

Abstracts de publicaciones internacionales ISI 2016

ANESTESIOLOGÍA Y REANIMACIÓN

REG ANESTH PAIN MED. 2016 MAY-JUN;41(3):368-73.

A RANDOMIZED COMPARISON BETWEEN CONVENTIONAL AND WAVEFORM-CONFIRMED LOSS OF RESISTANCE FOR THORACIC EPIDURAL BLOCKS.

Arnuntasupakul V, Van Zundert TC, Vijitpavan A, Aliste J, Engsusophon P, Leurcharusmee P, Ah-Kye S, Finlayson RJ, Tran DQ.

BACKGROUND AND OBJECTIVES: Epidural waveform analysis (EWA) provides a simple confirmatory adjunct for loss of resistance (LOR): when the needle tip is correctly positioned inside the epidural space, pressure measurement results in a pulsatile waveform. In this randomized trial, we compared conventional and EWA-confirmed LOR in 2 teaching centers. Our research hypothesis was that EWA-confirmed LOR would decrease the failure rate of thoracic epidural blocks. **METHODS:** One hundred patients undergoing thoracic epidural blocks for thoracic surgery, abdominal surgery, or rib fractures were randomized to conventional LOR or EWA-LOR. The operator was allowed as many attempts as necessary to achieve a satisfactory LOR (by feel) in the conventional group. In the EWA-LOR group, LOR was confirmed by connecting the epidural needle to a pressure transducer using a rigid extension tubing. Positive waveforms indicated that the needle tip was positioned inside the epidural space. The operator was allowed a maximum of 3 different intervertebral levels to obtain a positive waveform. If waveforms were still absent at the third level, the operator simply accepted LOR as the technical end point. However, the patient was retained in the EWA-LOR group (intent-to-treat analysis). After achieving a satisfactory tactile LOR (conventional group), positive waveforms (EWA-LOR group), or a third intervertebral level with LOR but no waveform (EWA-LOR group), the operator administered a 4-mL test dose of lidocaine 2% with epinephrine 5 µg/mL. Fifteen minutes after the test dose, a blinded investigator assessed the patient for sensory block to ice. **RESULTS:** Compared with LOR, EWA-LOR resulted in a lower rate of primary failure (2% vs 24%; $P = 0.002$). Subgroup analysis based on experience level reveals that EWA-LOR outperformed conventional LOR for novice ($P = 0.001$) but not expert operators. The performance time was longer in the EWA-LOR group (11.2 ± 6.2 vs 8.0 ± 4.6 minutes; $P = 0.006$). Both groups were comparable in terms of operator's level of expertise, depth of the epidural space, approach, and LOR medium. In the EWA-LOR group, operators obtained a pulsatile waveform with the first level attempted in 60% of patients. However, 40% of subjects required performance at a second or third level. **CONCLUSIONS:** Compared with its conventional counterpart, EWA-confirmed LOR results in a lower failure rate for thoracic epidural blocks (2% vs 24%) in our teaching centers. Confirmatory EWA provides significant benefits for inexperienced operators.

REG ANESTH PAIN MED. 2016 MAY-JUN;41(3):309-13.

PRIMARY FAILURE OF THORACIC EPIDURAL ANALGESIA IN TRAINING CENTERS: THE INVISIBLE ELEPHANT?

Tran DQ, Van Zundert TC, Aliste J, Engsusophon P, Finlayson RJ.

In teaching centers, primary failure of thoracic epidural analgesia can be due to multiple etiologies. In addition to the difficult anatomy of the thoracic spine, the conventional end point-loss-of-resistance-lacks specificity. Furthermore, insufficient training compounds the problem: learning curves are nonexistent, pedagogical requirements are often inadequate, supervisors may be

inexperienced, and exposure during residency is decreasing. Any viable solution needs to be multifaceted. Learning curves should be explored to determine the minimal number of blocks required for proficiency. The problem of decreasing caseload can be tackled with epidural simulators to supplement in vivo learning. From a technical standpoint, fluoroscopy and ultrasonography could be used to navigate the complex anatomy of the thoracic spine. Finally, correct identification of the thoracic epidural space should be confirmed with objective, real-time modalities such as neurostimulation and waveform analysis.

REG ANESTH PAIN MED. 2016 MAY-JUN;41(3):328-33.

A MULTICENTER RANDOMIZED COMPARISON BETWEEN INTRAVENOUS AND PERINEURAL DEXAMETHASONE FOR ULTRASOUND-GUIDED INFRACLAVICULAR BLOCK.

Leurcharusmee P, Aliste J, Van Zundert TC, Engsusophon P, Arnuntasupakul V, Tiyaprasertkul W, Tangjitbampenbun A, Ah-Kye S, Finlayson RJ, Tran DQ.

BACKGROUND AND OBJECTIVES: This multicenter, randomized trial compared intravenous (IV) and perineural (PN) dexamethasone for ultrasound (US)-guided infraclavicular brachial plexus block. Our research hypothesis was both modalities would result in similar durations of motor block. **METHODS:** One hundred fifty patients undergoing upper limb surgery with US-guided infraclavicular block were randomly allocated to receive IV or PN dexamethasone (5 mg). The local anesthetic agent (35 mL of lidocaine 1%-bupivacaine 0.25% with epinephrine 5 µg/mL) was identical in all subjects. Patients and operators were blinded to the nature of IV and PN injectates. During the performance of the block, the performance time, number of needle passes, procedural pain, and complications (vascular puncture, paresthesia) were recorded. Subsequently, a blinded observer assessed the success rate (defined as a minimal sensorimotor composite score of 14 of 16 points at 30 minutes), onset time as well as the incidence of surgical anesthesia (defined as the ability to complete surgery without local infiltration, supplemental blocks, IV opioids, or general anesthesia). Postoperatively (at 24 hours), the blinded observer contacted patients with successful blocks to enquire about the duration of motor block, sensory block, and postoperative analgesia. The main outcome variable was the duration of motor block. **RESULTS:** No intergroup differences were observed in terms of technical execution (performance time/number of needle passes/procedural pain/complications), onset time, success rate, and surgical anesthesia. However, compared to its IV counterpart, PN dexamethasone provided 19% to 22% longer durations for motor block (15.7 ± 6.2 vs 12.9 ± 5.5 hours; $P = 0.009$), sensory block (16.8 ± 4.4 vs 13.9 ± 5.4 hours; $P = 0.002$), and postoperative analgesia (22.1 ± 8.5 vs 18.6 ± 6.7 hours; $P = 0.014$). **CONCLUSIONS:** Compared with its IV counterpart, PN dexamethasone (5 mg) provides a longer duration of motor block, sensory block, and postoperative analgesia for US-guided infraclavicular block. Future dose-finding studies are required to elucidate the optimal dose of dexamethasone.

ANESTHESIOLOGY. 2016 FEB;124(2):417-27.

INFLAMMATION INCREASES NEURONAL SENSITIVITY TO GENERAL ANESTHETICS.

Avramescu S, Wang DS, Lecker I, To WT, Penna A, Whissell PD, Mesbah-Oskui L, Horner RL, Orser BA.

BACKGROUND: Critically ill patients with severe inflammation often exhibit heightened sensitivity to general anesthetics; however, the underlying mechanisms remain poorly understood. Inflammation increases the number of γ -aminobutyric acid type A (GABAA) receptors expressed on the surface of neurons, which supports the hypothesis that inflammation increases up-regulation of GABAA receptor activity by anesthetics, thereby enhancing the behavioral sensitivity to these drugs. **METHODS:** To mimic inflammation in vitro, cultured hippocampal and cortical neurons were pretreated with interleukin (IL)-1 β . Whole cell patch clamp methods were used to record currents evoked by γ -aminobutyric acid (GABA) (0.5 µM) in the absence and presence of etomidate or isoflurane. To mimic inflammation in vivo, mice were treated with lipopolysaccharide, and several anesthetic-related behavioral endpoints were examined. **RESULTS:** IL-1 β increased the amplitude of current evoked by GABA in combination with clinically relevant concentrations of either etomidate (3 µM) or isoflurane (250 µM) ($n = 5$ to 17, $P < 0.05$). Concentration-response plots for etomidate and isoflurane showed that IL-1 β increased the maximal current 3.3-fold ($n = 5$ to 9) and 1.5-fold ($n = 8$ to 11), respectively ($P < 0.05$ for both), whereas the half-maximal effective concentrations were unchanged. Lipopolysaccharide enhanced the hypnotic properties of both etomidate and isoflurane. The immobilizing properties of etomidate, but not isoflurane, were also increased by lipopolysaccharide. Both lipopolysaccharide and etomidate impaired contextual fear memory. **CONCLUSIONS:** These results provide proof-of-concept evidence that inflammation increases the sensitivity of neurons to general anesthetics. This increase in anesthetic up-regulation of GABAA receptor activity in vitro correlates with enhanced sensitivity for GABAA receptor-dependent behavioral endpoints in vivo.

NEUROTOXICOL TERATOL. 2016 OCT 26. PII: S0892-0362(16)30121-0.

REDUCED EXPRESSION OF α 5GABAA RECEPTORS ELICITS AUTISM-LIKE ALTERATIONS IN EEG PATTERNS AND SLEEP-WAKE BEHAVIOR.

Mesbah-Oskui L, Penna A, Orser BA, Horner RL.

A reduction in the activity of GABAA receptors, particularly α 5 subunit-containing GABAA receptors (α 5GABAARs), has been implicated in the etiology of Autism Spectrum Disorders (ASD). Genetically modified mice that lack α 5GABAARs (Gabra5^{-/-}) exhibit autism-like behaviors and both enhanced and impaired learning and memory, depending on the behavioral task. The aim of this study was to examine the electroencephalogram (EEG) activity and sleep-wake behaviors in Gabra5^{-/-} mice and wild-type mice. In addition, since some individuals with ASD can exhibit elevated innate immune response, mice were treated with lipopolysaccharide (LPS; 125mg/kg intraperitoneal injection) or vehicle and EEG and sleep-wake patterns were assessed. The results showed that Gabra5^{-/-} mice (n=3) exhibited elevated 0-2Hz EEG activity during all sleep-wake states (all $p < 0.04$), decreased 8-12Hz EEG activity during REM sleep ($p = 0.04$), and decreased sleep spindles under baseline conditions compared to wild-type controls (n=4) (all $p \leq 0.03$). Alterations in EEG activity and sleep-wake behavior were identified in Gabra5^{-/-} mice following treatment with LPS, however these changes were similar to those in wild-type mice. Our findings support the hypothesis that reduced α 5GABAAR activity contributes to an ASD phenotype. The results also suggest that Gabra5^{-/-} mice may serve as an animal model for ASD, as assessed through EEG activity and sleep-wake behaviors.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

LANCET PSYCHIATRY. 2016 DEC;3(12):1138-1146.

