpose of this study is to report parameters of glycemic control in patients with T2DM and mild obesity who underwent laparoscopic Roux-en-Y gastric bypass (RYGBP). This prospective clinical trial includes patients with T2DM with a body mass index (BMI) between 30 and 35 kg/m² who underwent laparoscopic RYGBP from July 2008 through October 2010. Thirty-one patients were included in the study, 15 men and 16 women, with an average age of 48.7 ± 8.6 years. The average time since onset of T2DM was 5.8 years. The average postoperative follow-up was 30.4 months. The average preoperative blood glucose and glycosylated hemoglobin were 152 ± 70 mg/dl and 7.7 ± 2.1 %, respectively. All of them were using oral hypoglycemic agents, and four patients were insulin dependent. Only one patient had a postoperative complication (hemoperitoneum). At 36 months follow-up, the average BMI decreased to 24.7 kg/m², all patients (31) showed improvement in their glycemic control, and 29 of them (93.6 %) met the criteria for remission of T2DM in the last control. Laparoscopic RYGBP is a safe and effective procedure that improves glycemic control in patients with T2DM and mild obesity at midterm follow-up.

ANN N Y ACAD SCI. 2013 OCT; 1300: 29-42.

OUTCOMES OF ESOPHAGEAL SURGERY, ESPECIALLY OF THE LOWER ESOPHAGEAL SPHINCTER.

Bonavina L, Siboni S, Saino GI, Cavadas D, Braghetto I, Csendes A, Korn O, Figueredo EJ, Swanstrom LL, Wassenaar E.

This paper includes commentaries on outcomes of esophageal surgery, including the mechanisms by which fundoduplication improves lower esophageal sphincter (LES) pressure; the efficacy of the Linx™ management system in improving LES function; the utility of radiologic characterization of antireflux valves following surgery; the correlation between endoscopic findings and reported symptoms following antireflux surgery; the links between laparoscopic sleeve gastrectomy and decreased LES pressure, endoscopic esophagitis, and gastroesophageal reflux disease (GERD); the less favorable outcomes following fundoduplication among obese patients; the application of bioprosthetic meshes to reinforce hiatal repair and decrease the incidence of paraesophageal hernia; the efficacy of endoluminal antireflux procedures, and the limited efficacy of revisional antireflux operations, underscoring the importance of good primary surgery and diligent work-up to prevent the necessity of revisional procedures.

ARQ BRAS CIR DIG. 2013 JAN-MAR;26(1):7-12.

DIGESTIVE TRACT RECONSTITUTION AFTER FAILED ESOPHAGO-GASTRO OR ESOPHAGO-COLOANASTOMOSIS.

Braghetto I, Cardemil G, Csendes A, Venturelli A, Herrera M, Korn O, Sepúlveda S, Rojas J.

Background: Severe dysphagia or even aphagia can occur after esophagectomy secondary to necrosis of the ascended organ with severe stricture or complete separation of the stumps. Catastrophic esophageal or gastric disruption drives the decision to “disconnect” the esophagus in order to prevent severe septic complications. The operations employed to re-establish esophageal discontinuity are not standardized and reoperations for re-establishment of the upper digestive transit are a real challenge. Methods: This is retrospective study collecting the authors experience during 17 years including 18 patients, 14 of them previously submitted to esophagectomy and four to esophagogastrectomy. They were operated on in order to re-establish the upper digestive tract. Results: Redo esophago-gastro-anastomosis was possible in 12 patients, 10 through cervical approach and combined with sternotomy in four in order to perform the new anastomosis. In five patients a new esophago-colo anastomosis was performed. Free jejunal graft interposition was performed in one patient. Complications occurred in ten patients (55.5 %): anastomotic leaks in three, strictures in four, sternal condritis in two and cervical abscess in one. No mortality was observed. Conclusion: There are different surgical options for the treatment of this difficult and risky clinical situation which must be treated with tailored procedures according to the anatomic segment available to be used, choosing the most conservative procedure.

OBES SURG. 2013 SEP;23(9):1481-6.

GASTRIC STENOSIS AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY IN MORBIDLY OBESE PATIENTS.

Burgos AM, Csendes A, Braghetto I.

Laparoscopic sleeve gastrectomy (LSG) is an effective bariatric procedure. The objective of this study is to describe a series of patients who were subjected to LSG and then developed gastric stenosis, with an emphasis on their treatment and a discussion of the possible underlying mechanisms. From January 2006 to October 2012, 717 patients with morbid obesity underwent LSG in our institution. Out of 717 patients, 571 (79.6 %) were women. The mean age was 36.9 years with a BMI of 37.3 kg/m². Five patients (0.69 %) developed gastric stenosis. Treatment of the stenosis was endoscopic dilatations; however, one patient required a conversion to laparoscopic Roux-en-Y gastric bypass. Stenosis after LSG is rare but requires early diagnosis and treatment.

J PLAST RECONSTR AESTHET SURG. 2013 NOV;66(11):1557-63.

SUCTION-ASSISTED LIPECTOMY FAILS TO IMPROVE CARDIOVASCULAR METABOLIC MARKERS OF DISEASE: A META-ANALYSIS.

Danilla S, Longton C, Valenzuela K, Cavada G, Norambuena H, Tabilo C, Erazo C, Benitez S, Sepulveda S, Schulz R, Andrades P.

Background: The purpose of this study was to determine whether suction-assisted lipectomy (SAL) decreases the incidence of early cardiovascular disease risk factors or its biochemical and clinical risk indicators. Methods: A systematic review of the literature was performed by conducting a predefined, sensitive search in MEDLINE without limiting the year of publication or language. The extracted data included the basal characteristics of the patients, the surgical technique, the amount of fat extracted, the cardiovascular risk factors and the biochemical and clinical markers monitored over time. The data were analysed using pooled curves, risk ratios and standardised means with meta-analytical techniques. Results: Fifteen studies were identified involving 357 patients. In all of the studies, measurements of predefined variables were recorded before and after the SAL procedure. The median follow-up was 3 months (interquartile range (IQR) 1-6, range 0.5-10.5). The mean amount of extracted fat ranged from

2063 to 16,300 ml, with a mean \pm standard deviation (SD) of 6138 ± 4735 ml. After adjusting for time and body mass index (BMI), leptin and fasting insulin were the only markers that were significantly associated with the amount of aspirated fat. No associations were observed for high sensitive C-reactive protein (hCRP), interleukin-6 (IL-6), adiponectin, resistin, tumour necrosis factor- α (TNF- α), Homeostasis Model of Assessment (HOMA), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides, free fatty acids or systolic blood pressure. Conclusions: Based on the results of our analysis, we conclude that there is no evidence to support the hypothesis that subcutaneous fat removal reduces early cardiovascular or metabolic disease, its markers or its risk factors.

NUTR HOSP. 2013 MAY-JUN;28(3):631-6.

[BONE MINERAL DENSITY DISMINUTION POST ROUX-Y BYPASS SURGERY].

Papapietro K, Massardo T, Riffo A, Díaz E, Araya AV, Adjemian D, Montesinos G, Castro G.

Introduction: Bariatric surgery has important metabolic complications such as bone mass loss. GOAL: To assess bone mineral density (BMD) after Roux-en-Y gastric by-pass (RYGB) in patients under standard calcium and vitamin D supplementation. Method: In patients with morbid obesity submitted to RYGB, 76 women and 22 men of diverse age, all with standard nutritional instruction including vitamin D and calcium, we measured BMD with a dual X-ray densitometer. They had lumbar spine and hips measurement 2-3 years post-surgery. Twenty females were followed up with BMD until a mean of 54 months. Using World Health Organization (WHO) criteria's, values were compared with young controls and same age and sex population, evaluating osteopenia and osteoporosis. Results: Inverse correlation was observed between BMD and age; positive between BMD and body mass index as well as with preoperative weight excess. In women younger than 45 years, we observed a diminished BMD in 26.8% of them, with no cases of osteoporosis. In older females, BMD was decreased in 65.7% ($p = 0.0011$); corresponding to 45.7% of osteopenia and 20% osteoporosis, more frequent in lumbar spine. In the female's subgroup followed longer, BMD diminished progressively mainly in left hip. In men, there was 36% of osteopenia and 14% of osteoporosis. Conclusion: Patients from both genders and diverse ages after BPYR presented osteopenia and osteoporosis, despite early supplement prescription of calcium and vitamin D. We consider important to perform serial BMD measurements and also to individualize therapy with risk factors control.

PLAST RECONSTR SURG. 2013 AUG;132(2):327-32.

ANALGESIC EFFICACY OF LIDOCAINE FOR SUCTION-ASSISTED LIPECTOMY WITH TUMESCENT TECHNIQUE UNDER GENERAL ANESTHESIA: A RANDOMIZED, DOUBLE-MASKED, CONTROLLED TRIAL.

Danilla S, Fontbona M, de Valdés VD, Dagnino B, Sorolla JP, Israel G, Searle S, Norambuena H, Cabello R.

Background: Suction-assisted lipectomy is one of the most common procedures performed in plastic surgery. To minimize blood loss and to obtain adequate analgesia, a liquid solution is infiltrated into the subcutaneous plane before suction. The objective of this study was to determine whether the use of lidocaine in the infiltration solution reduces postoperative pain. Methods: A prospective, randomized, double-masked, clinical trial was designed. Each side of patients' body zones to be treated with suction-assisted lipectomy was randomized to receive infiltration solution with or without lidocaine. Treatment allocation was performed using computer-generated random numbers in permuted blocks of eight. Pain was assessed using the visual analogue scale and registered 1, 6, 12, 18, and 24 hours after the procedure. Results: The trial was stopped after a first interim analysis. The use of lidocaine in the dilute solution reduced pain by 0.5 point on the visual analogue scale (95 percent CI, 0.3 to 0.8; $p < 0.001$). The effect was independent of the suctioned body zone ($p = 0.756$), and lasted until 18 hours after surgery. Its analgesic effect was lost at the 24-hour postoperative control. Pain increased an average of 0.018 point on the visual analogue scale per hour (95 percent CI, 0.001 to 0.036; $p = 0.043$). Conclusions: The use of lidocaine in the infiltration solution is effective in postoperative pain control until 18 hours after surgery. Nevertheless, its clinical effect is limited and clinically irrelevant, and therefore it is no longer used by the authors.

DEPARTAMENTO DE MEDICINA

SERVICIO DE GASTROENTEROLOGÍA

J MED ECON. 2014 JAN;17(1):65-76.

COST-EFFECTIVENESS OF TELAPREVIR IN COMBINATION WITH PEGYLATED INTERFERON ALPHA AND RIBAVIRIN IN PREVIOUSLY UNTREATED CHRONIC HEPATITIS C GENOTYPE 1 PATIENTS.

Cure S, Bianic F, Gavart S, Curtis S, Lee S, Dusheiko G.

BACKGROUND: Telaprevir (T, TVR) is a direct-acting antiviral (DAA) used for the treatment of genotype 1 chronic hepatitis C virus (HCV) infection. The sustained virological response (SVR) rates, i.e., undetectable HCV RNA levels 24 weeks after the end of treatment, is what differentiate treatments. This analysis evaluated the cost-effectiveness of TVR combined with pegylated interferon (Peg-IFN) alfa-2a plus ribavirin (RBV), with Peg-IFN and RBV (PR) alone or with boceprevir (B, BOC) plus Peg-IFN alfa-2b and RBV, in naive patients. **METHODS:** A Markov cohort model of chronic HCV disease progression reflected the pathway of naive patients initiating anti-HCV therapy. SVR rates were derived from a mixed-treatment comparison including results from Phase II and III trials of TVR and BOC, and trials comparing both PR regimens. SVR has significant impact on survival, quality-of-life, and costs. Incremental cost per life year (LY) gained and quality-adjusted-life-year (QALY) gained were computed at lifetime, adopting the (National Health Service) NHS perspective. Cost and health outcomes were discounted at 3.5%. Uncertainty was assessed using deterministic and probabilistic sensitivity analyses. Sub-group analyses were also performed by interleukin (IL)-28B genotype and fibrosis stage. **RESULTS:** Higher costs and improved outcomes were associated with T/PR relative to PR alone, resulting in an ICER of £12,733 per QALY gained. T/PR retained a significant SVR advantage over PR alone and was cost-effective regardless of IL-28B genotype and fibrosis stages. T/PR regimen 'dominated' B/PR, generating 0.2 additional QALYs and reducing lifetime cost by £2758. Sensitivity analyses consistently resulted in ICERs less than £30,000/QALY for the T/PR regimen over PR alone. **LIMITATIONS:** No head-to-head trial provides direct evidence of better efficacy of T/PR vs B/PR. **Conclusion:** The introduction of TVR-based therapy for genotype 1 HCV patients is cost-effective for naive patients at the £30,000 willingness-to-pay threshold, regardless of IL-28B genotype or fibrosis stage.

REV GASTROENTEROL MEX. 2013 OCT-DEC;78(4):203-10.

[THE PREVALENCE OF IRRITABLE BOWEL SYMPTOMS IN A POPULATION OF SHOPPING MALL VISITORS IN SANTIAGO DE CHILE].

Madrid-Silva AM, Defilippi-Caffri C, Landskron-Ramos G, Olguín-Herrera F, Reyes-Ponce A, Castro-Lara A, Larraín-Corp S, Martínez-Roje N, Cortés-Espinoza J.

Background: Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain or discomfort that is associated with altered bowel habit. Both its prevalence and clinical characteristics vary throughout Latin America. A percentage of patients does not seek medical attention, therefore a reliable prevalence figure can only be established by interviewing non-selected populations. **AIMS:** To study the prevalence and clinical characteristics of IBS symptoms in non-selected subjects in Santiago, Chile. **Methods:** A total of 437 shopping mall visitors above the age of 15 years (246 women) participated in the study by answering the Rome II validated questionnaire for IBS. The demographic and socioeconomic backgrounds, comorbidities, and a family history of IBS were registered. **Results:** A total of 64.1% subjects reported having gastrointestinal symptoms and 28.6% had symptoms suggestive of IBS. When the subjects with IBS symptoms were compared with the asymptomatic individuals, a predominance of women (65.6 vs. 42.9, $P < .001$) and a greater cholecystectomy frequency (33.6 vs. 12.9% $P < .05$) were observed in the former. The age of symptom onset was 30.4 years. An equal percentage of subjects (42.4%) presented with diarrhea and constipation and 15.2% presented with alternating IBS. Participants with a higher educational level reported a lower percentage of IBS ($P < .05$). A family history of the disease was present in 40% of the subjects with IBS, compared with 14.9% in the asymptomatic individuals ($P < .05$). Only 39.2% of the subjects had seen a physician for their symptoms and the treatment and tests ordered were inappropriate. **Conclusion:** The prevalence of IBS symptoms in the population studied is one of the highest described. Therefore, health teams should have the necessary knowledge and skill required for its management.

GASTROENTEROL HEPATOL. 2013 FEB;36(2):76-80.

[ACUTE LIVER FAILURE AFTER BARIATRIC SURGERY. A CASE REPORT AND LITERATURE REVIEW].

Sagredo S, Brahm J, Uribe M, Codoceo V, Smok G.

Non-alcoholic fatty liver disease is common among morbidly obese people. Bariatric surgery is increasingly used in this population to control weight but is not free of risks. We present the case of a 28-year-old morbidly obese woman who underwent gastroplasty with

intestinal resection and a gastro-jejunal anastomosis. Eleven months later, and with a weight reduction of 35%, the patient developed acute liver failure. A biopsy showed severe steatohepatitis and fibrosis. After prolonged hospital stay and management that consisted of support measures, nutritional assistance, N-acetyl cysteine, zinc and vitamin E, liver function was restored. A follow-up biopsy showed marked regression of the initial findings. Bariatric surgery has many beneficial effects. However, even with the most up-to-date techniques, complications can occur. Familiarity with these complications is important for their prevention and treatment.

SERVICIO REUMATOLOGÍA

CLIN EXP IMMUNOL. 2013 MAR;171(3):237-42.

EFFECT OF INTERLEUKIN-6 RECEPTOR BLOCKADE ON THE BALANCE BETWEEN REGULATORY T CELLS AND T HELPER TYPE 17 CELLS IN RHEUMATOID ARTHRITIS PATIENTS.

Pesce B, Soto L, Sabugo F, Wurmman P, Cuchacovich M, López MN, Sotelo PH, Molina MC, Aguillón JC, Catalán D.