SAFETY AND EFFICACY OF ADJUNCTIVE SECOND-GENERATION ANTIDEPRESSANT THERAPY WITH A MOOD STABILISER OR AN ATYPICAL ANTIPSYCHOTIC IN ACUTE BIPOLAR DEPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMISED PLACEBO-CONTROLLED TRIALS.

McGirr A, Vöhringer PA, Ghaemi SN, Lam RW, Yatham LN.

BACKGROUND: Although mania and hypomania define bipolar disorder, depressive episodes are more common and impairing, with few proven treatments. Adjunctive therapy with second-generation antidepressants is widely used to treat acute bipolar depression, but their efficacy and safety remain controversial. **METHODS:** In this systematic review and meta-analysis, we searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from inception to Jan 31, 2016, for randomised, double-blind, placebo-controlled trials of second-generation antidepressants adjunctive to a mood stabiliser or an antipsychotic in patients with acute bipolar depression. We extracted data from published reports. The primary outcome was change in clinician-rated depressive symptom score; secondary outcomes were clinical response, clinical remission, treatment-emergent mania or hypomania, and tolerability (using dropout rates as a proxy). We used pooled random-effects models, subgroup comparisons, and meta-regression for analyses. We made subgroup comparisons on the basis of mood stabiliser or antipsychotic treatment and did meta-regression examining trial duration. This study is registered with PROSPERO, number CRD#42015016024. **FINDINGS:** We identified six trials representing 1383 patients with bipolar depression. Second-generation antidepressants were associated with a small but significant improvement in clinician-rated depressive symptom score (standardised mean differences 0.165 [95% CI 0.051-0.278], $p = 0.004$). However, clinical response and remission rates did not differ significantly between patients receiving adjunctive antidepressants and those receiving placebo (1.158 [0.840-1.597], $p = 0.371$ for clinical response; 1.220 [0.874-1.703], $p = 0.243$ for remission). Acute treatment was not associated with an increased risk of treatment-emergent mania or hypomania (0.926 [0.576-1.491], $p = 0.753$), but 52 week extension periods were associated with an increase in risk (1.774 [1.018-3.091], $p = 0.043$). **INTERPRETATION:** Adjunctive second-generation antidepressants are associated with reduced symptoms of acute bipolar depression, but the magnitude of benefit is small because they do not increase clinical response or remission rates. However, these medications should be used only in the short term because prolonged use is associated with an increased risk of treatment-emergent mania or hypomania.

FRONT NEUROSCI. 2016 NOV 8;10:488. ECOLLECTION 2016.

FROM MOLECULES TO THE CLINIC: LINKING SCHIZOPHRENIA AND METABOLIC SYNDROME THROUGH SPHINGOLIPIDS METABOLISM.

Castillo RI, Rojo LE, Henriquez-Henriquez M, Silva H, Maturana A, Villar MJ, Fuentes M, Gaspar PA.

Metabolic syndrome (MS) is a prevalent and severe comorbidity observed in schizophrenia (SZ). The exact nature of this association is controversial and very often accredited to the effects of psychotropic medications and disease-induced life-style modifications, such as inactive lifestyle, poor dietary choices, and smoking. However, drug therapy and disease-induced lifestyle factors are likely not the only factors contributing to the observed converging nature of these conditions, since an increased prevalence of MS is also observed in first episode and drug-naïve psychosis populations. MS and SZ share common intrinsic susceptibility factors and etiopathogenic mechanisms, which may change the way we approach clinical management of SZ patients. Among the most relevant common pathogenic pathways of SZ and MS are alterations in the sphingolipids (SLs) metabolism and SLs homeostasis. SLs have important structural functions as they participate in the formation of membrane "lipid rafts." SLs also play physiological roles in cell differentiation, proliferation, and inflammatory processes, which might be part of MS/SZ common pathophysiological processes. In this article we review a plausible mechanism to explain the link between MS and SZ through a disruption in SL homeostasis. Additionally, we provide insights on how this hypothesis can lead to the developing of new diagnostic/therapeutic technologies for SZ patients.

EPIDEMIOL PSYCHIATR SCI. 2016 OCT;25(5):441-449.

PREVALENCE OF MENTAL DISORDERS AT ADMISSION TO THE PENAL JUSTICE SYSTEM IN EMERGING COUNTRIES: A STUDY FROM CHILE.

Mundt AP, Kastner S, Larrain S, Fritsch R, Priebe S.

BACKGROUND: Previous mental health surveys conducted in prisons within emerging countries recruited samples of all prisoners at any single point in time. However, this sampling strategy results in an overrepresentation of long-term prisoners as compared with those studies recruiting from all admissions over time. This study aimed to assess mental disorders in consecutively admitted prisoners soon after admission, in order to address service needs of people with short-term imprisonments and people at early stages of imprisonment. METHOD: Disorders were assessed in a sample of 229 male and 198 female prisoners, consecutively committed to the penal justice system in Santiago de Chile, using the structured Mini-Neuropsychiatric interview. Prevalence rates were calculated as per cent values. Ninety-five per cent confidence intervals were calculated for the proportions. RESULTS: Illicit drug and/or alcohol use disorders in the year prior to admission were present in 173 (76%) male and 64 (32%) female prisoners. The substances most frequently causing addiction were cocaine-based products in 108 (47%) male and 42 (21%) female prisoners. Current major depression was present in 124 (54%) male and 86 (43%) female prisoners, and current non-affective psychotic disorders in 18 (8%) male and in 10 (5%) female prisoners. High suicidal risk was present in 64 (28%) male prisoners and in 29 (15%) female prisoners. CONCLUSION: When consecutive prisoners are assessed at admission, rates of mental health and substance use disorders were higher than in previous studies in emerging countries that had sampled from all existing prisoners at a time. Affective disorders and suicide risk appear more prevalent than in admission studies conducted in Western high-income countries. Previous research may have systematically underestimated the extent of mental health problems in prisoners, which poses a major public health challenge in emerging countries.

ACTA PSYCHIATR SCAND. 2016 DEC;134(6):504-510.

THE INTERNATIONAL MOOD NETWORK (IMN) NOSOLOGY PROJECT: DIFFERENTIATING BORDERLINE PERSONALITY FROM BIPOLAR ILLNESS.

Vöhringer PA, Barroilhet SA, Alvear K, Medina S, Espinosa C, Alexandrovich K, Riumallo P, Leiva F, Hurtado ME, Cabrera J, Sullivan M, Holtzman N, Ghaemi SN3

OBJECTIVE: The differential diagnosis of bipolar illness vs. borderline personality is controversial. Both conditions manifest impulsive behavior, unstable interpersonal relationships, and mood symptoms. This study examines whether and which mood clinical features can differentiate between both conditions. METHOD: A total of 260 patients (mean \pm standard deviation age 41 \pm 13 years, 68% female) attending to a mood clinic were examined for diagnosis of bipolar illness and borderline personality disorder using SCID-I, SCID-II, and clinical mood criteria extracted from Mood Disorder Questionnaire (MDQ). They were analyzed using diagnoses as dependent variables. Predictors of bipolar and borderline diagnoses were identified by multivariable logistic regressions, and predictive validity of models was assessed using ROC curve analysis. RESULTS: Bipolar illness was strongly predicted by elevated

mood (OR = 4.02, 95% CI: 1.80-9.15), increased goal-directed activities (OR = 3.90, 95% CI: 1.73-8.96), and episodicity of mood symptoms (OR = 3.48, 95% CI 1.49-8.39). This triad model predicted bipolar illness with 88.7% sensitivity, 81.4% specificity, and obtained an auROC of 0.91 (95% CI: 0.76-0.96) and a positive predictive value of 85.1%. For borderline personality disorder, only female gender was a statistically significant predictor (OR = 3.41, 95% CI: 1.29-13.7), and the predictive model obtained an auROC of 0.67 (95% CI: 0.53-0.74). CONCLUSION: In a mood disorder clinic setting, manic criteria and episodic mood course distinguished bipolar illness from borderline personality disorder.

J FORENSIC LEG MED. 2016 AUG;42:56-62.

EXPOSURE TO PHYSICAL AND SEXUAL VIOLENCE PRIOR TO IMPRISONMENT PREDICTS MENTAL HEALTH AND SUBSTANCE USE TREATMENTS IN PRISON POPULATIONS.

Sánchez FC, Luna A, Mundt A.

The present study aimed to establish rates of exposure to physical or sexual violence (PSV) prior to imprisonment for prisoners in Spain and to explore whether people exposed to PSV access mental health treatment during imprisonment. In a sample of 2484 male and 225 female prisoners, socio-demographic variables, exposure to PSV prior to imprisonment and mental health treatments during imprisonment were assessed. Frequencies were calculated as per cent values with 95% confidence intervals (CI). The Risk Ratio (RR) of PSV and other socio-demographic variables to associate with mental health treatment during imprisonment was established. History of PSV was present in 35.2% (95% CI: 33.3-37.0) of the male and 40.0% (95% CI: 33.9-46.8) of the female prisoners. 70.7% (95% CI: 67.8-73.9) of the male and 76.9% (95% CI: 67.7-86.0) of the female prisoners with prior exposure to PSV were in mental health treatment during imprisonment. PSV was a significant predictor of mental health treatment during imprisonment in male (RR: 2.79; 95% CI 2.44-2.92) and female (RR: 1.94; 95% CI 1.76-2.23) prisoners. Most people with exposure to PSV prior to imprisonment access mental health treatment during imprisonment. Treatments may have to focus more on traumatic experiences.

PSYCHIATRY RES. 2016 MAY 30;239:226-31.

PSYCHOMETRIC PROPERTIES OF THE SYMPTOM CHECK-LIST-90-R IN PRISON INMATES.

Ignatyev Y, Fritsch R, Priebe S, Mundt AP.

The aim of this study was to investigate the reliability, construct and criterion validity of the Symptom Check-List-90-R (SCL-90-R) for prison inmates. A sample of 427 adult prisoners was assessed at admission to the penal justice system in the metropolitan region of Santiago de Chile using the SCL-90-R and the mini international neuropsychiatric interview. We tested internal consistency using Cronbach's alpha. We examined construct validity using Principal Components Analysis and Confirmatory Factor Analysis (PCA and CFA) as well as Mokken Scale Analysis. Receiver Operating Characteristic (ROC) analysis was conducted to examine external criterion validity against diagnoses established using structured clinical interviews. The SCL-90-R showed good internal consistency for all subscales ($\alpha = 0.76-0.89$) and excellent consistency for the global scale ($\alpha = 0.97$). PCA yielded a 1-factor structure, which accounted for 70.7% of the total variance. CFA and MSA confirmed the unidimensional structure. ROC analysis indicated useful accuracy of the SCL-90-R to screen for severe mental disorders. Optimal cut-off on the Global Severity Index between severe mental disorders and not having any severe mental disorder was 1.42. In conclusion, the SCL-90-R is a reliable and valid instrument, which may be useful to screen for severe mental disorders at admission to the prison system.