A new paradigm has emerged relating the pathogenesis of rheumatoid arthritis (RA), focused on the balance between T helper type 17 cells and regulatory T cells (T(regs)). In humans, both subpopulations depend on transforming growth factor (TGF)- β for their induction, but in the presence of inflammatory cytokines, such as interleukin (IL)-6, the generation of Th17 is favoured. Tocilizumab is a therapeutic antibody targeting the IL-6 receptor (IL-6R), which has demonstrated encouraging results in RA. The aim of this study was to evaluate the effect of tocilizumab on Th1 cells, Th17 cells, IL-17 and interferon (IFN)- γ double secretors Th17/Th1 cells, and T(regs) in RA patients. Eight RA patients received tocilizumab monthly for 24 weeks and blood samples were obtained every 8 weeks to study T cell populations by flow cytometry. The frequency of Th17 cells, Th1 cells and Th17/Th1 cells was evaluated in peripheral blood mononuclear cells (PBMCs) activated in vitro with a polyclonal stimulus. T(regs) were identified by their expression of forkhead box protein 3 (FoxP3) and CD25 by direct staining of PBMCs. Although no changes were detected in the frequency of Th1 or Th17 cells, the percentages of peripheral T(regs) increased after therapy. In addition, the infrequent Th17/Th1 subpopulation showed a significant increment in tocilizumab-treated patients. In conclusion, tocilizumab was able to skew the balance between Th17 cells and T(regs) towards a more protective status, which may contribute to the clinical improvement observed in RA patients.

SERVICIO DE ENDOCRINOLOGÍA

FOOD NUTR BULL. 2013 JUN;34(2):215-21.

ZINC AS A POTENTIAL COADJUVANT IN THERAPY FOR TYPE 2 DIABETES.

Ruz M, Carrasco F, Rojas P, Codoceo J, Inostroza J, Basfi-fer K, Valencia A, Vásquez K, Galgani J, Pérez A, López G, Arredondo M, Perez-Bravo F.

BACKGROUND: Type 2 diabetes is highly prevalent in populations having high rates of overweight and obesity. It is a chronic condition responsible for long-term severe dysfunction of several organs, including the kidneys, heart, blood vessels, and eyes. Although there are a number of pharmacologic products in the market to treat insulin resistance and impaired insulin secretion—the most prominent features of this disease—interventions directed at preserving the integrity and function of beta-cells in the long term are less available. The use of some nutrients with important cellular protective roles that may lead to a preservation of beta-cells has not been fully tested; among these, zinc may be an interesting candidate. **OBJECTIVE:** To assess the potential of zinc supplementation as adjuvant to diabetes therapy. **METHODS:** This article reviews the available information on the use of zinc as part of diabetes therapy. **RESULTS:** Cellular and animal models provide information on the insulin mimetic action of zinc, as well as its role as a regulator of oxidative stress, inflammation, apoptosis, and insulin secretion. Zinc supplementation studies in humans are limited, although some positive effects have been reported; mainly, a modest but significant reduction in fasting glucose and a trend to decreased glycated hemoglobin (HbA1c). **CONCLUSIONS:** Zinc supplementation may have beneficial effects on glycemic control. Nevertheless, among the studies considered, the vast majority lasted for 6 months or less, suggesting the importance of conducting long-duration studies given the characteristics of type 2 diabetes as a chronic disease.

HORM METAB RES. 2013 JUL;45(7):541-4.

EFFECT OF EXERCISE ON CIRCULATING LEVELS OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) IN OVERWEIGHT AND OBESE SUBJECTS.

Araya AV, Orellana X, Godoy D, Soto L, Fiedler J.

Exercise increases the expression of brain-derived neurotrophic factor (BDNF) in rodents and in healthy humans. Its relationship with weight loss and improvement in metabolic parameters, in obese human subjects, has not been elucidated. The aim of the study was to evaluate the effect of an aerobic exercise program on circulating levels of BDNF in overweight and obese subjects. We measured anthropometric and metabolic parameters in 15 male and female nondiabetic outpatients (age 38.3±9.5 years, BMI 27-35 kg/m²), before and after 30 sessions of aerobic exercise (3 sessions per week). Plasma (p), serum (s), and platelet (plat) BDNF concentrations were measured at basal condition and after completing 15 and 30 sessions of exercise. Subjects were advised to continue their usual food intake. A significant decrease in weight, BMI, waist circumference, diastolic blood pressure and total cholesterol was observed at the end of the study (p<0.02). Serum and platBDNF showed a significant increase during the training period (p=0.005 and 0.04 respectively). However, pBDNF showed no significant increase. Area under the curve of glucose at baseline, was inversely correlated with sBDNF (r= - 0.53, p=0.04) and platBDNF (r= - 0.6, p=0.01) after session 15. Also, platBDNF was correlated inversely with post load insulin and HOMA2-IR at the end of the training program (r= - 0.53, p=0.03 and r= - 0.52, p=0.04, respectively). In overweight and obese subjects, serum and platBDNF levels increase after 30 sessions of aerobic exercise. This is accompanied with the improvement of anthropometric and metabolic parameters and modest weight loss.

ARQ BRAS ENDOCRINOL METABOL. 2013 JUN;57(4):265-91.

CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF HYPOTHYROIDISM.

Brenta G, Vaisman M, Sgarbi JA, Bergoglio LM, de Andrada NC, Bravo PP, Orlandi AM, Graf H; Task Force on Hypothyroidism of the Latin American Thyroid Society (LATS).

INTRODUCTION: Hypothyroidism has long been known for its effects on different organ systems, leading to hypometabolism. However, subclinical hypothyroidism, its most prevalent form, has been recently related to cardiovascular risk and also to maternal-fetal complications in pregnant women. OBJECTIVES: In these clinical practice guidelines, several aspects of this field have been discussed with the clear objectives of helping physicians treat patients with hypothyroidism, and of sharing some of our Latin American-based clinical experience. MATERIALS AND METHODS: The Latin American Thyroid Society commissioned a Task Force on Hypothyroidism to develop evidence-based clinical guidelines on hypothyroidism. A systematic review of the available literature, focused on the primary databases of MedLine/PubMed and Lilacs/SciELO was performed. Filters to assess methodological quality were applied to select the best quality studies. The strength of recommendation on a scale from A-D was based on the Oxford Centre for Evidence-based Medicine, Levels of Evidence 2009, allowing an unbiased opinion devoid of subjective viewpoints. The areas of interest for the studies comprised diagnosis, screening, treatment and a special section for hypothyroidism in pregnancy. RESULTS: Several questions based on diagnosis, screening, treatment of hypothyroidism in adult population and specifically in pregnant women were posed. Twenty six recommendations were created based on the answers to these questions. Despite the fact that evidence in some areas of hypothyroidism, such as therapy, is lacking, out of 279 references, 73% were Grade A and B, 8% Grade C and 19% Grade D. CONCLUSIONS: These evidence-based clinical guidelines on hypothyroidism will provide unified criteria for management of hypothyroidism throughout Latin America. Although most of the studies referred to are from all over the world, the point of view of thyroidologists from Latin America is also given.

SERVICIO DE NEUMOLOGÍA**BIOL RES. 2013;46(2):207-13.**

RELATIONSHIP BETWEEN SEVERITY OF ADULT COMMUNITY-ACQUIRED PNEUMONIA AND IMPAIRMENT OF THE ANTIOXIDANT DEFENSE SYSTEM.

Castillo RL, Carrasco RA, Alvarez PI, Ruiz M, Luchsinger V, Zunino E, Martínez MA, Avendaño LF.

Oxidant/antioxidant imbalance has been reported in some infectious diseases, including community-acquired pneumonia (CAP). The aim was to assess the antioxidant status in adults with CAP and its relationship with clinical severity at

admission. Fifty-nine patients with CAP were enrolled and categorized at admission by the FINE score, from July 2010 to October 2012. In the same period 61 controls were enrolled. Plasma samples were obtained at admission for determination of the ferric reducing ability of plasma (FRAP) and lipid peroxidation (8-isoprostane). Erythrocyte reduced (GSH)/oxidized (GSSG) glutathione, malondialdehyde (MDA) and antioxidant enzyme activity were assessed. Antioxidant status in adults with CAP represented by FRAP and the GSH/GSSG ratio were 16.8% ($p=0.03$) and 39.7% ($p=0.04$) lower than control values, respectively. In addition, FRAP values showed a positive correlation with GSH/GSSG ratio ($r=0.852$; $p<0.02$; $n=59$). The CAP group showed greater lipid peroxidation in both plasma and erythrocytes. The FINE score correlated negatively with FRAP ($r= -0.718$; $p<0.05$; $n=59$) and positively with MDA and F2 isoprostane levels ($r=0.673$; $p<0.05$; $n=59$; $r=0.892$; $p<0.01$; $n=59$, respectively). Antioxidant status alterations correlated with clinical severity. The FRAP assay and lipid peroxidation biomarkers may provide a useful parameter for estimating the severity and the clinical outcome of patients with CAP.

THORAX. 2013 NOV;68(11):1000-6.

COMMUNITY-ACQUIRED PNEUMONIA IN CHILE: THE CLINICAL RELEVANCE IN THE DETECTION OF VIRUSES AND ATYPICAL BACTERIA.

Luchsinger V, Ruiz M, Zunino E, Martínez MA, Machado C, Piedra PA, Fasce R, Ulloa MT, Fink MC, Lara P, Gebauer M, Chávez F, Avendaño LF.

BACKGROUND: Adult community-acquired pneumonia (CAP) is a relevant worldwide cause of morbidity and mortality, however the aetiology often remains uncertain and the therapy is empirical. We applied conventional and molecular diagnostics to identify viruses and atypical bacteria associated with CAP in Chile. **METHODS:** We used sputum and blood cultures, IgG/IgM serology and molecular diagnostic techniques (PCR, reverse transcriptase PCR) for detection of classical and atypical bacteria (*Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumoniae*) and respiratory viruses (adenovirus, respiratory syncytial virus (RSV), human metapneumovirus, influenza virus, parainfluenzavirus, rhinovirus, coronavirus) in adults >18 years old presenting with CAP in Santiago from February 2005 to September 2007. Severity was qualified at admission by Fine's pneumonia severity index. **RESULTS:** Overall detection in 356 enrolled adults were 92 (26%) cases of a single bacterial pathogen, 80 (22%) cases of a single viral pathogen, 60 (17%) cases with mixed bacterial and viral infection and 124 (35%) cases with no identified pathogen. *Streptococcus pneumoniae* and RSV were the most common bacterial and viral pathogens identified. Infectious agent detection by PCR provided greater sensitivity than conventional techniques. To our surprise, no relationship was observed between clinical severity and sole or coinfections. **CONCLUSIONS:** The use of molecular diagnostics expanded the detection of viruses and atypical bacteria in adults with CAP, as unique or coinfections. Clinical severity and outcome were independent of the aetiological agents detected.

SERVICIO DE GENÉTICA

REPROD SCI. 2013 OCT;20(10):1207-14.

FAMILY-BASED ASSOCIATION STUDY BETWEEN SLC2A1, HK1, AND LEPR POLYMORPHISMS WITH MYELOMENINGOCELE IN CHILE.

Suazo J, Pardo R, Castillo S, Martin LM, Rojas F, Santos JL, Rotter K, Solar M, Tapia E.

Obese/diabetic mothers present a higher risk to develop offspring with myelomeningocele (MM), evidence supporting the role of energy homeostasis-related genes in neural tube defects. Using polymerase chain reaction-restriction fragment length polymorphism, we have genotyped SLC2A1, HK1, and LEPR single-nucleotide polymorphisms in 105 Chilean patients with MM and their parents in order to evaluate allele-phenotype associations by means of allele/haplotype transmission test (TDT) and parent-of-origin effects. We detected an undertransmission for the SLC2A1 haplotype T-A (rs710218-rs2229682; $P = .040$), which was not significant when only lower MM (90% of the cases) was analyzed. In addition, the leptin receptor rs1137100 G allele showed a significant increase in the risk of MM for maternal-derived alleles in the whole sample (2.43-fold; $P = .038$) and in lower MM (3.20-fold; $P = .014$). Our results support the role of genes involved in energy homeostasis in the risk of developing MM, thus sustaining the hypothesis of diverse pathways and genetic mechanisms acting in the expression of such birth defect.

SERVICIO DE GERIATRÍA

J ALZHEIMERS DIS. 2013;35(2):297-306.

THE CUIDEME STUDY: DETERMINANTS OF BURDEN IN CHILEAN PRIMARY CAREGIVERS OF PATIENTS WITH DEMENTIA.

Slachevsky A, Budinich M, Miranda-Castillo C, Núñez-Huasaf J, Silva JR, Muñoz-Neira C, Gloger S, Jimenez O, Martorell B, Delgado C.

BACKGROUND: Caring for a person with dementia is associated with well-documented increases in burden and distress and decreases in mental health and wellbeing. Studies assessing burden in caregivers of patients with dementia and its determinants are scarce in Latin America. **OBJECTIVE:** The main objective of this study was to assess the extent and the determinants of burden in informal primary caregivers of patients with dementia in Chile. **METHODS:** A descriptive study was conducted using clinically validated scales to assess dementia characteristics and to measure caregiver variables. Family socio-demographic characteristics and functional status, patient functional dependency and behavioral disturbances, and caregiver psychiatric morbidity were analyzed as independent variables to determine caregiver burden. **RESULTS:** Two hundred and ninety-two informal caregivers were included. There were more female (80%) than male caregivers, consisting mainly of daughters and spouses of the patients. Severe burden was reported in 63% of the caregivers, and 47% exhibited psychiatric morbidity. Burden was associated with caregiver psychiatric distress, family dysfunction, severity of neuropsychiatric symptoms and functional disability, but neither patient age, gender, nor socioeconomic status impacted burden. **CONCLUSION:** Our results underscore the importance of assessing the consequences of dementia in both caregivers and patients in order to evaluate the real biopsychosocial impact of dementia, as well as the importance of planning appropriate and effective public health interventions in Latin American countries. In addition, interventions targeting caregiver psychological distress, caregiver familial dysfunction, patient neuropsychiatric disorders, and patient functional disability could potentially diminish caregiver burden.

SERVICIO DE INMUNOLOGÍA

ALLERGOL IMMUNOPATHOL (MADR). 2013 JUL-AUG;41(4):233-8.

FIRST ANNUAL REGISTER OF ALLERGENIC POLLEN IN TALCA, CHILE.

Mardones P1, Grau M, Araya J, Córdova A, Pereira I, Peñailillo P, Silva R, Moraga A, Aguilera-Insunza R, Yepes-Núñez JJ, Palomo I.

BACKGROUND: There are no data on atmospheric pollen in Talca. In the present work, our aim is to describe the amount of pollen grain in the atmosphere of the city of Talca likely to cause pollinosis of its inhabitants. **METHODS:** A volumetric Hirst sampler (Burkard seven-day recording device) was used to study pollen levels. It was placed in the centre of Talca from May 2007 to April 2008. **RESULTS:** The highest airborne presence of pollen, as measured in weekly averages, was *Platanus acerifolia* with a maximum weekly daily average of 203 grains/m³ registered during September and October. The second highest was *Acer pseudoplatanus* with a maximum weekly daily average of 116 grains/m³. *Populus* spp. had a maximum weekly daily average 103 grains/m³. *Olea europaea* reached 19 grains/m³ in November. Grasses presented high levels of pollen counts with a maximum weekly daily average of 27 grains/m³ from the end of August until the end of January. Pollens of *Plantago* spp. *Rumex acetosella* and *Chenopodium* spp. had a similar distribution and were present from October to April with maximum weekly daily average of 7 grains/m³, 7 grains/m³ and 3 grains/m³ respectively. Significant concentrations of *Ambrosia artemisiifolia* were detected from February until April. **CONCLUSION:** The population of Talca was exposed to high concentrations of allergenic pollen, such as *P. acerifolia*, *A. pseudoplatanus*, and grasses in the months of August through November. The detection of *O. europaea* and *A. artemisiifolia* is important as these are emergent pollens in the city of Talca. Aerobiological monitoring will provide the community with reliable information about the level of allergenic pollens, improving treatment and quality of life of patients with respiratory allergy.

VIROL J. 2013 OCT 28;10(1):318.

HIV-1 TROPISM: A COMPARISON BETWEEN RNA AND PROVIRAL DNA IN ROUTINE CLINICAL SAMPLES FROM CHILEAN PATIENTS.

Ferrer P, Montecinos L, Tello M, Tordecilla R, Rodríguez C, Ferrés M, Pérez CM, Beltrán C, Guzmán MA, Afani A.

Background: HIV in Chile has a notification rate of 0.01%. Coreceptor antagonists are a family of antiretroviral drugs that are used with the prior knowledge of patients HIV-1 tropism. Viral RNA-based tropism detection requires a plasma viral load ≥ 1000 copies/mL, while proviral DNA-based detection can be performed regardless of plasma viral load. This test is useful in patients with low or

undetectable viral loads and would benefit with a proper therapy. The aim of this study was to determine the correlation between HIV RNA and proviral genotypic DNA tropism tests. Findings: Forty three Chilean patients were examined using population-based V3 sequencing, and a geno2pheno false-positive rate (FPR) cutoff values of 5, 5.75, 10 and 20%. With cutoff 5.75% a concordance of 88.4% in tropism prediction was found after a simultaneous comparison between HIV tropism assessment by RNA and DNA. In total, five discrepancies (11.6%) were found, 3 patients were RNA-R5/DNA-X4 and two were RNA-X4/DNA-R5. Proviral DNA enabled the prediction of tropism in patients with a low or undetectable viral load. For cutoff 5 and 5.75% genotypic testing using proviral DNA showed a similar sensitivity for X4 as RNA. We found that the highest sensitivity for detecting the X4 strain occurred with proviral DNA and cutoff of 10 and 20%. Viral loads were higher among X4 strain carriers than among R5 strain carriers ($p < 0.05$). Conclusions: A high degree of concordance was found between tropism testing with RNA and testing with proviral DNA. Our results suggest that proviral DNA-based genotypic tropism testing is a useful option for patients with low or undetectable viral load who require a different therapy.

PEDIATR ALLERGY IMMUNOL. 2013 NOV;24(7):671-7.

DEVELOPMENT OF THE SCALE OF PSYCHOSOCIAL FACTORS IN FOOD ALLERGY (SPS-FA).

Cortes A, Castillo A, Sciaraffia A.

Background: Food allergy (FA) is a growing condition among children and its psychological impact over the patients and their caregivers is well known, establishing a vicious circle that perpetuates stress levels. However, psychosocial factors are not commonly included in allergy treatments. Based on the lack of evidence of records about a scale that indicates the level of interaction between biopsychosocial factors in the patient-caregivers dyad for FA, the present research aims to develop a scale with these characteristics as a helpful tool to achieve a more comprehensive system of health care. Methods: A preliminary 28-item scale was generated (sample $N = 99$). The scale was adjusted in contents and language after expert opinion and application on patients. A factor analysis was carried out selecting the items from the final scale. Results: The final 9-item scale included three areas: impact on quality of life, social impact and conflicts. The scale had a good internal consistency (Cronbach's $\alpha = 0.870$) and correlated significantly with anxiety and depression measurements. Moreover, it was able to discriminate between study groups (members and non-members of peer support groups) and proved construct validity. Conclusions: The SPS-FA is the first scale for the assessment of the interaction of biopsychosocial factors on FA that includes the patient-caregiver dyad. Its application might be relevant for future research, and it can provide the clinician and the researcher with a solid tool to define which type of psychosocial support is required to provide a more comprehensive care in FA.

SERVICIO DE NEFROLOGÍA

NUTR HOSP. 2013 JUL-AUG;28(4):1306-12.

[BONE MINERAL DENSITY AND ADEQUACY OF DIETARY PATTERN OF PATIENTS WITH CHRONIC KIDNEY DISEASE IN HEMODIALYSIS].

Carrasco F, Cano M, Camousseigt J, Rojas P, Inostroza J, Torres R.

BACKGROUND: In chronic kidney disease (CKD) patients, malnutrition is common with loss of muscle mass and decreased bone mineral density (BMD), increasing the risk of morbidity. OBJECTIVE: To compare body composition, bone mineral density (BMD) and bone mineral content (BMC) between CKD patients and healthy subjects, and relate these parameters with energy, macronutrients and micronutrients intake. METHODS: Body composition was assessed 30 haemodialysis patients and compared with 28 healthy volunteers with DEXA. In patients, three 24 hours records of dietary intake were filled. RESULTS: A significantly lower BMD ($p < 0.01$) and BMC ($p < 0.0$) were found in CKD patients. There was a trend for patients to have lower fat free mass (FFM) than controls ($p = 0.06$). In men, differences in BMD and BMC lost significance when adjusting for fat mass FM (%) and FFM (kg). In CKD, 34.5% and 27.6% of patients had an adequate intake of energy and protein, respectively. However, it was observed a deficit of energy and protein intake in 31.0% and 44.8% of patients, respectively. No significant correlation was found in CKD patients between macronutrient and calcium intake and BMD or BMC. CONCLUSIONS: CKD have lower BMD and BMC than healthy volunteers. These differences lost significance in men, after adjusting for body composition parameters. A poor dietary adequacy was found in most patients with CKD, but no association was observed between these variables and body composition or bone mineral density.

DEPARTAMENTO DE DERMATOLOGÍA

SKIN THERAPY LETT. 2013 JUN;18(4):1-4.

SELECTED SKIN DISEASES WITH SYSTEMIC INVOLVEMENT.

Ruiz M, Valdés P, Tomecki K.

The skin is often a window to systemic disease that is available to the trained eye of the dermatologist. Herein, we focus on four dermatoses with associated systemic conditions of interest: scleromyxedema and monoclonal gammopathy, nephrogenic systemic fibrosis in the setting of renal insufficiency, dermatitis herpetiformis and celiac disease, and psoriasis as a risk factor for cardiovascular disease. Dermatologists can play a crucial role in recognizing the cutaneous manifestations linked with these conditions. Identifying the related underlying disorder will contribute to appropriate diagnosis and improved management.

SERVICIO DE ANATOMÍA PATOLÓGICA

BRAIN PATHOL. 2013 MAY;23(3):361-2.

24-YEAR-OLD WOMAN WITH AN INTERNAL AUDITORY CANAL MASS. HYBRID PERIPHERAL NERVE SHEATH TUMOR WITH SCHWANNOMA/PERINEURIOMA COMPONENTS.

Las Heras F, Martuza R, Caruso P, Rincon S, Stemmer-Rachamimov A.

Benign peripheral nerve sheath tumors are divided into schwannomas, neurofibromas and perineuriomas. In recent years, tumors with hybrid features, composed of multiple, discrete areas of different histological types, were described. These tumors may represent a diagnostic challenge. A 24-year-old woman with multiple sclerosis was found to have a 1.3 cm TV × 0.7 cm AP T2 intermediate lesion within the left internal auditory canal. Gross examination revealed a tan-white, well circumscribed mass. Histologic examination demonstrated a well demarcated, cellular, solid neoplasm with a biphasic pattern. Most of the tumor was composed of spindle cells arranged in fascicles with focal Verocay body formation and diffuse S100 positivity. A second, minor area showed concentric proliferation of neoplastic spindle cells around one or more axons. Tumor cells in this area were positive for perineurial markers, claudin-1 and Glut-1, and focally immunopositive for CD34. We present here a case of a benign peripheral nerve sheath tumor with histological and immunohistochemical features consistent with a dual pattern of differentiation of schwannoma and perineurioma, in the VIIIth cranial nerve. This is, to our knowledge, the first case of a hybrid perineurioma/schwannoma reported in a cranial nerve.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

ADV PSYCHOSOM MED. 2013;33:88-96.

ETHNOPSYCHOPHARMACOLOGY AND PHARMACOGENOMICS.

Silva H.

Significant differences in response to psychotropic drugs are observed in various ethnic and cultural groups. Ethnopsychiatry is the study of how culture and genetic differences in human groups determine and influence the response to psychotropic agents. Meanwhile, pharmacogenomics studies the influence of genetic variations in the response of patients to different drugs. Pharmacogenetic tests are used to predict drug response and the potential for adverse effects. There are important genetic variations that influence the metabolism and action of psychotropic drugs in different ethnic groups. As examples, the frequencies of CYP2D6 polymorphisms and of the long and short alleles of the promoter region of the serotonin transporter are analyzed. Studies found significant differences in the frequency of polymorphisms of both genes in different countries and ethnic groups. On the basis of this review, the importance of considering ethnic and cultural factors in the prescription of drugs and in the need of further pharmacogenetic studies in different countries and geographical regions is reaffirmed.

ADV PSYCHOSOM MED. 2013;33:115-22.

BIOETHICAL DIMENSIONS OF CULTURAL PSYCHOSOMATICS: THE NEED FOR AN ETHICAL RESEARCH APPROACH.

Lolas F.

Contemporary psychosomatics is a research-based technical discipline and its social power depends on how scientific knowledge is obtained and applied in practice, considering cultural contexts. This article presents the view that the dialogical principles on which bioethical discourse is based are more inclusive than professional ethics and philosophical reflection. The distinction is advanced between rule-guided behavior and norm-justifiable acts (substantiation and justification). The practical implications of good practices in the generation of valid, reliable, generalizable and applicable knowledge are emphasized. For practitioners and researchers, the need to reflect on the distinction between patient and research participant can avoid the therapeutic misunderstanding, a form of abuse of the doctor-patient relationship. In addition, in resource-poor settings, the dilemma presented by the know-do gap (inapplicability of research results due to financial or social constraints) is part of the ethics' realm of the profession. Future prospects include a wider use of research results in practice, but avoidance of the know-do gap (the disparity between what is known and what can be done, particularly in settings with limited resources) requires a synthetic and holistic approach to medical ethics, combining moral reflection, theoretical analysis and empirical data.

BMC PSYCHIATRY. 2013 APR 23;13:122.

DETECTING DEPRESSION AMONG ADOLESCENTS IN SANTIAGO, CHILE: SEX DIFFERENCES.

Araya R, Montero-Marin J, Barroilhet S, Fritsch R, Montgomery A.

Background: Depression among adolescents is common but most cases go undetected. Brief questionnaires offer an opportunity to identify probable cases but properly validated cut-off points are often unavailable, especially in non-western countries. Sex differences in the prevalence of depression become marked in adolescence and this needs to be accounted when establishing cut-off points. Method: This study involved adolescents attending secondary state schools in Santiago, Chile. We compared the self-reported Beck Depression Inventory-II with a psychiatric interview to ascertain diagnosis. General psychometric features were estimated before establishing the criterion validity of the BDI-II. Results: The BDI-II showed good psychometric properties with good internal consistency, a clear unidimensional factorial structure, and good capacity to discriminate between cases and non-cases of depression. Optimal cut-off points to establish caseness for depression were much higher for girls than boys. Sex discrepancies were primarily explained by differences in scores among those with depression rather than among those without depression. Conclusions: It is essential to validate scales with the populations intended to be used with. Sex differences are often ignored when applying cut-off points, leading to substantial misclassification. Early detection of depression is essential if we think that early intervention is a clinically important goal.

JAMA PEDIATR. 2013 NOV;167(11):1004-10. DOI: 10.1001/JAMAPEDIATRICS.2013.2361.

SCHOOL INTERVENTION TO IMPROVE MENTAL HEALTH OF STUDENTS IN SANTIAGO, CHILE: A RANDOMIZED CLINICAL TRIAL.

Araya R, Fritsch R, Spears M, Rojas G, Martinez V, Barroilhet S, Vöhringer P, Gunnell D, Stallard P, Guajardo V, Gaete J, Noble S, Montgomery AA.

Depression can have devastating effects unless prevented or treated early and effectively. Schools offer an excellent opportunity to intervene with adolescents presenting emotional problems. There are very few universal school-based depression interventions conducted in low- and middle-income countries. Objective: To assess the effectiveness of a school-based, universal psychological intervention to reduce depressive symptoms among adolescents from low-income families. Design, setting, and participants: A 2-arm, parallel, cluster, randomized clinical trial was conducted in secondary schools in deprived socioeconomic areas of Santiago, Chile. Almost all students registered in the selected schools consented to take part in the study. A total of 2512 secondary school students from 22 schools and 66 classes participated. Interventions: Students in the intervention arm attended 11 one-hour weekly and 2 booster classroom sessions of an intervention based on cognitive-behavioral models. The intervention was delivered by trained nonspecialists. Schools in the control arm received the standard school curriculum. Main outcomes and measures: Scores on the self-administered Beck Depression Inventory-II at 3 months (primary) and 12 months (secondary) after completing the intervention. Results: There were 1291 participants in the control arm and 1221 in the intervention arm. Primary outcome data were available for 82.1% of the participants. There was no evidence of any clinically important difference in mean depression scores between the groups (adjusted difference in mean, -0.19; 95% CI, -1.22 to 0.84) or for any of the other outcomes 3 months after completion of the intervention. No significant differences were found in any of the outcomes at 12 months. Conclusions and relevance: A well-designed and implemented school-based intervention did not reduce depressive symptoms among socioeconomically deprived

adolescents in Santiago, Chile. There is growing evidence that universal school interventions may not be sufficiently effective to reduce or prevent depressive symptoms.

FRONT PSYCHIATRY. 2013 OCT 9;4:116. ECOLLECTION 2013.

EFFICACY OF COMMUNITY TREATMENTS FOR SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS: A LITERATURE REVIEW.

Armijo J, Méndez E, Morales R, Schilling S, Castro A, Alvarado R, Rojas G.

Background: In Chile, the clinical guidelines “for the treatment of people from first episode of schizophrenia” aim to support individuals with schizophrenia to live independently, establishment occupational goals, and gain an adequate quality of life and social interaction. This requires the implementation of a treatment model that integrates psychosocial and pharmacological dimensions. Community intervention strategies ensure the achievement of these goals. Objectives: This study compiles and synthesizes available scientific evidence from the last 14 years on the effectiveness of community intervention strategies for schizophrenia and related psychotic disorders. Methodology: An electronic search was carried out using PUBMED, LILACS, and Science Direct as databases. Criteria of inclusion: (i) randomized clinical trials, (ii) Community-based interventions, (iii) diagnosis of schizophrenia or related psychotic disorder (section F2 of ICD-10). Exclusion Criteria: (i) treatments exclusively pharmacological, (ii) interventions carried out in inpatient settings, (iii) bipolar affective disorder or substance-induced psychosis (greater than 50% of sample). Results: Sixty-six articles were reviewed. Community strategies for integrated treatment from the first outbreak of schizophrenia significantly reduced negative and psychotic symptoms, days of hospitalization, and comorbidity with substance abuse and improved global functioning and adherence to treatment. In other stages, there were improved outcomes in negative and positive symptoms and general psychopathology. Psychoeducation for patients and families reduced the levels of self-stigma and domestic abuse, as well as improved knowledge of the disease and treatment adherence. Training focused on cognitive, social, and labor skills has been shown to improve yields in social functioning and employment status. Conclusion: Community-based intervention strategies are widely supported in the treatment of patients with schizophrenia.

J MED SCREEN. 2013;20(3):118-24.

DETECTING MOOD DISORDER IN RESOURCE-LIMITED PRIMARY CARE SETTINGS: COMPARISON OF A SELF-ADMINISTERED SCREENING TOOL TO GENERAL PRACTITIONER ASSESSMENT.

Vöhringer PA, Jimenez MI, Igor MA, Fores GA, Correa MO, Sullivan MC, Holtzman NS, Whitham EA, Barroilhet SA, Alvear K, Logvinenko T, Kent DM, Ghaemi NS.

Objectives: Although efficacious treatments for mood disorders are available in primary care, under-diagnosis is associated with under-treatment and poorer outcomes. This study compares the accuracy of self-administered screening tests with routine general practitioner (GP) assessment for detection of current mood disorder. Methods: 197 consecutive patients attending primary care centres in Santiago, Chile enrolled in this cross-sectional study, filling out the Patients Health Questionnaire-9 (PHQ-9) for depression and the Mood Disorder Questionnaire (MDQ) for bipolar disorder, after routine GP assessment. Diagnostic accuracy of these self-administered tools was compared with GP assessment, with gold standard diagnosis established by a structured diagnostic interview with trained clinicians (SCID-I). Results: The sample was 75% female, with a mean age of 48.5 (SD 16.8); 37% had a current mood disorder (positive SCID-I result for depression or bipolar disorder). Sensitivity of the screening instruments (SI) was substantially higher than GP assessment (SI: 0.8, [95% CI 0.71, 0.81], versus GP: 0.2, [95% CI 0.12, 0.25]: p-value < 0.0001), without sacrifice in specificity (SI: 0.9, [95% CI 0.86, 0.96], versus GP: 0.9, [95% CI 0.88, 0.97]: p-value = 0.7). This led to improvement in both positive predictive value (SI: 0.8, [95% CI 0.82, 0.90], versus GP: 0.6, [95% CI 0.50, 0.64]: p-value < 0.001) and negative predictive value (SI: 0.9, [95% CI 0.78, 0.91] versus GP: 0.7, [95% CI 0.56, 0.72]: p-value < 0.01). Conclusion: Self-administered screening tools are more accurate than GP assessment in detecting current mood disorder in low-income primary care. Such screening tests may improve detection of current mood disorder if implemented in primary care settings.