PARKINSONISM RELAT DISORD. 2017 FEB;35:17-24.

CHANGES IN NEURAL CIRCUITRY ASSOCIATED WITH DEPRESSION AT PRE-CLINICAL, PRE-MOTOR AND EARLY MOTOR PHASES OF PARKINSON'S DISEASE.

Borgonovo J, Allende-Castro C, Laliena A, Guerrero N, Silva H, Concha ML.

Although Parkinson's Disease (PD) is mostly considered a motor disorder, it can present at early stages as a non-motor pathology. Among the non-motor clinical manifestations, depression shows a high prevalence and can be one of the first clinical signs to appear, even a decade before the onset of motor symptoms. Here, we review the evidence of early dysfunction in neural circuitry associated with depression in the context of PD, focusing on pre-clinical, pre-motor and early motor phases of the disease. In the pre-clinical phase, structural and functional changes in the substantia nigra, basal ganglia and limbic structures are already observed. Some of these changes are linked to motor compensation mechanisms while others correspond to pathological processes common to PD and depression and thus could underlie the appearance of depressive symptoms during the pre-motor phase. Studies of the early

motor phase (less than five years post diagnosis) reveal an association between the extent of damage in different monoaminergic systems and the appearance of emotional disorders. We propose that the limbic loop of the basal ganglia and the lateral habenula play key roles in the early genesis of depression in PD. Alterations in the neural circuitry linked with emotional control might be sensitive markers of the ongoing neurodegenerative process and thus may serve to facilitate an early diagnosis of this disease. To take advantage of this, we need to improve the clinical criteria and develop biomarkers to identify depression, which could be used to determine individuals at risk to develop PD.

FRONT PSYCHOL. 2016 JUN 6;7:853.

CHILE: ACCEPTABILITY OF A TRAINING PROGRAM FOR DEPRESSION MANAGEMENT IN PRIMARY CARE.

Marín R, Martínez P, Cornejo JP, Díaz B, Peralta J, Tala Á, Rojas G.

BACKGROUND: In Chile, there are inconsistencies in the management of depression in primary care settings, and the National Depression Program, currently in effect, was implemented without a standardized training program. The objective of this study is to evaluate the acceptability of a training program on the management of depression for primary care health teams. **METHODS:** The study was a randomized controlled trial, and two primary centers from the Metropolitan Region of Santiago were randomly selected to carry out the intervention training program. Pre-post surveys were applied, to evaluate expectations and satisfaction with the intervention, respectively. Descriptive and content analysis was carried out. **RESULT:** The sample consisted of 41 health professionals, 56.1% of who reported that their expectations for the intervention were met. All of the training activities were evaluated with scores higher than 6.4 (on a 1-7 scale). The trainers, the methodology, and the learning environment were considered strengths and facilitators of the program, while the limited duration of the training, the logistical problems faced during part of the program, and the lack of educational material were viewed as weaknesses. **CONCLUSION:**The intervention was well accepted by primary health care teams. However, the clinical impact in patients still has to be evaluated.

J AFFECT DISORD. 2016 AUG;200:142-7.

HEALTHCARE TEAM TRAINING PROGRAMS AIMED AT IMPROVING DEPRESSION MANAGEMENT IN PRIMARY CARE: A SYSTEMATIC REVIEW.

Vöhringer PA, Castro A, Martínez P, Tala Á, Medina S, Rojas G.

BACKGROUND:Although evidence from Latin America and the Caribbean suggests that depression can be effectively treated in primary care settings, depression management remains unevenly performed. This systematic review evaluates all the international evidence on healthcare team training programs aimed at improving the outcomes of patients with depression. **METHODS:** Three databases were searched for articles in English or Spanish indexed up to November 20, 2014. Studies were included if they fulfilled the following conditions: clinical trials, meta-analyses, or systematic reviews; and if they evaluated a training or educational program intended to improve the management of depression by primary healthcare teams, and assessed change in depressive symptoms, diagnosis or response rates, referral rates, patients' satisfaction and/or quality of life, and the effectiveness of treatments. **RESULTS:** Nine studies were included in this systematic review. Five trials tested the effectiveness of multi-component interventions (training included), and the remaining studies evaluated the effectiveness of specific training programs for depression management. All the studies that implemented multi-component interventions were efficacious, and half of the training trials were shown to be effective. **LIMITATIONS:** Contribution of training programs alone to the effectiveness of multi-component interventions is yet to be established. The lack of specificity regarding health providers' characteristics might be a confounding factor. **CONCLUSIONS:** The review conducted suggests that stand-alone training programs are less effective than multi-component interventions. In applying the evidence gathered from developed countries to Latin America and the Caribbean, these training programs must consider and address local conditions of mental health systems, and therefore multi-component interventions may be warranted.

TELEMED J E HEALTH. 2016 JUL;22(7):577-83.

ACCEPTABILITY STUDY OF "ASCENSO": AN ONLINE PROGRAM FOR MONITORING AND SUPPORTING PATIENTS WITH DEPRESSION IN CHILE.

Espinosa HD, Carrasco Á, Moessner M, Cáceres C, Gloger S, Rojas G, Perez JC, Vanegas J, Bauer S, Krause M.

BACKGROUND: Major depression is a highly prevalent and severe mental disease. Despite the effective treatment options available, the risk of relapse is high. Interventions based on information and communication technologies generate innovative opportunities to provide support to patients after they completed treatment for depression. **MATERIALS AND METHODS:** This acceptability

study evaluated the Internet-based program Apoyo, Seguimiento y Cuidado de Enfermedades a partir de Sistemas Operativos (ASCENSO) in terms of its feasibility and acceptability in a sample of 35 patients in Chile. RESULTS: The study reveals high rates of acceptance and satisfaction among patients who actively used the program. As obstacles, patients mentioned technical problems, a lack of contact with other participants, and an insufficient connection between the program and the health service professionals. CONCLUSIONS: ASCENSO appears to be a promising complement to regular care for depression. Following improvements of the program based on participants' feedback, future research should evaluate its efficacy and cost-effectiveness.

J AFFECT DISORD. 2016 JAN 1;189:207-13.

THE COURSE OF MAJOR DEPRESSION DURING IMPRISONMENT - A ONE YEAR COHORT STUDY.

Baier A, Fritsch R, Ignatyev Y, Priebe S, Mundt AP.

BACKGROUND: First longitudinal studies in prisoners point to improvements of depressive symptoms during imprisonment. The aim of the present study was to assess the course of major depressive disorder during imprisonment and to identify factors influencing remission. METHODS: Prisoners with major depressive disorder in a sample of consecutive admissions to the penal justice system in Santiago de Chile were reassessed after one year of imprisonment. Psychiatric diagnoses were established using the Mini-International Neuropsychiatric Interview; psychological symptoms were assessed with the Symptom-Check-List 90 Revised (SCL-90-R). Mean symptom scores were compared at baseline and follow-up using Student's t-test. Odds ratios (OR) of comorbid disorders and socio-demographic factors at baseline to predict depression at follow-up were calculated. RESULTS: N=79 out of 80 inmates (99%) with major depression at baseline were included. Thirty-five prisoners (44%) had major depression at follow-up. The mean global severity score and all mean subscale scores of the SCL-90-R improved. High suicide risk was present in 37 prisoners (47%) at admission and in 11 (14%) at follow-up. The comorbid diagnosis of PTSD (OR 6.3; $p < 0.001$) at admission and having been previously imprisoned (OR 2.5; $p = 0.05$) predicted major depressive disorder at follow-up. LIMITATIONS: The study could not account for temporary improvements between the assessments. CONCLUSION: In spite of important symptom improvements, only about half of the prisoners with major depression at admission remit after one year of imprisonment. New interventions should target people with major depression and comorbid PTSD at admission.

PSYCHIATRY RES. 2016 MAR 30;237:361-5.

OBJECTIVE AND SUBJECTIVE BURDEN IN RELATIVES OF PATIENTS WITH SCHIZOPHRENIA AND ITS INFLUENCE ON CARE RELATIONSHIPS IN CHILE.

Caqueo-Urizar A, Urzúa A, Jamett PR, Irrazaval M.

This study examined the burden on family members of patients with schizophrenia in a Chilean community. Sixty-five caregivers underwent the Subjective and Objective Family Burden Interview. The results showed moderate to high levels of subjective burden and low levels of support from others in providing care. Burden and containment of disturbed behaviour were correlated with worse relationships between patients and caregivers, with the latter spending less time working outside the home. The assessed sample showed a similar pattern of burden to that of caregivers from developed countries; however, the extent of the burden tended to be higher in Chilean caregivers.

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

INT J DEV NEUROSCI. 2016 DEC 26;57:1-11.

SFPQ ASSOCIATES TO LSD1 AND REGULATES THE MIGRATION OF NEWBORN PYRAMIDAL NEURONS IN THE DEVELOPING CEREBRAL CORTEX.

Saud K, Cánovas J, Lopez CI, Berndt FA, López E, Maass JC, Barriga A, Kukuljan M.

The development of the cerebral cortex requires the coordination of multiple processes ranging from the proliferation of progenitors to the migration and establishment of connectivity of the newborn neurons. Epigenetic regulation carried out by the COREST/LSD1 complex has been identified as a mechanism that regulates the development of pyramidal neurons of the cerebral cortex. We now identify the association of the multifunctional RNA-binding protein SFPQ to LSD1 during the development of the cerebral cortex. In vivo reduction of SFPQ dosage by in utero electroporation of a shRNA results in impaired radial migration of newborn pyramidal neurons, in a similar way to that observed when COREST or LSD1 expressions are decreased. Diminished SFPQ expression also

associates to decreased proliferation of progenitor cells, while it does not affect the acquisition of neuronal fate. These results are compatible with the idea that SFPQ, plays an important role regulating proliferation and migration during the development of the cerebral cortex.

PLOS ONE. 2016 DEC 5;11(12):E0167286.

TRANSCRIPTOMIC ANALYSIS OF MOUSE COCHLEAR SUPPORTING CELL MATURATION REVEALS LARGE-SCALE CHANGES IN NOTCH RESPONSIVENESS PRIOR TO THE ONSET OF HEARING.

Maass JC, Gu R, Cai T, Wan YW, Cantellano SC, Asprer JS, Zhang H, Jen HI, Edlund RK, Liu Z, Groves AK.

Neonatal mouse cochlear supporting cells have a limited ability to divide and trans-differentiate into hair cells, but this ability declines rapidly in the two weeks after birth. This decline is concomitant with the morphological and functional maturation of the organ of Corti prior to the onset of hearing. However, despite this association between maturation and loss of regenerative potential, little is known of the molecular changes that underlie these events. To identify these changes, we used RNA-seq to generate transcriptional profiles of purified cochlear supporting cells from 1- and 6-day-old mice. We found many significant changes in gene expression during this period, many of which were related to regulation of proliferation, differentiation of inner ear components and the maturation of the organ of Corti prior to the onset of hearing. One example of a change in regenerative potential of supporting cells is their robust production of hair cells in response to a blockade of the Notch signaling pathway at the time of birth, but a complete lack of response to such blockade just a few days later. By comparing our supporting cell transcriptomes to those of supporting cells cultured in the presence of Notch pathway inhibitors, we show that the transcriptional response to Notch blockade disappears almost completely in the first postnatal week. Our results offer some of the first molecular insights into the failure of hair cell regeneration in the mammalian cochlea.

PLOS ONE. 2016 MAY 19;11(5):E0155991.

THE CORTICOFUGAL EFFECTS OF AUDITORY CORTEX MICROSTIMULATION ON AUDITORY NERVE AND SUPERIOR OLIVARY COMPLEX RESPONSES ARE MEDIATED VIA ALPHA-9 NICOTINIC RECEPTOR SUBUNIT.

Aedo C, Terreros G, León A, Delano PH.

BACKGROUND AND OBJECTIVE: The auditory efferent system is a complex network of descending pathways, which mainly originate in the primary auditory cortex and are directed to several auditory subcortical nuclei. These descending pathways are connected to olivocochlear neurons, which in turn make synapses with auditory nerve neurons and outer hair cells (OHC) of the cochlea. The olivocochlear function can be studied using contralateral acoustic stimulation, which suppresses auditory nerve and cochlear responses. In the present work, we tested the proposal that the corticofugal effects that modulate the strength of the olivocochlear reflex on auditory nerve responses are produced through cholinergic synapses between medial olivocochlear (MOC) neurons and OHCs via alpha-9/10 nicotinic receptors. METHODS: We used wild type (WT) and alpha-9 nicotinic receptor knock-out (KO) mice, which lack cholinergic transmission between MOC neurons and OHC, to record auditory cortex evoked potentials and to evaluate the consequences of auditory cortex electrical microstimulation in the effects produced by contralateral acoustic stimulation on auditory brainstem responses (ABR). RESULTS: Auditory cortex evoked potentials at 15 kHz were similar in WT and KO mice. We found that auditory cortex microstimulation produces an enhancement of contralateral noise suppression of ABR waves I and III in WT mice but not in KO mice. On the other hand, corticofugal modulations of wave V amplitudes were significant in both genotypes. CONCLUSION: These findings show that the corticofugal modulation of contralateral acoustic suppressions of auditory nerve (ABR wave I) and superior olivary complex (ABR wave III) responses are mediated through MOC synapses.

FRONT NEURAL CIRCUITS. 2016 DEC 27;10:108.

REBOXETINE IMPROVES AUDITORY ATTENTION AND INCREASES NOREPINEPHRINE LEVELS IN THE AUDITORY CORTEX OF CHRONICALLY STRESSED RATS.

Pérez-Valenzuela C, Gárate-Pérez MF, Sotomayor-Zárate R, Delano PH, Dagnino-Subiabre A.

Chronic stress impairs auditory attention in rats and monoamines regulate neurotransmission in the primary auditory cortex (A1), a brain area that modulates auditory attention. In this context, we hypothesized that norepinephrine (NE) levels in A1 correlate with the auditory attention performance of chronically stressed rats. The first objective of this research was to evaluate whether chronic stress affects monoamines levels in A1. Male Sprague-Dawley rats were subjected to chronic stress (restraint stress) and monoamines levels were measured by high performance liquid chromatographer (HPLC)-electrochemical detection. Chronically

stressed rats had lower levels of NE in A1 than did controls, while chronic stress did not affect serotonin (5-HT) and dopamine (DA) levels. The second aim was to determine the effects of reboxetine (a selective inhibitor of NE reuptake) on auditory attention and NE levels in A1. Rats were trained to discriminate between two tones of different frequencies in a two-alternative choice task (2-ACT), a behavioral paradigm to study auditory attention in rats. Trained animals that reached a performance of $\geq 80\%$ correct trials in the 2-ACT were randomly assigned to control and stress experimental groups. To analyze the effects of chronic stress on the auditory task, trained rats of both groups were subjected to 50 2-ACT trials 1 day before and 1 day after of the chronic stress period. A difference score (DS) was determined by subtracting the number of correct trials after the chronic stress protocol from those before. An unexpected result was that vehicle-treated control rats and vehicle-treated chronically stressed rats had similar performances in the attentional task, suggesting that repeated injections with vehicle were stressful for control animals and deteriorated their auditory attention. In this regard, both auditory attention and NE levels in A1 were higher in chronically stressed rats treated with reboxetine than in vehicle-treated animals. These results indicate that NE has a key role in A1 and attention of stressed rats during tone discrimination.

J NEUROSCI. 2016 JUL 6;36(27):7198-209.

SELECTIVE ATTENTION TO VISUAL STIMULI USING AUDITORY DISTRACTORS IS ALTERED IN ALPHA-9 NICOTINIC RECEPTOR SUBUNIT KNOCK-OUT MICE.

Terreros G, Jorratt P, Aedo C, Elgoyhen AB, Delano PH.

During selective attention, subjects voluntarily focus their cognitive resources on a specific stimulus while ignoring others. Top-down filtering of peripheral sensory responses by higher structures of the brain has been proposed as one of the mechanisms responsible for selective attention. A prerequisite to accomplish top-down modulation of the activity of peripheral structures is the presence of corticofugal pathways. The mammalian auditory efferent system is a unique neural network that originates in the auditory cortex and projects to the cochlear receptor through the olivocochlear bundle, and it has been proposed to function as a top-down filter of peripheral auditory responses during attention to cross-modal stimuli. However, to date, there is no conclusive evidence of the involvement of olivocochlear neurons in selective attention paradigms. Here, we trained wild-type and $\alpha 9$ nicotinic receptor subunit knock-out (KO) mice, which lack cholinergic transmission between medial olivocochlear neurons and outer hair cells, in a two-choice visual discrimination task and studied the behavioral consequences of adding different types of auditory distractors. In addition, we evaluated the effects of contralateral noise on auditory nerve responses as a measure of the individual strength of the olivocochlear reflex. We demonstrate that KO mice have a reduced olivocochlear reflex strength and perform poorly in a visual selective attention paradigm. These results confirm that an intact medial olivocochlear transmission aids in ignoring auditory distraction during selective attention to visual stimuli. SIGNIFICANCE STATEMENT: The auditory efferent system is a neural network that originates in the auditory cortex and projects to the cochlear receptor through the olivocochlear system. It has been proposed to function as a top-down filter of peripheral auditory responses during attention to cross-modal stimuli. However, to date, there is no conclusive evidence of the involvement of olivocochlear neurons in selective attention paradigms. Here, we studied the behavioral consequences of adding different types of auditory distractors in a visual selective attention task in wild-type and $\alpha 9$ nicotinic receptor knock-out (KO) mice. We demonstrate that KO mice perform poorly in the selective attention paradigm and that an intact medial olivocochlear transmission aids in ignoring auditory distractors during attention.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

INT UROGYNECOL J. 2016 DEC 6.

PREDICTING LEVATOR AVULSION FROM ICS POP-Q FINDINGS.

Pattillo Garnham A, Guzmán Rojas R, Shek KL, Dietz HP.

INTRODUCTION AND HYPOTHESIS: Levator avulsion is a common consequence of vaginal childbirth. It is associated with symptomatic female pelvic organ prolapse and is also a predictor of recurrence after surgical correction. Skills and hardware necessary for diagnosis by imaging are, however, not universally available. Diagnosis of avulsion may benefit from an elevated index of suspicion. The aim of this study was to examine the predictive value of the International Continence Society Pelvic Organ Prolapse Quantification (ICS POP-Q) for the diagnosis of levator avulsion by tomographic 4D translabial ultrasound. METHODS: This is a retrospective analysis of data obtained in a tertiary urogynaecological unit. Subjects underwent a standardised interview,

POP-Q examination and 4D translabial pelvic floor ultrasound. Avulsion of the puborectalis muscle was diagnosed by tomographic ultrasound imaging. We tested components of the ICS POP-Q associated with symptomatic prolapse and other known predictors of avulsion, including previous prolapse repair and forceps delivery with uni- and multivariate logistic regression. A risk score was constructed for clinical use. RESULTS: The ICS POP-Q components Ba, C, gh and pb were all significantly associated with avulsion on multivariate analysis, along with previous prolapse repair and forceps delivery. A score was assigned for each of these variables and patients were classified as low, moderate or high risk according to total score. The odds of finding an avulsion on ultrasound in patients in the "high risk" group were 12.8 times higher than in the "low risk" group. CONCLUSION: Levator avulsion is associated with ICS POP-Q measures. Together with simple clinical data, it is possible to predict the risk of avulsion using a scoring system. This may be useful in clinical practice by modifying the index of suspicion for the condition.

N ENGL J MED. 2016 MAR 17;374(11):1044-52.

A RANDOMIZED TRIAL OF A CERVICAL PESSARY TO PREVENT PRETERM SINGLETON BIRTH.