FRONT PSYCHIATRY. 2013 AUG 8;4:87.

COGNITIVE IMPAIRMENT IN BIPOLAR DISORDER AND SCHIZOPHRENIA: A SYSTEMATIC REVIEW.

Vöhringer PA, Barroilhet SA, Amerio A, Reale ML, Alvear K, Vergne D, Ghaemi SN.

Aims: Previous comparisons of cognitive decline among patients with bipolar disorder (BD) and schizophrenia (SZ) have found somehow quite similar profiles of deficits, but results have varied between studies. Therefore an extensive and thoughtful systematic review of the matter is warranted. Methods: Studies were found through systematic search (PubMed) following

PRISMA guidelines. To be included, studies must have assessed the following cognitive functions: executive functions, memory, IQ, attention-concentration, and perceptuomotor function. In order to make comparison between the two entities, studies should include BD patients with operationally defined euthymia, schizophrenic patients in remission, and third group of healthy control patients. Comparisons were made after controlling for years of schooling and residual affective symptoms. Results: We found that overall both SZ and BD patients present deficits on all neurocognitive measures compared to healthy controls. In particular, SZ patients show more severe and pervasive cognitive deficits while BD patients present a milder and more confined impairment. In addition, evidence from the literature suggests that SZ and BD patients share a similar cognitive impairment profile with different degrees of deficits. Therefore, the difference between the two groups seems to be more quantitative (degree of deficit) rather than qualitative (profile), supporting a dimensional approach to the two clinical entities. Limitations of the present review includes the impossibility to control for effects of medication, varying time required for assessment across studies, illness diagnosis reliability, and course severity. Conclusion: Patients with BD might exhibit a cognitive impairment that could be similar to SZ in terms of their profile, although patients with SZ may have more severe and widespread impairments.

J AFFECT DISORD. 2013 DEC;151(3):1125-31.

A CLINICAL PREDICTIVE SCORE FOR MOOD DISORDER RISK IN LOW-INCOME PRIMARY CARE SETTINGS.

Vöhringer PA, Jimenez MI, Igor MA, Forés GA, Correa MO, Sullivan MC, Holtzman NS, Whitham EA, Barroilhet SA, Alvear K, Logvinenko T, Kent DM, Ghaemi SN.

Background: Despite availability of validated screening tests for mood disorders, busy general practitioners (GPs) often lack the time to use them routinely. This study aimed to develop a simplified clinical predictive score to help screen for presence of current mood disorder in low-income primary care settings. Methods: In a cross-sectional study, 197 patients seen at 10 primary care centers in Santiago, Chile completed self-administered screening tools for mood disorders: the Patient Health questionnaire (PHQ-9) and the Mood Disorder Questionnaire (MDQ). To determine participants' current-point mood disorder status, trained clinicians applied a gold-standard diagnostic interview (SCID-I). A simplified clinical predictive model (CM) was developed based on clinical features and selected questions from the screening tools. Using CM, a clinical predictive score (PS) was developed. Full PHQ-9 and GP assessment were compared with PS. Results: Using multivariate logistic regression, clinical and demographic variables predictive of current mood disorder were identified for a simplified 8-point predictive score (PS). PS had better discrimination than GP assessment (auROC-statistic=0.80 [95% CI 0.72, 0.85] vs. 0.58 [95% CI 0.52, 0.62] p-value <0.0001), but not as good as the full PHQ-9 (0.89 [95% CI 0.85, 0.93], p-value=0.03). Compared with GP assessment, PS increased sensitivity by 50% at a fixed specificity of 90%. Administered in a typical primary care clinical population, it correctly predicted almost 80% of cases. Limitations: Further research must verify external validity of the PS. Conclusion: An easily administered clinical predictive score determined, with reasonable accuracy, the current risk of mood disorders in low-income primary care settings.

PLOS ONE. 2013 JUL 22;8(7):E69109.

PREVALENCE RATES OF MENTAL DISORDERS IN CHILEAN PRISONS.

Mundt AP, Alvarado R, Fritsch R, Poblete C, Villagra C, Kastner S, Priebe S.

Objective: High rates of mental disorders have been reported for prison populations worldwide, particularly in low- and middle-income countries (LMICs). The present study aimed to establish prevalence rates of mental disorders in Chilean prisoners. Method: A nationwide random sample of 1008 prisoners was assessed in 7 penal institutions throughout Chile. Twelve-month prevalence rates were established using the Composite International Diagnostic Interview (CIDI) and compared to the prevalence rates previously published for the general population. Results: Prevalence rates were 12.2% (95% CI, 10.2-14.1) for any substance use disorder, 8.3% (6.6-10.0) for anxiety disorders, 8.1% (6.5-9.8) for affective disorders, 5.7% (4.4-7.1) for intermittent explosive disorders, 2.2% (1.4-3.2) for ADHD of the adult, and 0.8% (0.3-1.3) for non-affective psychoses. Significantly higher prevalence rates among prisoners as compared to the general population in Chile were seen for major depression (6.1% vs. 3.7% males, $Z=2.58$, $p<0.05$) and illicit drug use (3.3% vs. 0.6% males with drug abuse, $Z=2.04$, $p<0.05$; 2.6% vs. 0.1% females with drug abuse, $Z=5.36$, $p<0.001$; 3.4% vs. 1.1% males with drug dependence, $Z=3.70$; $p<0.001$). Dysthymia (6.5% vs. 15.6%, $Z=-2.39$, $p<0.05$), simple (3.3% vs. 11.5%, $Z=-3.13$, $p<0.001$) and social phobias (3.9% vs. 9.7%, $Z=2.38$, $p<0.05$) were significantly less frequent in the female prison population than in the general population. One-year prevalence rates of alcohol abuse (2.3% vs. 3.9%; $Z=-2.04$; $p<0.05$) and dependence (2.7% vs. 8.2%; $Z=-5.24$; $p<0.001$) were less prevalent in the male prison population than in the general population. Conclusions: Service provision for prison populations in Chile should acknowledge high rates of depression and illicit drug use. Overall prevalence rates are lower than reported in other LMICs. Previous research in prison populations in LMICs might have overestimated prevalence rates of mental disorders.

FRONT PSYCHIATRY. 2013 JUN 17;4:45.

BDNF AND SCHIZOPHRENIA: FROM NEURODEVELOPMENT TO NEURONAL PLASTICITY, LEARNING, AND MEMORY.

Nieto R, Kukuljan M, Silva H.

Brain-Derived Neurotrophic Factor (BDNF) is a neurotrophin that has been related not only to neurodevelopment and neuroprotection, but also to synapse regulation, learning, and memory. Research focused on the neurobiology of schizophrenia has emphasized the relevance of neurodevelopmental and neurotoxicity-related elements in the pathogenesis of this disease. Research focused on the clinical features of schizophrenia in the past decades has emphasized the relevance of cognitive deficits of this illness, considered a core manifestation and an important predictor for functional outcome. Variations in neurotrophins such as BDNF may have a role as part of the molecular mechanisms underlying these processes, from the neurodevelopmental alterations to the molecular mechanisms of cognitive dysfunction in schizophrenia patients.

J CLIN PSYCHOPHARMACOL. 2013 APR;33(2):231-5. DOI: 10.1097/JCP.0B013E318287019C.

EFFECTIVENESS OF SHORT-TERM OLANZAPINE IN PATIENTS WITH BIPOLAR I DISORDER, WITH OR WITHOUT COMORBIDITY WITH SUBSTANCE USE DISORDER.

Sani G, Kotzalidis GD, Vöhringer P, Pucci D, Simonetti A, Manfredi G, Savoja V, Tamorri SM, Mazzarini L, Pacchiarotti I, Telesforo CL, Ferracuti S, Brugnoli R, Ambrosi E, Caloro M, Del Casale A, Koukopoulos AE, Vergne DE, Girardi P, Ghaemi SN.

OBJECTIVES: Prognosis of comorbid bipolar disorder (BD) and drug abuse is poor. We assessed the efficacy of olanzapine in manic or mixed BD patients, with (SUD) or without (N-SUD) comorbidity with substance use disorder (SUD) and its effect on drug abuse, days of abuse, and craving. METHODS: Eighty patients with BD-I (40 SUD) were hospitalized for a manic or mixed episode and received add-on olanzapine. Assessments were conducted at admission, discharge, and 4 and 8 weeks after discharge. Primary outcome was the proportion of responders and remitters in each group. We used a logistic regression model to adjust for possible confounders. We assessed craving and drug-abuse days with a visual analog scale and the Timeline Follow-Back. RESULTS: SUD and N-SUD were similar on response and remission, adjusted for sex, age, years ill, age at first episode, first episode depressive, number of hospitalizations, and duration of hospitalization (odds ratio, 1.09; 95% confidence interval, 1.02-2.29). Mood rating scores dropped significantly from baseline to end point in both groups. Timeline follow-back decreased in SUD from 22.5 to 7.3 at 8 weeks postdischarge, whereas craving dropped from 8.3 to 5.1 ($P < 0.03$). CONCLUSIONS: The effectiveness of short-term olanzapine in BD-I mania or mixed mania did not differ according to SUD comorbidity. Treatment was followed by less substance use/abuse and craving in comorbid bipolar-SUD patients.

DEPARTAMENTO DE ANESTESIOLOGÍA

FRONT PSYCHIATRY. 2013 MAY 20;4:37.

SMALL SACCADES AND IMAGE COMPLEXITY DURING FREE VIEWING OF NATURAL IMAGES IN SCHIZOPHRENIA.

Egaña JI, Devia C, Mayol R, Parrini J, Orellana G, Ruiz A, Maldonado PE.

In schizophrenia, patients display dysfunctions during the execution of simple visual tasks such as antisaccade or smooth pursuit. In more ecological scenarios, such as free viewing of natural images, patients appear to make fewer and longer visual fixations and display shorter scanpaths. It is not clear whether these measurements reflect alterations in their proficiency to perform basic eye movements, such as saccades and fixations, or are related to high-level mechanisms, such as exploration or attention. We utilized free exploration of natural images of different complexities as a model of an ecological context where normally operative mechanisms of visual control can be accurately measured. We quantified visual exploration as Euclidean distance, scanpaths, saccades, and visual fixation, using the standard SR-Research eye tracker algorithm (SR). We then compared this result with a computation that includes microsaccades (EM). We evaluated eight schizophrenia patients and corresponding healthy controls (HC). Next, we tested whether the decrement in the number of saccades and fixations, as well as their increment in duration reported previously in schizophrenia patients, resulted from the increasing occurrence of undetected microsaccades. We found that when utilizing the standard SR algorithm, patients displayed shorter scanpaths as well as fewer and shorter saccades and fixations. When we employed the EM algorithm, the differences in these parameters between patients and HC were no longer significant. On the other hand, we found that image complexity plays an important role in exploratory behaviors, demonstrating that this factor explains most of differences between eye-movement behaviors in schizophrenia patients. These results help elucidate the mechanisms of visual motor control that are affected in schizophrenia and contribute to the finding of adequate markers for diagnosis and treatment for this condition.

SERVICIO DE UROLOGÍA

UROLITHIASIS. 2013 JUN;41(3):253-6.

IMMEDIATE POSTOPERATIVE MORBIDITY IN PATIENTS WITH INDWELLING DOUBLE-J STENT VERSUS OVERNIGHT-EXTERNALIZED URETERAL CATHETER AFTER TUBELESS PERCUTANEOUS NEPHROLITHOTOMY: A PROSPECTIVE, RANDOMIZED STUDY.

Mercado A, Fernández MI, Recabal P, Fleck D, Ledezma R, Moya F, Sepúlveda F, Vilches R, Reyes D, Marchant F.

The conventional technique for percutaneous nephrolithotomy (PNL) ends by placing a nephrostomy tube within the access tract. However, feasibility and safety of tubeless PNL have been widely demonstrated. In this modification, a ureteral stent is usually left in place instead of the nephrostomy tube. The aim of this study is to compare the use of a postoperative indwelling double-J stent versus an overnight-externalized ureteral catheter in patients undergoing tubeless PNL. Sixty-eight patients undergoing tubeless PNL were randomized either for a postoperative double-J stent (group 1) or for an overnight-externalized ureteral catheter (group 2). Outcomes evaluated included postoperative pain, hospital stay length, incidence of hemorrhagic complications, residual lithiasis and urinary leakage. Groups were similar according to age, sex, body mass index and stone burden. There were no significant differences in terms of postoperative pain, incidence of perirenal hematomas, residual lithiasis and urinary leakage. However, patients in group 1 presented longer hospital stays (3.7 ± 1.7 vs. 1.9 ± 0.3 days; $p < 0.001$) and greater hematocrit drops (4.9 ± 2.2 vs. 2.1 ± 1.8 %; $p < 0.001$). Our results confirm that among patients undergoing tubeless PNL, both alternatives (i.e. leaving a double-J stent or an overnight-externalized ureteral catheter) are reliable and safe. However, further considerations, like the need of double-J stent removal under cystoscopy, need to be taken into account when deciding which modality to use.

BIOL RES. 2013;46(4):431-40.

TAPCELLS, THE CHILEAN DENDRITIC CELL VACCINE AGAINST MELANOMA AND PROSTATE CANCER.

Salazar-Onfray F, Pereda C, Reyes D, López MN.

Here we summarize 10 years of effort in the development of a biomedical innovation with global projections. This innovation consists of a novel method for the production of therapeutic dendritic-like cells called Tumor Antigen Presenting Cells (TAPCells®). TAPCells-based immunotherapy was tested in more than 120 stage III and IV melanoma patients and 20 castration-resistant prostate cancer patients in a series of phase I and I/II clinical trials. TAPCells vaccines induced T cell-mediated memory immune responses that correlated with increased survival in melanoma patients and prolonged prostate-specific antigen doubling time in prostate cancer patients. Importantly, more than 60% of tested patients showed a Delayed Type Hypersensitivity (DTH) reaction against the lysates, indicating the development of anti-tumor immunological memory that correlates with clinical benefits. The in vitro analysis of the lysate mix showed that it contains damage-associated molecular patterns such as HMBG-1 protein which are capable to improve, through Toll-like receptor-4, maturation and antigen cross-presentation of the dendritic cells (DC). In fact, a Toll-like receptor-4 polymorphism correlates with patient clinical outcomes. Moreover, Concholepas concholepas hemocyanin (CCH) used as adjuvant proved to be safe and capable of enhancing the immunological response. Furthermore, we observed that DC vaccination resulted in a three-fold increase of T helper-1 lymphocytes releasing IFN- γ and a two-fold increase of T helper-17 lymphocytes capable of producing IL-17 in DTH+ with respect to DTH- patients. Important steps have been accomplished for TAPCells technology transfer, including patenting, packaging and technology assessment. Altogether, our results indicate that TAPCells vaccines constitute an exceptional Chilean national innovation of international value.

BR J CANCER. 2013 SEP 17;109(6):1488-97.

TUMOUR CELL LYSATE-LOADED DENDRITIC CELL VACCINE INDUCES BIOCHEMICAL AND MEMORY IMMUNE RESPONSE IN CASTRATION-RESISTANT PROSTATE CANCER PATIENTS.

Reyes D, Salazar L, Espinoza E, Pereda C, Castellón E, Valdevenito R, Huidobro C, Inés Becker M, Lladser A, López MN, Salazar-Onfray F.