Nicolaidis KH, Syngelaki A, Poon LC, Picciarelli G, Tul N, Zamprakou A, Skyfta E, Parra-Cordero M, Palma-Dias R, Rodriguez Calvo J. BACKGROUND: Preterm birth is the leading cause of neonatal and infant death and of disability among survivors. It is unclear whether a pessary inserted around the cervix reduces the risk of preterm singleton birth. METHODS: We conducted a multicenter, randomized, controlled trial comparing pessary placement with expectant management (control) in girls and women who were pregnant with singletons (singleton pregnancies) and who had a cervical length of 25 mm or less at 20 weeks 0 days to 24 weeks 6 days of gestation. Participants in either group who had a cervical length of 15 mm or less, at randomization or at subsequent visits, received treatment with vaginal progesterone. The primary outcome was spontaneous delivery before 34 weeks of gestation. RESULTS: In an intention-to-treat analysis, there was no significant difference between the pessary group (465 participants) and the control group (467 participants) in the rate of spontaneous delivery before 34 weeks (12.0% and 10.8%, respectively; odds ratio in the pessary group, 1.12; 95% confidence interval, 0.75 to 1.69; P=0.57). There were no significant differences in the rates of perinatal death (3.2% in the pessary group and 2.4% in the control group, P=0.42), adverse neonatal outcome (6.7% and 5.7%, respectively; P=0.55), or neonatal special care (11.6% and 12.9%, respectively; P=0.59). The incidence of new or increased vaginal discharge was significantly higher in the pessary group than in the control group. CONCLUSIONS: Among girls and women with singleton pregnancies who had a short cervix, a cervical pessary did not result in a lower rate of spontaneous early preterm delivery than the rate with expectant management. (Funded by the Fetal Medicine Foundation; Current Controlled Trials number, ISRCTN01096902.).

ULTRASOUND OBSTET GYNECOL. 2016 AUG;48(2):239-42.

WARPING OF THE LEVATOR HIATUS: HOW SIGNIFICANT IS IT?

Dietz HP, Severino M, Kamisan Atan I, Shek KL, Guzman Rojas R.

OBJECTIVES: The levator hiatus is the largest potential hernial portal in the human body. Excessive distensibility is associated with female pelvic organ prolapse (POP). Distension occurs not just laterally but also caudally, resulting in perineal descent and hiatal deformation or 'warping'. The aim of this study was to quantify the warping effect in symptomatic women, to validate the depth of the rendered volume used for the 'simplified method' of measuring hiatal dimensions and to determine predictors for the degree of warping. METHODS: This was a retrospective study utilizing records of patients referred to a tertiary urogynecological service between November 2012 and March 2013. Patients underwent a standardized interview, clinical assessment using the POP quantification system of the International Continence Society and four-dimensional translabial ultrasound. The craniocaudal difference in the location of minimal distances in mid-sagittal and coronal planes was determined by offline analysis of ultrasound volumes, and provided a numerical measure of warping. We tested potential predictors, such as demographic factors, signs and symptoms of prolapse, levator avulsion and levator distensibility, for an association with warping. RESULTS: Full datasets were available for 190 women. The mean craniocaudal difference in location of minimal distances in mid-sagittal and coronal planes was -1.26 mm (range, -6.7 to 4.6 mm; P<0.001). This measure of warping was associated with hiatal area on Valsalva maneuver ($r=-0.284$; P<0.0001) and signs of significant prolapse on clinical and ultrasound examination (both P<0.0001). CONCLUSIONS: The plane of minimal dimensions of the levator ani hiatus is non-Euclidean, i.e. warped, and the degree of warping is associated with hiatal distension, or 'ballooning', and with POP. However, the degree of warping is minor, the largest difference we found in the location of the plane of minimal dimensions being 6.7 mm. Hence, our results support the determination of hiatal area in a rendered volume of 1-2 cm in depth.

INT UROGYNECOL J. 2016 JUN;27(6):909-13.

IS THE LEVATOR-URETHRA GAP HELPFUL FOR DIAGNOSING AVULSION?

Dietz HP, Garnham AP, Rojas RG.

INTRODUCTION AND HYPOTHESIS: Levator avulsion is a risk factor for female pelvic organ prolapse (POP) and recurrence after POP surgery. Imaging diagnosis requires the observation of an abnormal muscle insertion on tomographic ultrasound imaging (TUI). This study was designed to compare the diagnostic performance of the qualitative diagnosis (visual qualitative assessment) to measurement of the distance between muscle insertion and urethra [levator-urethra gap; (LUG)]. **METHODS:** This was a retrospective analysis of data obtained in a tertiary urogynecological unit. All patients presented with symptoms of pelvic floor dysfunction and underwent 4D translabial pelvic floor ultrasound (US), supine, and after voiding. Avulsion was defined qualitatively as abnormal muscle insertion and quantitatively as LUG \geq 25 mm on at least three consecutive central axial plane slices, with one examiner using both methods. We examined the correlation between both methods and validated them against clinical prolapse, significant organ descent on US, and hiatal ballooning. **RESULTS:** Between January and July 2013, 233 patients were seen, of whom 202 had complete volume data sets. The qualitative method diagnosed avulsion in 22 % and the quantitative method in 24.3 %. Agreement was good, with a kappa of 0.79 (0.70-0.87). Avulsion diagnosed by either method was associated with clinical and sonographic prolapse and hiatal ballooning, with odds ratios nonsignificantly higher for the quantitative method. **CONCLUSION:** Qualitative analysis of slices on TUI and a method using LUG measurement show good agreement for the diagnosis of avulsion. The LUG method is at least equally as valid in its capacity to predict significant prolapse on clinical examination and US, as well as ballooning of the levator hiatus.

ULTRASOUND OBSTET GYNECOL. 2016 OCT;48(4):516-519.

DOES IT MATTER WHETHER LEVATOR AVULSION IS DIAGNOSED PRE- OR POSTOPERATIVELY?

Abdul Jalil SS, Guzman Rojas R, Dietz HP.

OBJECTIVE: Levator ani muscle avulsion is found in 15-30% of parturients and is associated with recurrence of pelvic organ prolapse (POP) following surgery, although most published evidence on recurrence relates to postoperative diagnosis. We performed a study to determine whether a diagnosis of avulsion after pelvic floor surgery can be used as a proxy for preoperative diagnosis. **METHODS:** This was a retrospective study of 207 patients who were seen before and after surgery for POP between February 2007 and May 2013. All assessments included a three/four-dimensional transperineal tomographic ultrasound examination. Volume data were stored and analyzed at a later date by an operator who was blinded against all clinical data. The primary outcome measure was agreement between preoperative and postoperative diagnoses of avulsion, as evaluated by Cohen's kappa. Secondary outcome measures were the associations of pre- and postoperative diagnoses of levator avulsion with prolapse recurrence, defined as International Continence Society POP-Q Stage \geq 2 in any compartment. **RESULTS:** Mean follow-up after surgery was 1.3 (range, 0.3-5.5) years. Levator avulsion was found preoperatively in 111 (53.6%) patients and postoperatively in 109 (52.7%). The kappa value for the association between pre- and postoperative avulsion was 0.864 (95% CI, 0.796-0.933), signifying high agreement. The odds ratio of prolapse recurrence in women with a preoperative diagnosis of avulsion was 2.5 (95% CI, 1.3-4.5) and in those with a postoperative diagnosis it was 2.3 (95% CI, 1.3-4.2). **CONCLUSIONS:** The diagnosis of levator avulsion by tomographic pelvic floor ultrasound is equally valid before and after pelvic reconstructive surgery for POP, and both diagnoses show excellent agreement. This implies that a postoperative diagnosis of avulsion can be used as a proxy for preoperative diagnosis. Hence, avulsion can be identified postoperatively and used for subgroup analysis in prospective surgical intervention trials to define high-risk patients.

GENET MOL BIOL. 2016 OCT-DEC;39(4):573-579.

UNIPARENTAL ANCESTRY MARKERS IN CHILEAN POPULATIONS.

Vieira-Machado CD, Tostes M, Alves G, Nazer J, Martinez L, Wettig E, Pizarro Rivadeneira O, Diaz Caamaño M, Larenas Ascui J, Pavez P, Dutra MD, Castilla EE, Orioli IM.

The presence of Native Americans, Europeans, and Africans has led to the development of a multi-ethnic, admixed population in Chile. This study aimed to contribute to the characterization of the uniparental genetic structure of three Chilean regions. Newborns from seven hospitals in Independencia, Providencia, Santiago, Curicó, Cauquenes, Valdivia, and Puerto Montt communes, belonging to the Chilean regions of Santiago, Maule, and Los Lagos, were studied. The presence of Native American mitochondrial DNA (mtDNA) haplogroups and two markers present in the non-recombinant region of the Y chromosome, DYS199 and DYS287, indicative of Native American and African ancestry, respectively, was determined. A high Native American matrilineal contribution and a low Native American and African patrilineal contributions were found in all three studied regions.

As previously found in Chilean admixed populations, the Native American matrilineal contribution was lower in Santiago than in the other studied regions. However, there was an unexpectedly higher contribution of Native American ancestry in one of the studied communes in Santiago, probably due to the high rate of immigration from other regions of the country. The population genetic sub-structure we detected in Santiago using few uniparental markers requires further confirmation, owing to possible stratification for autosomal and X-chromosome markers.

BJOG. 2016 MAY;123(6):995-1003.

DOES THE EPI-NO(®) BIRTH TRAINER PREVENT VAGINAL BIRTH-RELATED PELVIC FLOOR TRAUMA? A MULTICENTRE PROSPECTIVE RANDOMISED CONTROLLED TRIAL.

Kamisan Atan I, Shek KL, Langer S, Guzman Rojas R, Caudwell-Hall J, Daly JO, Dietz HP.

OBJECTIVE: Vaginal childbirth may result in levator ani injury secondary to overdistension during the second stage of labour. Other injuries include perineal and anal sphincter tears. Antepartum use of a birth trainer may prevent such injuries by altering the biomechanical properties of the pelvic floor. This study evaluates the effects of Epi-No(®) use on intrapartum pelvic floor trauma. **DESIGN:** Multicentre prospective randomised controlled trial. **SETTING:** Two tertiary obstetric units in Australia. **POPULATION:** Nulliparous women carrying an uncomplicated singleton term pregnancy. **METHODS:** Participants were assessed clinically and with 4D translabial ultrasound in the late third trimester, and again at 3-6 months postpartum. Women randomised to the intervention group were asked to use the Epi-No(®) device from 37 weeks of gestation until delivery. **MAIN OUTCOME MEASURES:** Levator ani, anal sphincter, and perineal trauma diagnosed clinically and/or with translabial ultrasound imaging. **RESULTS:** Of 660 women randomised, 504 (76.4%) returned for assessment at a mean of 5 months postpartum. There was no significant difference in the incidence of levator avulsion [12 versus 15%; relative risk (RR) 0.82, 95% confidence interval (95% CI) 0.51-1.32; absolute risk reduction (ARR) 0.03, 95% CI -0.04 to 0.09; P = 0.39], irreversible hiatal overdistension (13 versus 15%; RR 0.86, 95% CI 0.52-1.42; ARR 0.02, 95% CI -0.05 to 0.09; P = 0.51), clinical anal sphincter trauma (7 versus 6%; RR 1.12, 95% CI 0.49-2.60; ARR -0.01, 95% CI -0.05 to 0.06; P = 0.77), and perineal tears (51 versus 53%; RR 0.96, 95% CI 0.78-1.17; ARR 0.02, 95% CI -0.08 to 0.13; P = 0.65). A marginally higher rate of significant defects of the external anal sphincter on ultrasound was observed in the intervention group (21 versus 14%; RR 1.44, 95% CI 0.97-2.20; ARR -0.06, 95% CI -0.13 to 0.05; P = 0.07). **CONCLUSION:** Antenatal use of the Epi-No(®) device is unlikely to be clinically beneficial in the prevention of intrapartum levator ani damage, or anal sphincter and perineal trauma.

REPROD SCI. 2016 JAN 1:1933719116678689.

MOLECULAR MECHANISMS OF ANDROSTENEDIOL IN THE REGULATION OF THE PROLIFERATIVE PROCESS OF HUMAN ENDOMETRIAL CELLS.

Plaza-Parrochia F, Oróstica L, García P, Vera C, Romero C, Valladares L, Vega M.

Proliferation in endometria of women with polycystic ovarian syndrome (PCOS) is increased, similar to the biosynthesis of androstenediol (estrogenic metabolite). As previously shown, in human endometrial cells, androstenediol increases CYCLIN D1 levels and KI67 and decreases P27 content. The objective of the present investigation was to determine the mechanisms by which androstenediol promotes endometrial cell-cycle progression. Estrogen receptor α (ER α) activation and changes in CYCLIN D1 and P27 levels were evaluated by Western blot in T-HESC and St-T1b endometrial cell lines, using receptor antagonists; activation of PI3K-protein kinase B (AKT) and mitogen-activated protein kinases-extracellular signal-regulated kinases (MAPK-ERK)1/2 pathways was evaluated using PI3K, MAPK/ERK kinase (MEK)1/2, and RNA-polymerase II inhibitors. The data showed that androstenediol treatment significantly increases CYCLIN D1 and decreases P27 levels through ER α activation (P < .05). In addition, an increase in AKT/ERK1/2 phosphorylations was determined (P < .05). In the presence of RNA-polymerase II inhibitor, phosphorylation of AKT/ERK1/2 decreased (P < .05), meaning that endometrial cells need transcriptional activity to activate the kinases involved. It was also observed that PI3K action is required for P27 and CYCLIN D1 changes. Therefore, the action of androstenediol in endometria depends on PI3K-AKT and MAPK-ERK1/2 pathways activation, together with cell transcriptional machinery. This could be of clinical significance, as in pathologies such as PCOS, increased endometrial levels of androstenediol together with a high prevalence of endometrial hyperplasia and adenocarcinoma have been reported.

CURR PHARM DES. 2016;22(36):5614-5624.

ALTERED STEROID METABOLISM AND INSULIN SIGNALING IN PCOS ENDOMETRIA: IMPACT IN TISSUE FUNCTION.

Oróstica L, Rosas C, Plaza-Parrochia F, Astorga I, Gabler F, García V, Romero C, Vega M.

BACKGROUND: Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine/metabolic disorder characterized by hyperandrogenemia and in most cases, by hyperinsulinemia in addition to obesity. Besides ovarian dysfunction, endometrial physiology is also disrupted since this tissue is highly dependent on the action of steroids; in case of conception cycles, high percentage of abortion is observed. Because of the endocrine/metabolic alterations, PCOS-women present high probability to develop hyperplasia and endometrial cancer, where an imbalance of cell proliferation/apoptosis processes is detected. Additionally, insulin pathway and the endometrial energetic homeostasis are also compromised. **METHODS:**The aim of this review was to report molecular alterations related to insulinresistance and/or obesity in PCOS-women endometria that could drive to infertility. For this, several methods were employed: immunohistochemistry, qPCR, western-blot, glucoseuptake, cell cultures, among others. **RESULTS:** Diminished levels and activity of several insulin signaling pathway molecules, like IRS-1/AS160/PKC, were detected. Concomitantly, a defect in the synthesis and GLUT4 translocation to cell surface is induced. Oral administration of metformin (insulin sensitizer) to PCOS-patients increases GLUT4 endometrial levels, improving fertility of those patients. Another relevant feature is the high percentage of obesity in PCOS-women; adiponectin is an obesity marker and elicits an insulin-sensitizer action, being diminished in plasma of obese PCOSwomen similar to its endometrial level, adiponectin-receptors and APPL1, an adapter molecule of adiponectin pathway. Moreover, obesity and PCOS can induce a pro-inflammatory environment, exaggerating the alterations in insulin pathway. **CONCLUSION:** The evidences obtained in PCOS-endometria clearly indicate that these molecular defects could partially explain the reproductive failures of these patients.

EUR J OBSTET GYNECOL REPROD BIOL. 2016 JAN;196:6-10.

TRANSCUTANEOUS POSTERIOR TIBIAL NERVE STIMULATION VERSUS EXTENDED RELEASE OXYBUTYNIN IN OVERACTIVE BLADDER PATIENTS. A PROSPECTIVE RANDOMIZED TRIAL.

Manríquez V, Guzmán R, Naser M, Aguilera A, Narvaez S, Castro A, Swift S, Digesu GA.

INTRODUCTION AND HYPOTHESIS: The aim of this study was to evaluate the effectiveness of transcutaneous posterior tibial nerve stimulation (T.C. PTNS) versus extended release oxybutynin (E.R.O.) in patients with overactive bladder. **MATERIALS AND METHODS:** Seventy female patients were randomized to receive either 10mg E.R.O. daily or T.C. PTNS, using a TENS machine program with the 20Hz, 200 cycles/s, and normal stimulation setting for two 30-min sessions, each week for a 12-week period. Pre-treatment and after the 12-week intervention, each patient completed a 3-day voiding diary and a self-report quality of life questionnaire (OAB-q). Statistical analysis was performed using Stata V12.1. **RESULTS:** Sixty-four patients completed the treatment protocol. There were no significant differences between study groups in terms of age, body mass index, past hormone replacement therapy, smoking habits, menopause status, and parity. Prior to treatment, there were also no significant differences in the analysis of the 3-day voiding diary or in the OAB-q questionnaire results. Following the 12-week study, there was a statistically significant reduction in frequency of urination, urgency episodes, and urge incontinent episodes compared to pre-treatment values. However, there were no significant differences in these values between intervention groups after 12-weeks of therapy. There was a similar improvement in OAB-q scores in both treatment groups following therapy, and the T.C. PTNS group showed a statistically significant improvement over the E.R.O. in domain 2 of the OAB-q questionnaire. The other two domains showed similar improvement in both study groups. **CONCLUSION:** T.C. PTNS and E.R.O. demonstrated similar improvements in subjects with OAB in a 12-week study.

BJOG. 2016 APR;123(5):815-9.

CAESAREAN HYSTERECTOMY FOR PLACENTA PRAEVIA/ACCRETA USING AN APPROACH VIA THE POUCH OF DOUGLAS.

Selman AE.

Placenta praevia/accreta is associated with significant maternal morbidity and mortality and is a common cause of obstetric hysterectomy. This paper describes posterior retrograde abdominal hysterectomy, a new surgical technique for caesarean hysterectomy, in 11 women with placenta percreta, increta or accreta. There were no intraoperative or postoperative maternal complications, and only one fetus required admission to the neonatal unit, for prematurity. Our technique in placenta praevia/accreta allows easy identification of the vagina and early uterine devascularisation, as well as safe resection of the involved urinary bladder in women with placenta percreta showing bladder penetration. Analytical studies are needed to confirm our findings.

REPROD SCI. 2016 JUN;23(6):761-70..

HYPERANDROGENISM DECREASES GRP78 PROTEIN LEVEL AND GLUCOSE UPTAKE IN HUMAN ENDOMETRIAL STROMAL CELLS. Rosas C, Oróstica L, Poblete C, Carvajal R, Gabler F, Romero C, Lavandero S, Vega M.

BACKGROUND: Women with polycystic ovary syndrome (PCOS) exhibit a low fertility by chronic hyperandrogenemia. Different evidence have shown that androgens could regulate the endoplasmic reticulum (ER) homeostasis and glucose metabolism. However, it is unclear whether androgens can exert these effects on human endometrial stromal cells. Our goal was to study the protein content of GRP78 (an ER homeostasis marker) in endometria from women with PCOS and healthy women and to assess the GRP78 protein levels and its relationship with glucose uptake on a human endometrial stromal cell line stimulated with testosterone. METHODS: Immunohistochemistry assays for GRP78 were performed on endometrial samples obtained from women with PCOS (n = 8) and control women subjected to hysterectomy (n = 8). Western blot analysis for GRP78 and glucose uptake was assessed in a telomerase-immortalized human endometrial stromal cell line (T-HESC) exposed to testosterone for 24 or 48 hours and challenged to an insulin short-term stimulation. Tukey test was performed for human samples comparison. Student t test or ANOVA-Bonferroni test was carried out according to the in vitro experiment. $P < .05$ was considered as significant. RESULTS: GRP78 stromal immunostaining was reduced in PCOS endometria compared to controls ($P < .05$). The T-HESC shows a testosterone-dependent downregulation of GRP78 protein content ($P < .05$), concomitant with half-reduction in glucose uptake compared to controls ($P < .05$). Moreover, enhanced small interfering RNA against GRP78 messenger RNA leads to a decrease in glucose uptake ($P < .05$). Such effects were reverted by hydroxyflutamide, an inhibitor of androgen receptor. CONCLUSION: These results suggest that hyperandrogenemic PCOS environment could compromise the endometrial homeostasis confirmed by the decrease in glucose uptake induced by testosterone and exhibited by stromal cells.

REPROD SCI. 2016 FEB;23(2):211-8.

LEVELS OF REGULATORY PROTEINS ASSOCIATED WITH CELL PROLIFERATION IN ENDOMETRIA FROM UNTREATED PATIENTS HAVING POLYCYSTIC OVARIAN SYNDROME WITH AND WITHOUT ENDOMETRIAL HYPERPLASIA.

Bacallao K, Plaza-Parrochia F, Cerda A, Gabler F, Romero C, Vantman D, Vega M.

Polycystic ovarian syndrome (PCOS) has been associated with endometrial hyperplasia and cancer. The aim of this study was to establish whether the expression of proliferation regulatory proteins in the endometria of patients having PCOS, with or without hyperplasia, differs from control women. Control endometria (CE), patients having PCOS without and with endometrial hyperplasia (PCOSE and HPCOSE, respectively), and that of women with endometrial hyperplasia (HE) were used. The phosphorylated estrogen receptor form (pER α), similar to mother against decapentaplegic (SMAD) 2, SMAD3, and SMAD4, vascular epithelial growth factor (VEGF), and phosphorylated SMAD (pSMAD) 2 and pSMAD3 were detected by immunohistochemistry or Western blot. The results show higher levels of pER α in HE versus CE ($P < .05$), while higher VEGF levels were found in PCOSE and HE ($P < .05$) compared to CE; SMAD2 diminished in HE ($P < .05$) versus CE. Consequently, the higher levels of VEGF and pER α in PCOSE could represent early changes in the progression of PCOSE toward hyperplasia and cancer, whereas changes observed in SMAD proteins support the differential origin of the pathologies of HPCOSE and HE.