Background: Recently, we produced a tumour antigen-presenting cells (TAPCells) vaccine using a melanoma cell lysate, called TRIMEL, as an antigen source and an activation factor. Tumour antigen-presenting cells induced immunological responses and increased melanoma patient survival. Herein, we investigated the effect of TAPCells loaded with prostate cancer cell lysates (PCCL) as an antigen source, and TRIMEL as a dendritic cell (DC) activation factor; which were co-injected with the Concholepas concholepas haemocyanin (CCH) as an adjuvant on castration-resistant prostate cancer (CRPC) patients. Methods: The lysate mix

capacity, for inducing T-cell activation, was analysed by flow cytometry and Elispot. Delayed-type hypersensitivity (DTH) reaction against PCCL, frequency of CD8(+) memory T cells (T_m) in blood and prostate-specific antigen (PSA) levels in serum were measured in treated patients. Results: The lysate mix induced functional mature DCs that were capable of activating PCCL-specific T cells. No relevant adverse reactions were observed. Six out of 14 patients showed a significant decrease in levels of PSA. DTH(+) patients showed a prolonged PSA doubling-time after treatment. Expansion of functional central and effector CD8(+) T_m were detected. Conclusion: Treatment of CRPC patients with lysate-loaded TAPCells and CCH as an adjuvant is safe: generating biochemical and memory immune responses. However, the limited number of cases requires confirmation in a phase II clinical trial.

UROLITHIASIS. 2013 JUN;41(3):253-6.

IMMEDIATE POSTOPERATIVE MORBIDITY IN PATIENTS WITH INDWELLING DOUBLE-J STENT VERSUS OVERNIGHT-EXTERNALIZED URETERAL CATHETER AFTER TUBELESS PERCUTANEOUS NEPHROLITHOTOMY: A PROSPECTIVE, RANDOMIZED STUDY.

Mercado A, Fernández MI, Recabal P, Fleck D, Ledezma R, Moya F, Sepúlveda F, Vilches R, Reyes D, Marchant F.

The conventional technique for percutaneous nephrolithotomy (PNL) ends by placing a nephrostomy tube within the access tract. However, feasibility and safety of tubeless PNL have been widely demonstrated. In this modification, a ureteral stent is usually left in place instead of the nephrostomy tube. The aim of this study is to compare the use of a postoperative indwelling double-J stent versus an overnight-externalized ureteral catheter in patients undergoing tubeless PNL. Sixty-eight patients undergoing tubeless PNL were randomized either for a postoperative double-J stent (group 1) or for an overnight-externalized ureteral catheter (group 2). Outcomes evaluated included postoperative pain, hospital stay length, incidence of hemorrhagic complications, residual lithiasis and urinary leakage. Groups were similar according to age, sex, body mass index and stone burden. There were no significant differences in terms of postoperative pain, incidence of perirenal hematomas, residual lithiasis and urinary leakage. However, patients in group 1 presented longer hospital stays (3.7 ± 1.7 vs. 1.9 ± 0.3 days; $p < 0.001$) and greater hematocrit drops (4.9 ± 2.2 vs. 2.1 ± 1.8 %; $p < 0.001$). Our results confirm that among patients undergoing tubeless PNL, both alternatives (i.e. leaving a double-J stent or an overnight-externalized ureteral catheter) are reliable and safe. However, further considerations, like the need of double-J stent removal under cystoscopy, need to be taken into account when deciding which modality to use.

UROL ONCOL. 2013 NOV;31(8):1522-6.

PCA3 SENSITIVITY AND SPECIFICITY FOR PROSTATE CANCER DETECTION IN PATIENTS WITH ABNORMAL PSA AND/OR SUSPICIOUS DIGITAL RECTAL EXAMINATION. FIRST LATIN AMERICAN EXPERIENCE.

Ramos CG, Valdevenito R, Vergara I, Anabalón P, Sánchez C, Fulla J.

Introduction: Prostate Cancer Gene 3 (PCA3) is a recently described and highly specific urinary marker for prostate cancer (CaP). Its introduction in clinical practice to supplement low specificity of prostate specific antigen (PSA) can improve CaP diagnosis and follow-up. However, before its introduction, it is necessary to validate the method of PCA3 detection in distinct geographic populations. Objectives: Our aim was to describe for the first time in Latin America, the application of the PROGENSA PCA3 assay for PCA3 detection in urine in Chilean men and its utility for CaP diagnosis in men with an indication of prostate biopsy. Materials and methods: Sixty-four Chilean patients (mean age, 64 years) with indication of prostate biopsy because of elevated PSA and/or suspicious digital rectal examination (DRE) were prospectively recruited. PCA3 scores were assessed from urine samples obtained after DRE, before biopsy, and compared with PSA levels and biopsy outcome. Results: The median PSA value and mean PCA3 score were 5.8 ng/ml and 31.7, respectively. Using a cutoff PCA3 score of 35, the sensitivity and specificity for detecting CaP were 52% and 87%, respectively. The receiver operating characteristic (ROC) curve analysis showed an area under the curve of 0.77 for PCA3 and 0.57 for PSA, for the same group of patients. In patients with previous negative biopsy, PCA3 specificity increased by 2.2%. Conclusions: This is the first report in Latin America on the use of PCA3 in diagnosing CaP. Our results are comparable to those reported in other populations in the literature, demonstrating the reproducibility of the test. PCA3 score was highly specific and we specially recommend its use in patients with persistent elevated PSA and prior negative biopsies.

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

J ASSOC RES OTOLARYNGOL. 2013 AUG;14(4):495-508.

P27KIP1 KNOCKDOWN INDUCES PROLIFERATION IN THE ORGAN OF CORTI IN CULTURE AFTER EFFICIENT SHRNA LENTIVIRAL TRANSDUCTION.

Maass JC1, Berndt FA, Cánovas J, Kukuljan M.

The cells in the organ of Corti do not exhibit spontaneous cell regeneration; hair cells that die after damage are not replaced. Supporting cells can be induced to transdifferentiate into hair cells, but that would deplete their numbers, therefore impairing epithelium physiology. The loss of p27Kip1 function induces proliferation in the organ of Corti, which raises the possibility to integrate it to the strategies to achieve regeneration. Nevertheless, it is not known if the extent of this proliferative potential, as well as its maintenance in postnatal stages, is compatible with providing a basis for eventual therapeutic manipulation. This is due in part to the limited success of approaches to deliver tools to modify gene expression in the auditory epithelium. We tested the hypothesis that the organ of Corti can undergo significant proliferation when efficient manipulation of the expression of regulators of the cell cycle is achieved. Lentiviral vectors were used to transduce all cochlear cell types, with efficiencies around 4 % for hair cells, 43 % in the overall supporting cell population, and 74 % within lesser epithelial ridge (LER) cells. Expression of short hairpin RNA targeting p27Kip1 encoded by the lentiviral vectors led to measurable proliferation in the organ of Corti and increase in LER cells number but not hair cell regeneration. Our results revalidate the use of lentiviral vectors in the study and in the potential therapeutic approaches for inner ear diseases, as well as demonstrate that efficient manipulation of p27Kip1 is sufficient to induce significant proliferation in the postnatal cochlea.

PLOS ONE. 2013;8(1):E55011.

ANALYSIS OF FGF-DEPENDENT AND FGF-INDEPENDENT PATHWAYS IN OTIC PLACODE INDUCTION.

Yang L, O'Neill P, Martin K, Maass JC, Vassilev V, Ladher R, Groves AK.

The inner ear develops from a patch of thickened cranial ectoderm adjacent to the hindbrain called the otic placode. Studies in a number of vertebrate species suggest that the initial steps in induction of the otic placode are regulated by members of the Fibroblast Growth Factor (FGF) family, and that inhibition of FGF signaling can prevent otic placode formation. To better understand the genetic pathways activated by FGF signaling during otic placode induction, we performed microarray experiments to estimate the proportion of chicken otic placode genes that can be up-regulated by the FGF pathway in a simple culture model of otic placode induction. Surprisingly, we find that FGF is only sufficient to induce about 15% of chick otic placode-specific genes in our experimental system. However, pharmacological blockade of the FGF pathway in cultured chick embryos showed that although FGF signaling was not sufficient to induce the majority of otic placode-specific genes, it was still necessary for their expression *in vivo*. These inhibitor experiments further suggest that the early steps in otic placode induction regulated by FGF signaling occur through the MAP kinase pathway. Although our work suggests that FGF signaling is necessary for otic placode induction, it demonstrates that other unidentified signaling pathways are required to co-operate with FGF signaling to induce the full otic placode program.

BIOL RES. 2013;46(3):239-42.

PREVALENCE OF THE 35DELG MUTATION IN THE GJB2 GENE IN TWO SAMPLES OF NON-SYNDROMIC DEAF SUBJECTS FROM CHILE.

Cifuentes L, Arancibia M, Torrente M, Acuña M, Farfán C, Ríos C.

Hearing loss is the most common inherited sensorial deficiency in humans; about 1 in 1000 children suffer from severe or profound hearing loss at birth. Mutations in the GJB2 gene are the most common cause of prelingual, non-syndromic autosomal recessive deafness in many populations; the c.35delG mutation is the most common in Caucasian populations. The frequency of the c.35delG mutation was estimated in two samples of deaf patients from Santiago, Chile. Unrelated non-syndromic sensorineural deaf patients were examined: Group 1 consisted of 47 unrelated individuals with neurosensory deafness referred to the Chilean Cochlear Implant Program; Group 2 included 66 school children with prelingual deafness attending special education institutions for deaf people.

Individuals with profound to moderate isolated neurosensory hearing loss with unknown etiology were included. The presence of the c.35delG mutation was evaluated by the allele-specific polymerase chain reaction method (PCR), and in some cases it was confirmed by direct DNA sequencing of the coding region of the GJB2 gene. Deaf relatives were present in 20.3% of the cases. We found 19.5% (22/113) patients with the c.35delG mutation, 6 of them homozygous; these rates are similar to frequencies found in other Latin American countries.

ACTA OTORRINOLARINGOL ESP. 2013 MAR 16. PII: S0001-6519(13)00026-5.

DECANNULATION AND ASSESSMENT OF DEGLUTITION IN THE TRACHEOSTOMIZED PATIENT IN NON-NEUROCRITICAL INTENSIVE CARE.

Alvo A, Olavarria C.

With intensive care patients, decannulation and deglutition disorders are frequent reasons for otorhinolaryngological assessment. The objective of a tracheostomy is to maintain a patent airway. It does not necessarily prevent episodes of aspiration and may even favour them. When the cause that led to the tracheostomy resolves, a decannulation may be proposed. Deglutition is a complex act involving the coordinated interaction of several structures of the aerodigestive tract. Fibre-optic endoscopy and videofluoroscopy are 2 useful, complementary tools for the evaluation of patients with swallowing disorders. In managing these patients, a thorough knowledge of laryngeal and swallowing physiology, as well as of the different therapeutic alternatives, is required. Although it is not uncommon for swallowing disorders to coexist in tracheostomy patients, decannulation evaluation is not synonymous with deglutition assessment. A patient could be a candidate for decannulation and have a swallowing disorder, or a tracheostomy patient could swallow adequately. Knowing and understanding these concepts will lead to more efficient management and help to clarify communication between the intensive care physician and the otorhinolaryngologist. Ideally, a multidisciplinary team should be formed to evaluate and manage these patients.

UNIDAD DE PACIENTES CRÍTICOS

AM J RESPIR CRIT CARE MED. 2013 AUG 15;188(4):440-8.

EFFECTS OF PRONE POSITIONING ON LUNG PROTECTION IN PATIENTS WITH ACUTE RESPIRATORY DISTRESS SYNDROME.

Cornejo RA, Díaz JC, Tobar EA, Bruhn AR, Ramos CA, González RA, Repetto CA, Romero CM, Gálvez LR, Llanos O, Arellano DH, Neira WR, Díaz GA, Zamorano AJ, Pereira GL.

Rationale: Positive end-expiratory pressure (PEEP) and prone positioning may induce lung recruitment and affect alveolar dynamics in acute respiratory distress syndrome (ARDS). Whether there is interdependence between the effects of PEEP and prone positioning on these variables is unknown. Objectives: To determine the effects of high PEEP and prone positioning on lung recruitment, cyclic recruitment/derecruitment, and tidal hyperinflation and how these effects are influenced by lung recruitability. Methods: Mechanically ventilated patients (Vt 6 ml/kg ideal body weight) underwent whole-lung computed tomography (CT) during breath-holding sessions at airway pressures of 5, 15, and 45 cm H₂O and Cine-CTs on a fixed thoracic transverse slice at PEEP 5 and 15 cm H₂O. CT images were repeated in supine and prone positioning. A recruitment maneuver at 45 cm H₂O was performed before each PEEP change. Lung recruitability was defined as the difference in percentage of nonaerated tissue between 5 and 45 cm H₂O. Cyclic recruitment/de-recruitment and tidal hyperinflation were determined as tidal changes in percentage of nonaerated and hyperinflated tissue, respectively. Measurements and main results: Twenty-four patients with ARDS were included. Increasing PEEP from 5 to 15 cm H₂O decreased nonaerated tissue (501 ± 201 to 322 ± 132 grams; P < 0.001) and increased tidal-hyperinflation (0.41 ± 0.26 to 0.57 ± 0.30%; P = 0.004) in supine. Prone positioning further decreased nonaerated tissue (322 ± 132 to 290 ± 141 grams; P = 0.028) and reduced tidal hyperinflation observed at PEEP 15 in supine patients (0.57 ± 0.30 to 0.41 ± 0.22%). Cyclic recruitment/de-recruitment only decreased when high PEEP and prone positioning were applied together (4.1 ± 1.9 to 2.9 ± 0.9%; P = 0.003), particularly in patients with high lung recruitability. Conclusions: Prone positioning enhances lung recruitment and decreases alveolar instability and hyperinflation observed at high PEEP in patients with ARDS.

J CRIT CARE. 2013 AUG;28(4):451-60.

EFFECTS OF THE IMPLEMENTATION OF A PREVENTIVE INTERVENTIONS PROGRAM ON THE REDUCTION OF MEDICATION ERRORS IN CRITICALLY ILL ADULT PATIENTS.

Romero CM, Salazar N, Rojas L, Escobar L, Griñén H, Berasaín MA, Tobar E, Jirón M.

Purpose: Medication errors (MEs) are a major factor limiting the effectiveness and safety of pharmacological therapies in critically ill patients. The purpose was to determine if a preventive interventions program (PIP) is associated with a significant reduction on prevalence of patients with MEs in intensive care unit (ICU). Methods: A prospective before-after study was conducted in a random sample of adult patients in a medical-surgical ICU. Between 2 observational phases, a PIP (bundle of interventions to reduce MEs) was implemented by a multidisciplinary team. Direct observation was used to detect MEs at baseline and postintervention. Each medication process, that is, prescription, transcription, dispensing, preparation, and administration, was compared with what the prescriber ordered; if there was a difference, the error was described and categorized. Medication errors were defined according to the National Coordinating Council for Medication Error Reporting and Prevention. Results: A total of 410 medications for 278 patients were evaluated. A 31.7% decrease on the prevalence of patients with MEs (41.9%-28.6%; $P < .05$) was seen. Main variations occurred in anti-infectives for systemic use and prescription and administration stage. Conclusions: The implementation of PIP by a multidisciplinary team resulted in a significant reduction on the prevalence of patients with ME at an adult ICU.

J CLIN MONIT COMPUT. 2013 FEB;27(1):71-9.

COMPARISON OF TWO DIFFERENT GENERATIONS OF "NIRS" DEVICES AND TRANSDUCERS IN HEALTHY VOLUNTEERS AND ICU PATIENTS.

Luengo C, Resche-Rigon M, Damoiseil C, Kerever S, Creteur J, Payen D.

The purpose of this study is to compare Near Infrared Spectroscopy (NIRS) thenar eminence parameters obtained with 2 different devices from the same manufacturer (InSpectra Models 325 and 650, Hutchinson Tech, Min USA), and 2 different probes (15 vs. 25 mm spacing), in healthy volunteers (HV) and ICU patients. Prospective, observational study in ICU setting. Simultaneous, cross over NIRS inter-device comparison and comparison between different probes (25 vs. 15 mm spacing) were done at baseline and during vascular occlusion tests (VOTs). Forty patients (19 septic shock, 21 trauma), and 29 HV were included. NIRS inter-device comparison showed similar baseline $StO(2)$ values in HV and patients. The VOT result were significantly different for minimal $StO(2)$ value reached during VOT ($StO(2min)$) (intraclass concordance coefficient (ICC) = 0.18), the occlusion slope (ICC = 0.16) and the reperfusion slope ($StO(2reperf)$) (ICC = 0.26). The probe comparison was also significantly different for VOT parameters ($StO(2min)$) (ICC = 0.43), occlusion (ICC = 0.50) and $StO(2reperf)$ (ICC = 0.48). The low concordance, poor agreement and large bias (ICC and Bland & Altman) observed, were related both to the device used and the probe spacing. $StO(2)$ data obtained with NIRS model 650 and 15 mm probe differ from values obtained with the previous device (325 and probe spacing 25 or 15 mm). This difference is not related to the population tested, but to the device and probe spacing. As a consequence, despite similar trends for variations between HV and patients during VOT, threshold and predictive values for outcome should be revisited with the new device before the acceptance for routine clinical use.

INTENSIVE CARE MED. 2013 AUG;39(8):1435-43.

EFFECTS OF DOBUTAMINE ON SYSTEMIC, REGIONAL AND MICROCIRCULATORY PERFUSION PARAMETERS IN SEPTIC SHOCK: A RANDOMIZED, PLACEBO-CONTROLLED, DOUBLE-BLIND, CROSSOVER STUDY.

Hernandez G, Bruhn A, Luengo C, Regueira T, Kattan E, Fuentealba A, Florez J, Castro R, Aquevedo A, Pairumani R, McNab P, Ince C.

PURPOSE: The role of dobutamine during septic shock resuscitation is still controversial since most clinical studies have been uncontrolled and no physiological study has unequivocally demonstrated a beneficial effect on tissue perfusion. Our objective was to determine the potential benefits of dobutamine on hemodynamic, metabolic, peripheral, hepatosplanchnic and microcirculatory perfusion parameters during early septic shock resuscitation. METHODS: We designed a randomized, controlled, double-blind, crossover study comparing the effects of 2.5-h infusion of dobutamine (5 mcg/kg/min fixed-dose) or placebo in 20 septic shock patients with cardiac index ≥ 2.5 l/min/m² and hyperlactatemia. Primary outcome was sublingual perfused microvascular density. RESULTS: Despite an increasing cardiac index, heart rate and left ventricular ejection fraction, dobutamine had no effect on sublingual perfused vessel density [9.0 (7.9-10.1) vs. 9.1 n/mm (7.9-9.9); $p = 0.24$] or microvascular flow index [2.1 (1.8-2.5) vs. 2.1 (1.9-2.5); $p = 0.73$] compared to placebo. No differences between dobutamine and placebo were found for the lactate levels, mixed venous-arterial pCO_2 gradient, thenar muscle oxygen saturation, capillary refill time or gastric-to-arterial pCO_2 gradient. The

indocyanine green plasma disappearance rate [14.4 (9.5-25.6) vs. 18.8 %/min (11.7-24.6); $p = 0.03$] and the recovery slope of the muscle oxygen saturation after a vascular occlusion test [2.1 (1.1-3.1) vs. 2.5 %/s (1.2-3.4); $p = 0.01$] were worse with dobutamine compared to placebo. CONCLUSIONS: Dobutamine failed to improve sublingual microcirculatory, metabolic, hepatosplanchnic or peripheral perfusion parameters despite inducing a significant increase in systemic hemodynamic variables in septic shock patients without low cardiac output but with persistent hypoperfusion.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

STROKE. 2013 APR;44(4):1169-71.

ACCURACY OF DIFFUSION-WEIGHTED IMAGING IN THE DIAGNOSIS OF STROKE IN PATIENTS WITH SUSPECTED CEREBRAL INFARCT.

Brunser AM, Hoppe A, Illanes S, Díaz V, Muñoz P, Cárcamo D, Olavarria V, Valenzuela M, Lavados P.

Background And Purpose: The Accuracy Of Diffusion-Weighted Imaging (Dwi) For The Diagnosis Of Acute Cerebral Ischemia Among Patients With Suspected Ischemic Stroke Arriving To An Emergency Room Has Not Been Studied In Depth. Methods: Dwi Was Performed In 712 Patients With Acute Or Subacute Focal Symptoms That Suggested An Acute Ischemic Stroke (Ais), 609 Of Them With Ais. Results: Dwi Demonstrated A Sensitivity Of 90% And Specificity Of 97%, A Positive Likelihood Ratio Of 31 And A Negative Likelihood Ratio Of 0.1 For Detecting Ais. The Overall Accuracy Was 95%. Of Those Patients Who Demonstrated Abnormal Dwi Studies, 99.5% Were Ais Patients, And Of Those Patients With Normal Dwi Studies 63% Were Stroke Mimics. Conclusions: Dwi Is Accurate In Detecting Ais In Unselected Patients With Suspected Ais; A Negative Study Should Alert For Nonischemic Conditions.

J STROKE CEREBROVASC DIS. 2013 OCT;22(7):1140-5.

EXCLUSION CRITERIA FOR INTRAVENOUS THROMBOLYSIS IN STROKE MIMICS: AN OBSERVATIONAL STUDY.

Brunser AM, Illanes S, Lavados PM, Muñoz P, Cárcamo D, Hoppe A, Olavarria VV, Delgado I, Díaz V.

BACKGROUND: Stroke mimics (SMs) are frequent in emergency departments (EDs), but are treated infrequently with intravenous recombinant tissue plasminogen activator (rt-PA) thrombolysis. We aimed at identifying the factors that lead to the exclusion of SMs from thrombolytic therapy. METHODS: Consecutive patients presenting to the ED between December 2004 and March 2011 with symptoms that suggested acute ischemic stroke were included. RESULTS: Eight hundred forty-two patients were included in this study; 113 (13.4%) were considered SMs; these patients were younger ($P = .01$), more frequently diabetic ($P = .001$), arrived later to the ED ($P = .03$), had lower National Institutes of Health Stroke Scale scores ($P < .001$), and higher frequencies of negative diffusion-weighted imaging studies ($P = .002$). The most common causes of cases of SM were toxic metabolic disorders ($n = 34$ [30.1%]) and seizures ($n = 22$ [19.5%]). The most frequent cause of consultation was aphasia ($n = 43$ [37.6%]). SM patients had a total of 152 contraindications for rt-PA, with 34 (30%) patients having >1 contraindication. The most frequent of these were being beyond the therapeutic window for thrombolysis ($n = 96$) and having deficits not measurable by the National Institutes of Health Stroke Scale or very mild symptoms before the start of rt-PA ($n = 37$). Twenty-four (21.2%) patients had both contraindications simultaneously. Two patients (1.76%) in the SM group were candidates for rt-PA but did not receive this treatment because they or their family rejected it. Of 729 stroke patients, 87 (11.9%) did receive rt-PA. CONCLUSIONS: SM patients frequently had exclusion criteria for systemic thrombolysis, the most frequent being presenting beyond the established thrombolytic window.

MULT SCLER. 2013 FEB;19(2):145-52.

TOWARDS ESTABLISHING MS PREVALENCE IN LATIN AMERICA AND THE CARIBBEAN.

Melcon MO, Melcon CM, Bartoloni L, Cristiano E, Duran JC, Grzesiuk AK, Fragoso YD, Brooks JB, Díaz V, Romero García KM, Cabrera Gomez JA, Abad P, Islas MA, Gracia F, Diaz de Bedoya VF, Ruiz ME, Hackembruch JH, Oehninger C, Ketzoian CN, Soto A; Grupo Colaborativo Multicéntrico para el Estudio de la Esclerosis Múltiple en América Latina y el Caribe (GEEMAL).

A very high prevalence of multiple sclerosis (MS) has been reported in some Western European and North American countries. The few surveys of MS epidemiology in South America reveal lower prevalence rates, implying that susceptibility varies between distinct ethnic groups, thus forming an important determinant of the geographic distribution of the disease. The objective of this study is to review MS prevalence estimates in different Latin American and Caribbean countries. We reviewed surveys of regional MS prevalence from 1991 to 2011. Sources included an online database, authors' reports

and proceedings or specific lectures from regional conferences. We obtained a total of 30 prevalence surveys from 15 countries, showing low/medium MS prevalence rates. Both the number and the quality of prevalence surveys have greatly improved in this region over recent decades. This is the first collaborative study to map the regional frequency of MS. Establishment of standardized methods and joint epidemiological studies will advance future MS research in Latin America and the Caribbean.

MOV DISORD. 2013 JUL;28(8):1150-1.

PLASMA URATE IN REM SLEEP BEHAVIOR DISORDER.

Uribe-San Martín R1, Venegas Francke P, López Illanes F, Jones Gazmuri A, Salazar Rivera J, Godoy Fernández J, Santín Martínez J, Juri C.

BACKGROUND: Rapid eye movement (REM) sleep behavior disorder (RBD) is associated with a high risk of developing Parkinson's disease (PD). Higher urate levels are associated with a lower risk of PD. We conducted a study to evaluate plasma urate levels in patients with RBD and their role in the development of PD. **METHODS:** We evaluated plasma urate levels in a cohort of 24 patients with idiopathic RBD. Patients were divided into 2 groups according to the presence or absence of PD. Other known markers of the risk of developing PD, such as olfaction testing, and substantia nigra (SN) hyperechogenicity, were evaluated in the 2 groups. **RESULTS:** No differences were observed regarding age, years of evolution of the RBD, SN hyperechogenicity, or plasma urate levels between the 2 groups. In patients without PD, there was a positive correlation between years of evolution of RBD and the levels of uric acid ($R(2) = 0.88$). Patients without PD and those who had more than 5 years of RBD exhibited higher levels of uric acid than patients with PD ($P=0.02$). **CONCLUSIONS:** Higher levels of plasma urate were associated with a longer duration of RBD without converting to PD. Future prospective studies would be needed to confirm this finding. Disorder Society

NEUROLOGIA. 2013 SEP;28(7):400-7.

[MEMORY, FLUENCY, AND ORIENTATION: A FIVE-MINUTE SCREENING TEST FOR COGNITIVE DECLINE].

Delgado Derio C, Guerrero Bonnet S, Troncoso Ponce M, Araneda Yañez A, Slachevsky Chonchol A, Behrens Pellegrino MI.

Background: The prevalence of cognitive impairment (CI) will double in the next 20 years, making early detection a key priority. **Objectives:** Validation of a 5-minute CI screening test. **Methods:** Adults aged 60 and older were recruited from memory clinics and the community at large in the Santiago, Chile metropolitan area. Based on clinical examination they were categorized as No CI (NCI), Mild CI (MCI) and dementia sufferers (DS). We measured the validity of a new test, MEFO, evaluating memory (5 points), phonetic verbal fluency (2 points) and orientation (6 points) by comparing its results with those from the MMSE. **Results:** We evaluated 214 subjects, comprising 49 with dementia, 47 with MCI, and 118 with no CI. The MEFO differentiated between all 3 groups whereas the MMSE did not discriminate between the MCI and NCI groups. The area under the ROC curve (AUC) for the MEFO distinguishing NCI subjects from dementia sufferers was 0.97; for NCI vs CI (dementia+MCI), 0.89; and for NCI vs MCI, 0.80. On the MMSE these values were 0.95, 0.84, and 0.73, respectively. A cut-off score of 6/7 on the MEFO identified dementia sufferers with a sensitivity of 86% and a specificity of 96%. A cut-off score of 8/9 distinguished CI from NCI subjects with a sensitivity of 83% and a specificity of 75%. **Conclusions:** The MEFO is a valid and reliable test for discriminating between dementia and CI sufferers and subjects with no CI. Its validity is similar to that the MMSE under these conditions, but it is more effective for identifying subjects with MCI and its administration time is shorter.

OFICINA APOYO INVESTIGACIÓN CLÍNICA

J ASSIST REPROD GENET. 2013 APR;30(4):531-8.

GREATER PREVALENCE OF Y CHROMOSOME Q1A3A HAPLOGROUP IN Y-MICRODELETED CHILEAN MEN: A CASE-CONTROL STUDY.

Lardone MC, Marengo A, Parada-Bustamante A, Cifuentes L, Piottante A, Ebensperger M, Valdevenito R, Castro A.

Purpose: To determine the prevalence of South Amerindian Y chromosome in Chilean patients with spermatogenic failure and their association with classical and/or AZFc-partial Y chromosome deletions. **Methods:** We studied 400 men, 218 with secretory azo/oligozoospermia (cases) and 182 controls (116 fertile and/or normozoospermic, and 66 azoospermic with normal spermatogenesis). After a complete testicular characterization (physical evaluation, hormonal and/or biopsy) peripheral blood was drawn to obtain

DNA for Y chromosome microdeletions, AZFc-partial deletions and biallelic analysis by allele specific polymerase chain reaction (PCR) of the M3 (rs3894) single nucleotide polymorphism (SNP). Results: Classical AZF microdeletions were found in 23 cases (Y-microdeleted). AZFc-partial deletions were observed in 10 cases (6 "gr/gr", 3 "b2/b3" and 1 "b1/b3") and 4 controls (4 "gr/gr"). The AZFc-partial deletions were mainly associated with the absence of DAZ1/DAZ2 (64 %). No significant differences in the prevalence of AZFc-partial deletions were observed between cases and controls. We observed a significant higher proportion of the Q1a3a haplogroup in Y-microdeleted men compared to patients with spermatogenic failure without deletions and control men ($P < 0.01$ and $P < 0.05$, respectively by Bonferroni test). Among them, patients with AZFb deletions had an increased prevalence of the Q1a3a haplogroup compared to controls, cases without deletions and to those with complete or partial-AZFc deletions ($P < 0.01$, Bonferroni test). Conclusions: The Q1a3a South Amerindian lineage seems to increase the susceptibility to non AZFc microdeletions. On the other hand, in Chilean population the AZFc-partial deletions ("gr/gr", "b1/b3" and/or "b2/b3") does not seem to predispose to severe spermatogenic impairment.

CANCER IMMUNOL IMMUNOTHER. 2013 APR;62(4):761-72.

THE IMMUNOLOGICAL RESPONSE AND POST-TREATMENT SURVIVAL OF DC-VACCINATED MELANOMA PATIENTS ARE ASSOCIATED WITH INCREASED TH1/TH17 AND REDUCED TH3 CYTOKINE RESPONSES.

Durán-Aniotz C, Segal G, Salazar L, Pereda C, Falcón C, Tempio F, Aguilera R, González R, Pérez C, Tittarelli A, Catalán D, Nervi B, Larrondo M, Salazar-Onfray F, López MN.

Introduction: Immunization with autologous dendritic cells (DCs) loaded with a heat shock-conditioned allogeneic melanoma cell lysate caused lysate-specific delayed type hypersensitivity (DTH) reactions in a number of patients. These responses correlated with a threefold prolonged long-term survival of DTH(+) with respect to DTH(-) unresponsive patients. Herein, we investigated whether the immunological reactions associated with prolonged survival were related to dissimilar cellular and cytokine responses in blood. Materials and methods: Healthy donors and melanoma patient's lymphocytes obtained from blood before and after vaccinations and from DTH biopsies were analyzed for T cell population distribution and cytokine release. Results/discussion: Peripheral blood lymphocytes from melanoma patients have an increased proportion of Th3 (CD4(+) TGF- β (+)) regulatory T lymphocytes compared with healthy donors. Notably, DTH(+) patients showed a threefold reduction of Th3 cells compared with DTH(-) patients after DCs vaccine treatment. Furthermore, DCs vaccination resulted in a threefold augment of the proportion of IFN- γ releasing Th1 cells and in a twofold increase of the IL-17-producing Th17 population in DTH(+) with respect to DTH(-) patients. Increased Th1 and Th17 cell populations in both blood and DTH-derived tissues suggest that these profiles may be related to a more effective anti-melanoma response. Conclusions: Our results indicate that increased proinflammatory cytokine profiles are related to detectable immunological responses in vivo (DTH) and to prolonged patient survival. Our study contributes to the understanding of immunological responses produced by DCs vaccines and to the identification of follow-up markers for patient outcome that may allow a closer individual monitoring of patients.

INTERNATIONAL JOURNAL OF MORPHOLOGY, 31(2), 392-398

EFFECTO DE CELECOXIB EN UNA VARIANTE MULTIRRESISTENTE DEL TUMOR TA3. UNA DESCRIPCIÓN HISTOLÓGICA

Carlos Rosas C.; Ignacio Roa; Mariana Sinning O.; Marcela Fuenzalida B., David Lemus A.