J CANCER RES CLIN ONCOL. 2016 JAN;142(1):47-58.

ROLE OF DIHYDROTESTOSTERONE (DHT) ON TGF- β 1 SIGNALING PATHWAY IN EPITHELIAL OVARIAN CANCER CELLS.

Kohan-Ivani K, Gabler F, Selman A, Vega M, Romero C.

PURPOSE: One of the hypotheses regarding the genesis of epithelial ovarian cancer involves the action of androgens on the proliferation of epithelial ovarian cells, as well as inclusion cysts. The purpose of the present study was to evaluate whether DHT causes changes in the TGF- β 1 pathway that might modify the anti-proliferative effect of the latter. METHODS: The levels of TGF- β 1 protein, of its receptors (TGFBR1 and TGFBR2), of Smad2/3 (canonical signaling pathway protein) and of p21 (cell cycle protein) were assessed in ovarian tissues, epithelial ovarian cancer cell lines (A2780) and control cell lines (HOSE) through the use of immunohistochemistry and immunocytochemistry. Additionally, cell lines were treated with 100 nmol/L DHT, 10 ng/mL of TGF- β 1 and DHT + TGF- β 1 during 72 h in the presence and absence of a siRNA against androgen receptor. After treatment, TGFBR1 and TGFBR2 levels were detected through Western blotting and p21 was assessed through immunocytochemistry. RESULTS: Epithelial ovarian cancer tissues showed a decrease in TGF- β 1 I receptor ($p < 0.05$) and a change in Smad2/3 protein levels. Additionally, after treatment of cell lines with DHT, protein levels of TGF- β 1 receptors (TGFBR1-TGFBR2) showed a decrease ($p < 0.05$) that might cause a potential disorder in TGF- β 1 response, represented by

the significant decrease in p21 protein levels in the presence of DHT ($p < 0.001$). CONCLUSIONS: Overall, our results indicate a defect in the canonical TGF- β signaling pathway in epithelial ovarian cancer caused by androgen action, thus suggesting eventual changes in such tissue proliferation rates.

INT UROGYNECOL J. 2016 FEB;27(2):229-32.

DIGITATION ASSOCIATED WITH DEFECCATION: WHAT DOES IT MEAN IN UROGYNAECOLOGICAL PATIENTS?

Hai-Ying C, Guzmán Rojas R, Hall JC, Atan IK, Dietz HP.

INTRODUCTION AND HYPOTHESIS: Obstructed defecation is a common symptom complex in urogynaecological patients, and perineal, vaginal and/or anal digitation may be required for defecation. Translabial ultrasound can be used to assess anorectal anatomy, similar to defecation proctography. The aim of the present study was to determine the association between different forms of digitation (vaginal, perineal and anal) and abnormal posterior compartment anatomy. METHODS: A total of 271 patients were analysed in a retrospective study utilising archived ultrasound volume datasets. Symptoms of obstructed defecation (straining at stool, incomplete bowel emptying, perineal, vaginal and anal digitation) were ascertained on interview. Postprocessing of stored 3D/4D translabial ultrasound datasets obtained on maximal Valsalva was used to diagnose descent of the rectal ampulla, rectocele, enterocele and rectal intussusception at a later date, blinded to all clinical data. RESULTS: Digitation was reported by 39 % of our population. The position of the rectal ampulla on Valsalva was associated with perineal ($p=0.02$) and vaginal ($p=0.02$) digitation. The presence of a true rectocele was significantly associated with perineal ($p=0.04$) and anal ($p=0.03$) digitation. Rectocele depth was associated with all three forms of digitation ($P=0.005-0.02$). The both of symptoms of obstructed defecation was strongly associated with digitation (all $P < 0.001$), with no appreciable difference in both among the three forms. CONCLUSION: Digitation is common, and all forms of digitation are associated with abnormal posterior compartment anatomy. It may not be necessary to distinguish between different forms of digitation in clinical practice.

GYNECOL OBSTET INVEST. 2016;81(1):78-83.

ASSESSMENT OF PROTEIN:CREATININE RATIO VERSUS 24-HOUR URINE PROTEIN IN THE DIAGNOSIS OF PREECLAMPSIA.

Valdés E, Sepúlveda-Martínez Á, Tong A, Castro M, Castro D.

BACKGROUND/AIMS: Current evidence has tried to extrapolate the use of the protein:creatinine ratio (PCR) in a single urine sample as a rapid diagnostic tool for preeclampsia (PE). The present study addresses the effectiveness of the PCR in the differential diagnosis of the pregnancy hypertensive disorder (PHD). METHODS: This is a prospective study conducted on patients admitted during 1 year with a diagnosis of PHD. These pregnant women were assessed for the correlation between the 24-hour test and the PCR to detect significant proteinuria. A ROC curve was made to determine the PCR cutoff value that would offer the best positive predictive value (PPV) as an early predictor of global and severe PE. RESULTS: A total of 72 patients with 24-hour proteinuria and PCR were studied (49 with PE). A significant correlation between the quick and the deferred sampling was observed ($r = 0.60$; $p < 0.001$). The ROC analysis showed a PCR of 0.36 as the best cutoff value for the diagnosis of global PE (PPV 96.4%; false-positive rate 4.4%; AUC 0.8802) and a cutoff value of 4.58 (sensitivity: 100%; PPV 87.5%; false-positive rate 3.5%; AUC 0.9805) as the best cutoff for the diagnosis of severe proteinuria. CONCLUSIONS: PCR proved to be an effective test for the differential diagnosis of PHS.

INT UROGYNECOL J. 2016 JUN;27(6):939-44.

THE PREVALENCE OF ABNORMAL POSTERIOR COMPARTMENT ANATOMY AND ITS ASSOCIATION WITH OBSTRUCTED DEFECCATION SYMPTOMS IN UROGYNECOLOGICAL PATIENTS.

Guzman Rojas R, Kamisan Atan I, Shek KL, Dietz HP.

INTRODUCTION AND HYPOTHESIS: Symptoms of obstructive defecation (OD) are common in women. Transperineal ultrasound (TPUS) has been used for the evaluation of defecatory disorders. The aim of our study was to determine the overall prevalence of anatomical abnormalities of the posterior compartment and their correlations with OD in women seen in a tertiary urogynecology clinic. METHODS: This is a retrospective study on 750 women seen at a tertiary urogynaecological unit who had undergone a standardized interview, clinical examination, and 4D TPUS. Univariate and multivariate logistic regression analyses were undertaken to study the association between examination findings and symptoms of OD. This study was approved by the local human research ethics committee (Nepean Blue Mountains Local Health District Human Research Ethics Committee, IRB approval no. 13-16). RESULTS: The datasets of 719 women were analyzed. Mean age was 56.1 (18.4-87.6) years. Ninety-seven patients (13 %) reported fecal incontinence, 190 (26 %) constipation, and 461 (64 %) symptoms of OD. On examination, 405 women (56 %) were diagnosed

with significant posterior compartment prolapse (POP-Q \geq stage 2), which was associated with symptoms of OD ($p < 0.0001$). On ultrasound, 103 (14 %) patients had an enterocele, 382 (53 %) a true rectocele and 31 (4.3 %) had rectal intussusception. On multivariate analysis true rectocele ($p = 0.003$) and rectal intussusception ($p = 0.004$) remained significantly associated with symptoms of OD. CONCLUSION: Both symptoms of OD and anatomical abnormalities of the posterior compartment are highly prevalent in urogynecological patients. Ultrasound findings of a true rectocele and rectal intussusception are significantly associated with obstructed defecation.

FETAL DIAGN THER. 2016;39(3):186-91.

CORD OCCLUSION IN MONOCHORIONIC TWINS WITH EARLY SELECTIVE INTRAUTERINE GROWTH RESTRICTION AND ABNORMAL UMBILICAL ARTERY DOPPLER: A CONSECUTIVE SERIES OF 90 CASES.

Parra-Cordero M1, Bennasar M, Martínez JM, Eixarch E, Torres X, Gratacós E.

OBJECTIVE: To describe perinatal outcomes achieved with cord occlusion (CO) in monochorionic twins with severe selective intrauterine growth restriction (sIUGR) and abnormal umbilical artery Doppler in the IUGR twin (types II and III). METHODS: We studied a consecutive series of 90 cases of sIUGR with abnormal Doppler treated with CO of the IUGR fetus. Abnormal Doppler was defined as continuous (type II, $n = 41$) or intermittent (type III, $n = 49$) absent/reversed end-diastolic flow. All cases presented at least one of the following severity criteria: gestational age (GA) < 22 weeks, inter-twin estimated weight discordance $> 35\%$, reversed end-diastolic umbilical artery flow or ductus venosus pulsatility index > 95 th centile. We prospectively recorded pregnancy course and perinatal outcome. RESULTS: Median GA at surgery was 20.6 weeks and mean duration 22.4 min. Miscarriage (< 24 weeks) occurred in 3.3% (3/90) and preterm delivery < 32 weeks in 7.1% (6/84) of continuing pregnancies. GA at delivery was 36.4 weeks and neonatal survival of the larger twin was achieved in 93.3%. CONCLUSION: In a consecutive series studied by an experienced team, CO in monochorionic twins with severe sIUGR type II or III was associated with delivery > 32 weeks in 92.9% and neonatal survival of the normal twin in 93.3% of pregnancies.

FETAL DIAGN THER. 2016;40(4):298-302.

INCREASED PR INTERVAL IN FETUSES OF PATIENTS WITH INTRAHEPATIC CHOLESTASIS OF PREGNANCY.

Rodríguez M1, Moreno J, Márquez R, Eltit R, Martínez F, Sepúlveda-Martínez A, Parra-Cordero M.