In the study of cancer diverse cellular lines are in use, each with its own characteristics. One of these tumor lines is the TA3 tumor variant, multi resistant to drugs. Although diverse studies exist in reference to this tumor line, there are no detailed morphological descriptions of this one, nor those that observe the effect of Celecoxib, a COX-2 tissue inhibitor. We used 18 mice divided in 3 groups that received PBS inoculation; TA3 tumor cell inoculation; cell tumor inoculation + treatment with Celecoxib (1000ppm) respectively. The mice were sacrificed and histologically processed with H & E, PAS and Arteta stain. The study revealed that tumor showed a marked heterogeneity, some areas of necrosis and central and peripheral neovascularization. Furthermore, Celecoxib significantly reduced tumor invasion in the liver ($p < 0.05$). Other organs did not show significant differences when compared with the treated group. The results are similar to partial descriptions realized in the past and are comparable to other tumor lines. It is estimated that the route of medication administration is critical for result interpretation. These results are important in the discussion of other research where Celecoxib is used as an antiangiogenic drug and serves as base for future research within this tumor line.

BANCO DE SANGRE

J TRANSL MED. 2013 MAY 24;11:128.

A SHORT PROTOCOL USING DEXAMETHASONE AND MONOPHOSPHORYL LIPID A GENERATES TOLEROGENIC DENDRITIC CELLS THAT DISPLAY A POTENT MIGRATORY CAPACITY TO LYMPHOID CHEMOKINES.

García-González P, Morales R, Hoyos L, Maggi J, Campos J, Pesce B, Gárate D, Larrondo M, González R, Soto L, Ramos V, Tobar P, Molina MC, Pino-Lagos K, Catalán D, Aguillón JC.

Background: Generation of tolerogenic dendritic cells (ToIDCs) for therapy is challenging due to its implications for the design of protocols suitable for clinical applications, which means not only using safe products, but also working at defining specific biomarkers for ToIDCs identification, developing shorter DCs differentiation methods and obtaining ToIDCs with a stable phenotype. We describe here, a short-term protocol for ToIDCs generation, which are characterized in terms of phenotypic markers, cytokines secretion profile, CD4+ T cell-stimulatory ability and migratory capacity. Methods: ToIDCs from healthy donors were generated by modulation with dexamethasone plus monophosphoryl lipid A (MPLA-tDCs). We performed an analysis of MPLA-tDCs in terms of yield, viability, morphology, phenotypic markers, cytokines secretion profile, stability, allogeneic and antigen-specific CD4+ T-cell stimulatory ability and migration capacity. Results: After a 5-day culture, MPLA-tDCs displayed reduced expression of costimulatory and maturation molecules together to an anti-inflammatory cytokines secretion profile, being able to maintain these tolerogenic features even after the engagement of CD40 by its cognate ligand. In addition, MPLA-tDCs exhibited reduced capabilities to stimulate allogeneic and antigen-specific CD4+ T cell proliferation, and induced an anti-inflammatory cytokine secretion pattern. Among potential tolerogenic markers studied, only TLR-2 was highly expressed in MPLA-tDCs when compared to mature and immature DCs. Remarkable, like mature DCs, MPLA-tDCs displayed a high CCR7 and CXCR4 expression, both chemokine receptors involved in migration to secondary lymphoid organs, and even more, in an in vitro assay they exhibited a high migration response towards CCL19 and CXCL12. Conclusion: We describe a short-term protocol for ToIDC generation, which confers them a stable phenotype and migratory capacity to lymphoid chemokines, essential features for ToIDCs to be used as therapeutics for autoimmunity and prevention of graft rejection.

DEPARTAMENTO CARDIOVASCULAR

J OROFAC PAIN. 2013 FALL;27(4):361-6.

ISOBOLOGRAPHIC ANALYSIS IN MICE OF THE INTERACTION OF GABAPENTIN AND NORTRIPTYLINE IN RELIEVING OROFACIAL PAIN.

Miranda HF, Noriega V, Zanetta P, Prieto JC.

Aims: To evaluate the nature of the antinociceptive interaction of systemic administration of a combination of the anticonvulsant gabapentin with the antidepressant nortriptyline, by isobolographic analysis in the formalin orofacial pain test of mice. Methods: The study was carried out in 168 male CF-1 mice weighing 30 g, and the protocol was to test each drug (at dosages of 1, 3, 10, 30, and 100 mg/kg of gabapentin and 0.1, 1, 3, 10, and 30 mg/kg of nortriptyline; ip) alone and in combination. The isobolographic assay has two phases: phase 1 corresponds to the 5-minute period starting immediately after the formalin injection and reflects a tonic acute pain due to peripheral nociceptor sensitization; phase 2 is recorded as the 10-minute period starting 20 minutes after the formalin injection and reflects an inflammatory pain state. Results were analyzed by Student t test for independent means. Results: Gabapentin was 1.61 times more potent in phase 2 than in phase 1, and nortriptyline 1.37 times more potent in phase 2 than in phase 1. The combination of both drugs was synergic, with an index of interaction of 0.134 and 0.148 for phase 1 and phase 2, respectively. Differences in the pharmacological profiles of gabapentin and nortriptyline could underlie the synergism of the two drugs. Conclusion: The findings of this study are important, because they are concordant with some clinical studies and also raise the possibility of potential clinical advantages of combining gabapentin and nortriptyline in pain management, since the low doses of the components may potentially have a lower incidence of adverse reactions.

PHARMACOL REP. 2013;65(1):80-8.

SYSTEMIC SYNERGISM BETWEEN CODEINE AND MORPHINE IN THREE PAIN MODELS IN MICE.

Miranda HF, Noriega V, Zepeda RJ, Sierralta F, Prieto JC.

Background: The combination of two analgesic agents offers advantages in pain treatment. Codeine and morphine analgesia is due to activation of opioid receptor subtypes. Methods: This study, performed in mice using isobolographic analysis, evaluated the type of interaction in intraperitoneal (ip) or intrathecal (it) coadministration of codeine and morphine, in three nociceptive behavioral models. Results: Intrathecal morphine resulted to be 7.5 times more potent than ip morphine in the writhing test, 55.6 times in the tail flick test and 1.7 times in phase II of the orofacial formalin test; however, in phase I of the same test ip was 1.2 times more potent than it morphine. Intrathecal codeine resulted being 3.4 times more potent than ip codeine in the writhing test, 1.6 times in the tail flick test, 2.5 times in phase I and 6.7 times in phase II of the orofacial formalin test. Opioid coadministration had a synergistic effect in the acute tonic pain (acetic acid writhing test), acute phasic pain (tail flick test) and inflammatory pain (orofacial formalin test). The interaction index ranged between 0.284 (writhing ip) and 0.440 (orofacial formalin phase II ip). Conclusion: This synergy may relate to the different pathways of pain transmission and to the different intracellular signal transduction. The present findings also raise the possibility of potential clinical advantages in combining opioids in pain management.

CLIN SCI (LOND). 2013 JAN;124(1):1-15.

CARDIOPROTECTION AGAINST ISCHAEMIA/REPERFUSION BY VITAMINS C AND E PLUS N-3 FATTY ACIDS: MOLECULAR MECHANISMS AND POTENTIAL CLINICAL APPLICATIONS.

Rodrigo R, Prieto JC, Castillo R.

The role of oxidative stress in ischaemic heart disease has been thoroughly investigated in humans. Increased levels of ROS (reactive oxygen species) and RNS (reactive nitrogen species) have been demonstrated during ischaemia and post-ischaemic reperfusion in humans. Depending on their concentrations, these reactive species can act either as benevolent molecules that promote cell survival (at low-to-moderate concentrations) or can induce irreversible cellular damage and death (at high concentrations). Although high ROS levels can induce NF- κ B (nuclear factor κ B) activation, inflammation, apoptosis or necrosis, low-to-moderate levels can enhance the antioxidant response, via Nrf2 (nuclear factor-erythroid 2-related factor 2) activation. However, a clear definition of these concentration thresholds remains to be established. Although a number of experimental studies have demonstrated that oxidative stress plays a major role in heart ischaemia/reperfusion pathophysiology, controlled clinical trials have failed to prove the efficacy of antioxidants in acute or long-term treatments of ischaemic heart disease. Oral doses of vitamin C are not sufficient to promote ROS scavenging and only down-regulate their production via NADPH oxidase, a biological effect shared by vitamin E to abrogate oxidative stress. However, infusion of vitamin C at doses high enough to achieve plasma levels of 10 mmol/l should prevent superoxide production and the pathophysiological cascade of deleterious heart effects. In turn, n-3 PUFA (polyunsaturated fatty acid) exposure leads to enhanced activity of antioxidant enzymes. In the present review, we present evidence to support the molecular basis for a novel pharmacological strategy using these antioxidant vitamins plus n-3 PUFAs for cardioprotection in clinical settings, such as post-operative atrial fibrillation, percutaneous coronary intervention following acute myocardial infarction and other events that are associated with ischaemia/reperfusion.

J AM COLL CARDIOL. 2013 OCT 15;62(16):1457-65

A RANDOMIZED CONTROLLED TRIAL TO PREVENT POST-OPERATIVE ATRIAL FIBRILLATION BY ANTIOXIDANT REINFORCEMENT.

Rodrigo R, Korantzopoulos P, Cereceda M, Asenjo R, Zamorano J, Villalabeitia E, Baeza C, Aguayo R, Castillo R, Carrasco R, Gormaz JG.

OBJECTIVES: This study was designed to assess whether the reinforcement of the antioxidant system, through n-3 fatty acids plus antioxidant vitamin supplementation, could reduce the incidence of post-operative atrial fibrillation. BACKGROUND: Therapy to prevent post-operative atrial fibrillation remains suboptimal. Although oxidative stress plays a key role in the pathogenesis of this arrhythmia, antioxidant reinforcement has produced controversial results. METHODS: A total of 203 patients scheduled for on-pump cardiac surgery were randomized to placebo or supplementation with n-3 polyunsaturated fatty acids (2 g/day) (eicosapentaenoic acid:docosahexaenoic acid ratio 1:2), vitamin C (1 g/day), and vitamin E (400 IU/day). The primary outcome

was the occurrence of post-operative atrial fibrillation. Secondary outcomes were the biomarkers related to oxidative stress and inflammation. RESULTS: Post-operative atrial fibrillation occurred in 10 of 103 patients (9.7%) in the supplemented group versus 32 of 100 patients (32%) in the placebo group ($p < 0.001$). Early after surgery, placebo patients presented with increased levels of biomarkers of inflammation and oxidative stress, which were markedly attenuated by antioxidant supplementation. The activity of catalase, superoxide dismutase, and glutathione peroxidase in atrial tissue of the supplemented patients was 24.0%, 17.1%, and 19.7% higher than the respective placebo values ($p < 0.05$). The atrial tissue of patients who developed atrial fibrillation showed NADPH oxidase p47-phox subunit protein and mRNA expression 38.4% and 35.7% higher, respectively, than patients in sinus rhythm ($p < 0.05$). CONCLUSIONS: This safe, well-tolerated, and low-cost regimen, consisting of n-3 polyunsaturated fatty acids plus vitamins C and E supplementation, favorably affected post-operative atrial fibrillation, increased antioxidant potential, and attenuated oxidative stress and inflammation. (Prevention of Post-Operative Atrial Fibrillation: Pathophysiological Characterization of a Pharmacological Intervention Based on a Novel Model of Nonhypoxic Pre-Conditioning; ISRCTN45347268).

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

ULTRASOUND IN OBSTETRICS & GYNECOLOGY. 2013; 41(ISSUE 3): 348-359

ISUOG PRACTICE GUIDELINES (UPDATED): SONOGRAPHIC SCREENING EXAMINATION OF THE FETAL HEART

Carvalho, JS, Allan, LD, Chaoui, R, Muñoz H.

The International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) is a scientific organization that encourages safe clinical practice and high-quality teaching and research related to diagnostic imaging in women's healthcare. The ISUOG Clinical Standards Committee (CSC) has a remit to develop Practice Guidelines and Consensus Statements that provide healthcare practitioners with a consensus-based approach for diagnostic imaging. They are intended to reflect what is considered by ISUOG to be the best practice at the time at which they are issued. Although ISUOG has made every effort to ensure that Guidelines are accurate when issued, neither the Society nor any of its employees or members accept any liability for the consequences of any inaccurate or misleading data, opinions or statements issued by the CSC. The ISUOG CSC documents are not intended to establish a legal standard of care because interpretation of the evidence that underpins the Guidelines may be influenced by individual circumstances, local protocol and available resources. Approved Guidelines can be distributed freely with the permission of ISUOG

ULTRASOUND OBSTET GYNECOL. 2013 MAR 21.

IS THERE A ROLE FOR CERVICAL ASSESSMENT AND UTERINE ARTERY DOPPLER PERFORMED DURING THE FIRST TRIMESTER OF PREGNANCY AS A SCREENING TEST FOR SPONTANEOUS PRETERM DELIVERY?

Parra-Cordero M, Sepúlveda-Martínez A, Rencoret G, Valdés E, Pedraza D, Muñoz H.

OBJECTIVE: To evaluate the role of cervical length (CL) and uterine artery Doppler (UtAD) at 11+0 to 13+6 weeks as a predictor of spontaneous preterm delivery (sPTD) in a Chilean population. METHODS: This is a prospective study involving 3,480 asymptomatic women with singleton pregnancies attending for a nuchal translucency scan at 11+0-13+6 weeks gestation who underwent a transvaginal scan for evaluation of CL and UtAD. After excluding iatrogenic deliveries <34 weeks, 3,310 pregnant women were finally studied. Maternal characteristics and ultrasound variables, adjusted and expressed as the multiple of median (MoM) of the unaffected group, were studied using a logistic regression analysis. RESULTS: The rate of sPTD <34 weeks was 0.9% (n=31). Previous PTB was present in 7.4% of multiparous women. Patients who subsequently had sPTD were characterized by a significantly higher prevalence of previous PTB (12.9 vs. 3.7%, $p < 0.05$) than the controls. No significant difference was found in the CL and UtAD between the two groups. The logistic regression analysis showed that a smoking habit and previous PTB were significantly associated with sPTD <34 weeks. The combination of these two findings provided a detection rate of 26% with an 8% FPR. CONCLUSION: Neither UtAD nor CL during the first trimester was shown to be a useful predictor of early sPTD. However, a combined model that includes a smoking habit and previous PTB might predict approximately one-third of the women destined to deliver <34 weeks with an 8% FPR.

FETAL DIAGN THER. 2013;33(4):268-71.

CHORIOAMNIONITIS CAUSED BY LISTERIA MONOCYTOGENES: A CASE REPORT OF ULTRASOUND FEATURES OF FETAL INFECTION. Hasbún J, Sepúlveda-Martínez A, Haye MT, Astudillo J, Parra-Cordero M.

Maternal listeriosis is often associated with mild symptoms for the patient, but fetal infection can lead to severe adverse perinatal outcome. The most described antenatal symptoms are reduced fetal movements and an abnormal fetal heart rate trace. We present a case of fetal listeriosis suspected by ultrasound findings of fetal gastrointestinal compromise, neonatal diagnosis and outcome.

ULTRASOUND OBSTET GYNECOL. 2013 MAY;41(5):538-44.

PREDICTION OF EARLY AND LATE PRE-ECLAMPSIA FROM MATERNAL CHARACTERISTICS, UTERINE ARTERY DOPPLER AND MARKERS OF VASCULOGENESIS DURING FIRST TRIMESTER OF PREGNANCY.

Parra-Cordero M, Rodrigo R, Barja P, Bosco C, Rencoret G, Sepúlveda-Martínez A, Quezada S.

OBJECTIVE: To develop a predictive model for pre-eclampsia using clinical, biochemical and ultrasound markers during the first trimester of pregnancy. METHODS: This was a nested case-control study within a pre-eclampsia screening project that involved 5367 asymptomatic pregnant women undergoing routine transvaginal uterine artery (UtA) Doppler at 11 +0 to 13 +6 weeks. Following exclusions, there were 70 pregnant women who later developed pre-eclampsia and 289 control patients enrolled during the first trimester who had serum or plasma samples taken at enrolment available for the purposes of this study. Of these, 17 pregnancies were diagnosed with early-onset (delivery < 34 weeks) pre-eclampsia and 53 with late-onset (delivery ≥ 34 weeks) pre-eclampsia. The lowest, highest and mean of left and right UtA pulsatility indices (PI) were calculated. Blood samples were stored at -84 °C until biochemical analysis for markers of vasculogenesis was performed. The distributions of the lowest UtA-PI and the biochemical markers were adjusted for maternal characteristics, expressed as multiples of the median (MoM), and compared between groups. Logistic regression analysis was used to evaluate if any variable was significantly associated with pre-eclampsia. RESULTS: Pregnancies that later developed pre-eclampsia were associated with higher maternal prepregnancy body mass index. An increased lowest UtA-PI was significantly associated with both early- and late-onset disease. Placental growth factor (PIGF) MoM was significantly reduced in women who later developed early- or late-onset pre-eclampsia compared with controls (median (interquartile range), 0.69 (0.33-1.46) and 1.10 (0.39-1.56), respectively, vs 1.19 (0.65-1.84), $P < 0.05$). Different combined models were generated by logistic regression analysis, and the detection rate with a fixed 10% false-positive rate was 47% and 29% for early- and late-onset pre-eclampsia, respectively. CONCLUSION: Pregnancies that later developed early or late pre-eclampsia were characterized by impaired placentation and an anti-angiogenic state during the first trimester of pregnancy. Regression models which include maternal characteristics, UtA Doppler and PIGF can apparently predict approximately half of pregnancies that will be complicated by early-onset pre-eclampsia. We believe more research in several areas is needed to aid in the creation of a better and more population-specific screening test for pre-eclampsia during the first trimester of pregnancy.

LABORATORIO ENDOCRINOLOGÍA Y MEDICINA DE LA REPRODUCCIÓN

HORM METAB RES. 2013 SEP;45(9):640-5.

TESTOSTERONE MODULATES THE EXPRESSION OF MOLECULES LINKED TO INSULIN ACTION AND GLUCOSE UPTAKE IN ENDOMETRIAL CELLS.

Ormazabal P, Romero C, Quest AF, Vega M.

Polycystic ovary syndrome (PCOS) is a common hyperandrogenic disorder associated with insulin resistance. Insulin exerts its metabolic function by activating the PI3K/Akt pathway and favoring glucose uptake. Caveolin-1 is a scaffolding protein which increases insulin receptor (IR) stability. Alternatively, activation of IR increases caveolin-1 phosphorylation on tyrosine-14. Furthermore, endometrial tissue from PCOS patients is proposed to be insulin resistant; however, the particular role of testosterone in modulating the metabolic effects of insulin remains unexplored in endometrial stromal cells. To evaluate whether androgens modulate the response to insulin, T-HESCs cells were stimulated with 100 nM testosterone for 24 h and changes in the protein levels of caveolin-1, IR, and Akt were determined by Western blotting (WB). After testosterone treatment, the consequences of acute insulin stimulation were evaluated by WB analysis of phospho-S473Akt and phospho-Y14Caveolin-1, as well as by measuring glucose incorporation analyzing 2-deoxyglucose (2-DOG) uptake. For cells pretreated with testosterone, higher IR, IRS-1, and caveolin-1

protein levels compared with control conditions were detected. However, in testosterone treated cells acute insulin stimulation did not increase phospho-S473Akt and phospho-Y14caveolin-1 levels and reduced 2-DOG uptake was observed compared to control cells. Our results suggest that testosterone may have a detrimental role on the metabolic effects of insulin in endometrial stromal cell cultures. Thus, the high androgen levels in patients with PCOS may favor insulin resistance observed in endometria from these women.

HORM METAB RES. 2013 APR;45(4):291-6.

DECREASED PHOSPHORYLATION OF Y¹⁴ CAVEOLIN-1 IN ENDOMETRIAL TISSUE OF POLYCYSTIC OVARY SYNDROME PATIENTS MAY BE RELATED WITH AN INSULIN RESISTANT STATE IN THIS TISSUE.

Ormazabal P, Romero C, Gabler F, Quest AF, Vega M.

Endometrial tissue of patients with polycystic ovary syndrome (PCOS) shows an impaired expression of insulin signaling molecules. Tyrosine phosphorylation of the insulin receptor (IR) by insulin promotes glucose uptake by activating the PI3K/Akt pathway. IR stability and function depend on the presence of the protein caveolin-1. Activation of IR increases phosphorylation of Y¹⁴ caveolin-1. Since the endometrium of PCOS patients is proposed to be insulin resistant, we evaluated the phosphorylation of IR and caveolin-1 in endometria of patients with insulin resistance (PCOSE-IR) compared to controls (CE). To explore the mechanism associated with this condition, cultured endometrial cells (T-HESC) were exposed to high glucose (25 mM, 24 h), an experimental condition that leads to insulin resistance in other cell types. Endometrial protein levels of phospho-Y⁹⁷² IR, phospho-Y¹⁴ caveolin-1 and caveolin-1 were determined by Western blotting. In cultured cells, protein levels of caveolin-1, IR, and Akt were evaluated by Western blotting. After acute insulin stimulation, phospho-S⁴⁷³ Akt, phospho-Y¹⁴ caveolin-1, and 2-deoxyglucose (2-DOG) uptake were determined. PCOSE-IR samples showed high protein levels of caveolin-1, but reduced phospho-Y¹⁴ caveolin-1 compared to CE. No differences were observed for phospho-Y⁹⁷² IR between both groups. Cells pretreated with glucose showed a reduction in protein levels of IR and caveolin-1 and were unable to increase 2-DOG uptake, phospho-S⁴⁷³ Akt and phospho-Y¹⁴ caveolin-1 after insulin stimulation. In conclusion, in PCOSE-IR the impaired phosphorylation of IR downstream molecules such as phospho-Y¹⁴ caveolin-1 suggests a diminished insulin sensitivity in endometria, condition that could be supported in vitro by the ability of T-HESCs to become insulin resistant when they are exposed to high glucose.

HUM REPROD. 2013 AUG;28(8):2235-44.

METFORMIN AUGMENTS THE LEVELS OF MOLECULES THAT REGULATE THE EXPRESSION OF THE INSULIN-DEPENDENT GLUCOSE TRANSPORTER GLUT4 IN THE ENDOMETRIA OF HYPERINSULINEMIC PCOS PATIENTS.

Carvajal R, Rosas C, Kohan K, Gabler F, Vantman D, Romero C, Vega M.

Study question: Does treatment with the insulin sensitizer metformin modify the levels and activation of proteins related to the expression of the insulin-dependent glucose transporter (GLUT4), such as adenosine monophosphate-activated protein kinase (AMPK) and myocyte enhancer factor 2A (MEF2A), in endometria from hyperinsulinemic hyperandrogenemic polycystic ovary syndrome (PCOS h-Ins) patients? Summary answer: In PCOS h-Ins patients, metformin increases endometrial levels of GLUT4 mRNA and protein levels by normalizing the quantity and activation of molecules that regulate GLUT4 expression to healthy values. These changes could improve endometrial metabolic function. What is already known: PCOS is an endocrine-metabolic disorders closely associated with insulin resistance. In particular, the insulin signaling pathway is impaired in endometria from these patients and the concentration of GLUT4, as well as the molecules involved in its translocation to the cell surface, is decreased. However, there are limited data about the mechanisms that regulate the GLUT4 expression in the endometria and the effect of metformin on them. Study design, size and duration: This is a case-control study in the setting of a research unit, approved by the Ethical Committees of our institution. The groups whose endometria were studied were PCOS h-Ins (n = 8); PCOS patients with hyperandrogenemia hyperinsulinemia taking only metformin for at least 3 months (PCOS-MTF, n = 8) and healthy fertile women at the time of hysterectomy because of benign pathology as controls (CE, n = 8). Participants/materials, setting, methods: Steroids and sex hormone-binding globulin were measured and glucose and insulin levels were evaluated during an oral glucose tolerance test. Protein levels for α AMPK (catalytic subunit of AMPK), phosphorylated (p)-AMPK α Thr(172) (activating phosphorylation site), MEF2A, p-MEF2AThr312 (activating phosphorylation site) and GLUT4 were assessed by western blot and immunohistochemistry. In addition, GLUT4 gene expression was evaluated by RT-PCR. Main results and the role of chance: We found significantly lower levels of MEF2A and p-MEF2AThr312 in PCOS h-Ins compared with CE endometria (P < 0.05). Also, we detected lower levels of p-AMPK α Thr(172) in PCOS h-Ins endometria compared with the PCOS-MTF group (P < 0.05). The ratios of phospho-AMPK/total AMPK and phospho-MEF2A/total MEF2A were significantly increased in the PCOS-MTF compared with the PCOS h-Ins group (P < 0.05). The RT-PCR experiments showed lower levels of GLUT4 mRNA transcripts in PCOS h-Ins compared with PCOS-MTF-treated group (P < 0.05), the protein levels of GLUT4

were decreased in a similar way. Limitations, reasons for caution: The limited number of patients included in this study who presented large clinical variability. Therefore, it would be necessary to recruit a greater number of patients to minimize our data dispersion in order to prove the clinical benefits of metformin described by others. Wider implications of the findings: Since the insulin sensitizer metformin increases the expression of the GLUT4, it may improve endometrial physiology in PCOS patients and, therefore, promote better reproductive outcomes. These results suggest that in PCOS patients, metformin may act directly at the endometrial level and decrease insulin resistance condition by increasing the expression of GLUT4 and, in this way, indirectly restore endometrial function.

BREAST CANCER RES TREAT. 2013 JAN;137(2):559-69.

GENETIC VARIANTS IN FGFR2 AND MAP3K1 ARE ASSOCIATED WITH THE RISK OF FAMILIAL AND EARLY-ONSET BREAST CANCER IN A SOUTH-AMERICAN POPULATION.

Jara L, Gonzalez-Hormazabal P, Cerceño K, Di Capua GA, Reyes JM, Blanco R, Bravo T, Peralta O, Gomez F, Waugh E, Margarit S, Ibañez G, Romero C, Pakomio J, Roizen G.

Genome-Wide Association Studies have identified several loci associated with breast cancer (BC) in populations of different ethnic origins. One of the strongest associations was found in the FGFR2 gene, and MAP3K1 has been proposed as a low-penetrance BC risk factor. In this study, we evaluated the associations among FGFR2 SNPs rs2981582, rs2420946, and rs1219648; and MAP3K1 rs889312, with BC risk in 351 BRCA1/2-negative Chilean BC cases and 802 controls. All the SNPs studied were significantly associated with increased BC risk in familial BC and in non-familial early-onset BC, in a dose-dependent manner. Subjects with 3 risk alleles were at a significantly increased risk of BC compared with subjects with 0-2 risk alleles, in both familial BC and early-onset non-familial BC (OR = 1.47, 95 % CI 1.04-2.07, P = 0.026 and OR = 2.04 95 % CI 1.32-3.24, P < 0.001, respectively). In the haplotype analysis, the FGFR2 rs2981582 T / rs2420946 T / rs1219648 G haplotype (ht2) was associated with a significantly increased BC risk compared with the rs2981582 C / rs2420946 C / rs1219648 A haplotype in familial BC and in non-familial early-onset BC (OR = 1.32, 95 % CI 1.06-1.65, P = 0.012; OR = 1.46, 95 % CI 1.11-1.91, P = 0.004, respectively). When the FGFR2 ht2 and MAP3K1 rs889312 were evaluated as risk alleles, the risk of BC increased in a dose-dependent manner as the number of risk alleles increased (P trend <0.0001), indicating an additive effect. Nevertheless, there is no evidence of an interaction between FGFR2 ht2 and the MAP3K1 rs889312 C allele. These findings suggest that genetic variants in the FGFR2 and MAP3K1 genes may contribute to genetic susceptibility to BC.

DEPARTAMENTO DE RADIOLOGÍA

RESPIR MED. 2013 APR;107(4):570-9.

CT AND PHYSIOLOGIC DETERMINANTS OF DYSPNEA AND EXERCISE CAPACITY DURING THE SIX-MINUTE WALK TEST IN MILD COPD.

Díaz AA, Morales A, Díaz JC, Ramos C, Klaassen J, Saldías F, Aravena C, Díaz R, Lisboa C, Washko GR, Díaz O.

OBJECTIVES: We aimed to explore physiological responses to the six-minute walk test (6MWT) and assess computed tomographic (CT) features of the lungs and thigh muscle in order to determine contributors to dyspnea intensity and exercise limitation in dyspneic and non-dyspneic subjects with GOLD-1 COPD and controls. METHODS: We compared Borg dyspnea ratings, ventilatory responses to 6MWT, and CT-measures of emphysema, airway lumen caliber, and cross-sectional area of the thigh muscle (RTMCT-CSA) in 19 dyspneic, 22 non-dyspneic, and 30 control subjects. RESULTS: Dyspneic subjects walked less and experienced greater exertional breathlessness than non-dyspneic (105 m less and 2.4 Borg points more, respectively) and control subjects (94 m less and 2.6 Borg points more, respectively) (P < 0.05 for all comparisons). At rest, dyspneic subjects had significant greater expiratory airflow obstruction, air trapping, ventilation/perfusion mismatch, burden of emphysema, narrower airway lumen, and lower RTMCT-CSA than comparison subjects. During walking dyspneic subjects had a decreased inspiratory capacity (IC) along with high ventilatory demand. Dyspneic subjects exhibited higher end-exercise tidal expiratory flow limitation and oxygen saturation drop than comparison subjects. In regression analysis, dyspnea intensity was best explained by Δ IC and forced expiratory volume in 1 s %predicted. RTMCT-CSA and Δ IC were independent determinants of distance walked. CONCLUSIONS: Among subjects with mild COPD, those with daily-life dyspnea have worse exercise outcomes; distinct lung and thigh muscle morphologic features; and different pulmonary physiologic characteristics at rest and exercise. Δ IC was the main contributor to dyspnea intensity and Δ IC and thigh muscle wasting were determinants of exercise capacity.

ANTHROPOL ANZ. 2013;70(1):101-11.

FORENSIC PALEORADIOLOGY: IDENTIFICATION OF A PUBLIC FIGURE MURDERED IN 1837.

Castro M, Díaz J, Riquelme JL, Rivas P, Richter P.

Two unidentified graves were found during construction of a new crypt at the Metropolitan Cathedral in Santiago, Chile. One of the bodies was sent to the Teaching Hospital of the University of Chile for forensic identification. The fully mummified corpse was suspected to be that of Diego Portales, a prominent Chilean politician who was assassinated in 1837. The condition of the corpse determined that the best way to establish a positive identification was by means of a multislice CT scan, since the body had been autopsied and embalmed using unknown substances. This paper presents the results of the virtual autopsy of the remains and compares these results with the original autopsy report of 1837. The embalming method is also discussed, based on chemical analysis using inductively coupled mass spectroscopy (ICP-MS) and cold vapour atomic absorption spectrometry (HG-CVAAS).

COMITÉ INFECCIONES INTRAHOSPITALARIAS

INFECT CONTROL HOSP EPIDEMIOL. 2013 MAY;34(5):479-86.

COPPER SURFACES REDUCE THE RATE OF HEALTHCARE-ACQUIRED INFECTIONS IN THE INTENSIVE CARE UNIT.

Salgado CD, Sepkowitz KA, John JF, Cantey JR, Attaway HH, Freeman KD, Sharpe PA, Michels HT, Schmidt MG.

OBJECTIVE. Healthcare-acquired infections (HAIs) cause substantial patient morbidity and mortality. Items in the environment harbor microorganisms that may contribute to HAIs. Reduction in surface bioburden may be an effective strategy to reduce HAIs. The inherent biocidal properties of copper surfaces offer a theoretical advantage to conventional cleaning, as the effect is continuous rather than episodic. We sought to determine whether placement of copper alloy-surfaced objects in an intensive care unit (ICU) reduced the risk of HAI. **DESIGN.** Intention-to-treat randomized control trial between July 12, 2010, and June 14, 2011. **SETTING.** The ICUs of 3 hospitals. **PATIENTS.** Patients presenting for admission to the ICU. **METHODS.** Patients were randomly placed in available rooms with or without copper alloy surfaces, and the rates of incident HAI and/or colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus* (VRE) in each type of room were compared. **RESULTS.** The rate of HAI and/or MRSA or VRE colonization in ICU rooms with copper alloy surfaces was significantly lower than that in standard ICU rooms (0.071 vs 0.123; $P = .020$). For HAI only, the rate was reduced from 0.081 to 0.034 ($P = .013$). **CONCLUSIONS.** Patients cared for in ICU rooms with copper alloy surfaces had a significantly lower rate of incident HAI and/or colonization with MRSA or VRE than did patients treated in standard rooms. Additional studies are needed to determine the clinical effect of copper alloy surfaces in additional patient populations and settings.