OBJECTIVE: To evaluate the fetal mechanical PR interval in fetuses from pregnancies with intrahepatic cholestasis of pregnancy (ICP). METHODS: A case-control study was conducted in the Maternal-Fetal Medicine Unit at Hospital Carlos Van Buren between 2011 and 2013. Fetal echocardiography was performed in patients with ICP and normal pregnancies. Demographic and clinical characteristics were compared using the Mann-Whitney U test for continuous variables. A p value < 0.05 was considered significant. RESULTS: 51 patients with ICP were compared with 51 unaffected pregnancies. There were no significant differences in neither demographic nor clinical characteristics between the two groups. The fetal PR interval was significantly longer in the ICP group when compared to the control group (134.6 ± 12 vs. 121.4 ± 10 ms, $p < 0.001$). Moreover, four fetuses from the ICP group had a mechanical PR interval > 150 ms, which is compatible with a first-degree atrioventricular block. Two fetuses were identified in the neonatal period and were transferred to pediatric cardiology for follow-up, with a normal mechanical PR after the first month of life. CONCLUSIONS: We demonstrated that the fetal cardiac conduction system is altered in fetuses of patients with ICP. Further research is necessary to determine whether this alteration is related to stillbirths seen in ICP.

CURR STEM CELL RES THER. 2016;11(5):420-5.

PLACENTAL HYPOXIA DEVELOPED DURING PREECLAMPSIA INDUCES TELOCYTES APOPTOSIS IN CHORIONIC VILLI AFFECTING THE MATERNAL-FETUS METABOLIC EXCHANGE.

Bosco CB, Díaz EG, Gutierrez RR, González JM, Parra-Cordero M, Rodrigo RS, Barja PY.

Telocytes (TC) are a new type of stromal cells initially found and studied in digestive and extra-digestive organs. These cells have a small cell body with 2 to 5 thin and extremely long cytoplasmic prolongations named telopodes. In recent years, TC have also been described in placental chorionic villi, located in a strategic position between the smooth muscle cells from fetal vessels and the myofibroblasts in the stromal villi. Unlike other organs, the placenta is not innervated and considering the strategic location of TC it has been postulated that TC function would be related to signal transduction mechanisms involved in the regulation of the fetal vessels blood flow, as well as in the shortening/lengthening of the chorionic villi, providing the necessary rhythmicity to the process of maternal/fetal metabolic exchange. Preeclampsia (PE) is a systemic syndrome that affects 4%-6% of pregnancies worldwide. It

is characterized by a placental state of ischemia-hypoxia which triggers an oxidative stress stage with the concomitant production of reactive oxygen species (ROS) leading to an increase in the degree of placental apoptosis. Placental vascular tone is regulated by the vasodilator nitric oxide (NO) and, in PE cases, NO is diverted towards the formation of peroxynitrite, a powerful oxidative agent whose activity leads to an increase of placental apoptosis degree that compromises TC and myofibroblasts, a key feature we would like to emphasize in this work.

FETAL DIAGN THER. 2016 AUG 12.

MATERNAL PLASMA NERVE GROWTH FACTOR AT THE 11+0-13+6 WEEKS' SCAN AS A POTENTIAL ANGIOGENIC MARKER OF PREECLAMPSIA: A PILOT STUDY.

Sepúlveda-Martínez A, Garrido M, Caamano E, Vega M, Romero C, Parra-Cordero M.

OBJECTIVE: The aim of this study was to determine the role of nerve growth factor (NGF) in the first-trimester screening for preeclampsia (PE). **METHODS:** Uterine artery Doppler (UtAD) was determined transvaginally. Maternal concentrations of NGF were assessed in 42 patients who subsequently developed PE and in 95 controls. Quantile and multivariate regression analyses were performed for the NGF and UtAD adjustment and expressed as the multiple of the median (MoM) of the unaffected group. Logistic regression analysis was conducted to identify the best model for the prediction of PE. **RESULTS:** The maternal plasma concentration of NGF exhibited a trend towards lower values in patients who subsequently developed early-onset PE (e-PE) compared to controls (10.7 vs. 38.2 pg/ml, respectively; $p =$ not significant). The median MoM NGF in the all-PE, e-PE and control groups was 0.97 (95% CI 0.13-3.36), 0.62 (95% CI 0.16-2.19) and 1.00 (95% CI 0.20-2.94), respectively ($p =$ not significant). The best predictors of PE were previous PE, chronic hypertension and UtAD. With a false-positive rate of 10%, the detection rates (DRs) of all-PE and e-PE were 38 and 50%, respectively. The addition of MoM NGF did not improve the DR of PE. **CONCLUSION:** First-trimester NGF tends to be lower in patients who subsequently develop e-PE.

FETAL DIAGN THER. 2016 AUG 12.

SECOND-TRIMESTER ANTERIOR CERVICAL ANGLE IN A LOW-RISK POPULATION AS A MARKER FOR SPONTANEOUS PRETERM DELIVERY.

Sepúlveda-Martínez A, Díaz F, Muñoz H, Valdés E, Parra-Cordero M.

OBJECTIVE: The aim of this article is to assess the use of the anterior cervical angle (ACA) as a predictor of spontaneous preterm delivery (sPTD) at 20+0-24+6 weeks of gestation in an unselected population. **METHODS:** We conducted a nested case-control study that included 93 women who later delivered spontaneously <34 weeks of gestation and 225 controls. The ACA was assessed retrospectively on all selected images using ImageJ® software. The concordance correlation coefficient was determined for the assessment of interobserver variability. Continuous variables were adjusted by maternal characteristics and expressed as the z-score or multiples of the expected normal median (MoM) of the unaffected group. Logistic regression analysis was used to evaluate whether any maternal characteristics and ultrasound variables were significantly associated with sPTD <34 weeks. **RESULTS:** ACA z-score values were significantly greater in women who later delivered <34 weeks compared to controls (ACA z-score = 1.32 ± 0.57 vs. -0.09 ± 0.35 ; $p = 0.035$). The best prediction of sPTD <34 weeks was provided by a model that combined cervical length (CL) MoM, ACA z-score and maternal characteristics. For a fixed false-positive rate of 10%, the detection rate for this model was 37.6%. **CONCLUSION:** A model combining maternal history, CL and ACA at 20+0-24+6 weeks of gestation can predict approximately 40% of the severe preterm births.

INT J OBES (LOND). 2016 NOV;40(11):1715-1722.

PROINFLAMMATORY ENVIRONMENT AND ROLE OF TNF- α IN ENDOMETRIAL FUNCTION OF OBESE WOMEN HAVING POLYCYSTIC OVARIAN SYNDROME.

Oróstica L, Astorga I, Plaza-Parrochia F, Vera C, García V, Carvajal R, Gabler F, Romero C, Vega M.

BACKGROUND/OBJECTIVES: A high percentage of women having polycystic ovarian syndrome (PCOS) exhibit hyperinsulinemia and obesity. Transforming necrosis factor- α (TNF- α) is an adipokine that increases in obesity and negatively affects insulin action in several tissues, including the endometrium. In fact, it has been reported that insulin signaling is altered in the endometrium of PCOS women, affecting its reproductive function. The aim of this study was to determine the proinflammatory environment and TNF- α signaling in endometrium from obese women with PCOS, and also to evaluate the effect of TNF- α on endometrial cell energy homeostasis. **METHODS:** Serum and endometrial tissues were obtained from four study groups: normal-weight,

normal-weight-PCOS, obese and obese-PCOS (hyperandrogenemia/hyperinsulinemia) (n=7 per group). Serum TNF- α level was assayed by enzyme-linked immunosorbent assay (ELISA); endometrial TNF- α level and its receptors (TNFR1/TNFR2) as well as nuclear factor (NF)- κ B content were determined by immunohistochemistry. Finally, we evaluated TNF- α effect on glucose uptake in cultured human endometrial stromal cells (T-HESC) treated or not with testosterone/insulin resembling partially the PCOS condition. RESULTS: TNF- α plasma levels were similar between groups, whereas cytokine levels and macrophage number increased in endometrium from obese-PCOS women (P<0.001). Both receptor types were higher in obese vs normal-weight women, particularly TNFR2 content in the obese-PCOS group (P<0.001). Furthermore, an increased NF- κ B nuclear content in endometrium from obese-PCOS was observed (P<0.001). Finally, TNF- α treatment of T-HESC cultures exhibited a decrease of glucose uptake (P<0.05), although similar to cells treated with testosterone or testosterone/insulin/TNF- α . CONCLUSIONS: These results suggest that the PCOS condition induces an inflammatory state exacerbated when obesity is present, where a higher TNF- α signaling is observed, all of which could affect glucose uptake in the tissue and may cause fertility failures in these women.

EUR J OBSTET GYNECOL REPROD BIOL. 2016 SEP;204:1-4.

TREATMENT OF FEMALE STRESS URINARY INCONTINENCE WITH ERBIUM-YAG LASER IN NON-ABLATIVE MODE.

Pardo JI, Solà VR, Morales AA.

OBJECTIVE: To evaluate the efficacy of laser photothermal therapy in a group of Chilean women with SUI. MATERIAL AND METHODS: Longitudinal prospective study based on 42 women with mild-to-severe SUI, intervened with non ablative Er:YAG laser, between July 2014 and October 2015, in Santiago, Chile. The therapy efficacy was evaluated through the difference between every patient's scores obtained, before and after treatment, with the International Consultation on Incontinence Questionnaire - Urinary Incontinence Short Form (ICIQ-SF), at a confidence level of 95%. Also, the patient satisfaction with treatment was reported through an ordinal scale. RESULTS: ICIQ-SF median score was 11 before treatment and 3 after 6 months, with a significant difference per patient (p<0.001). 78.6% (n=33) reported improvement and 38.1% (n=16), a complete healing of SUI at follow up. 66.7% (n=28) reported high satisfaction and 81.8% (n=27) of sexually active women, also reported improvement of sexual gratification. Only mild pain during the procedure was reported as adverse effect. CONCLUSIONS: on this short-term pilot study, non-ablative Er:YAG laser procedure seems to be a safe and efficacious alternative for patients with SUI. Further controlled studies will help to validate the use of non-ablative Er:YAG for treatment of SUI.

MEDICINA FÍSICA Y REHABILITACIÓN

J CRIT CARE. 2017 FEB;37:85-90.

OCCUPATIONAL THERAPY FOR DELIRIUM MANAGEMENT IN ELDERLY PATIENTS WITHOUT MECHANICAL VENTILATION IN AN INTENSIVE CARE UNIT: A PILOT RANDOMIZED CLINICAL TRIAL.

Álvarez EA, Garrido MA, Tobar EA, Prieto SA, Vergara SO, Briceño CD, González FJ.

PURPOSE: Delirium has negative consequences such as increased mortality, hospital expenses and decreased cognitive and functional status. This research aims to determine the impact of occupational therapy intervention in duration, incidence and severity of delirium in elderly patients in the intensive care unit; secondary outcome was to assess functionality at hospital discharge. METHODS: This is a pilot randomized clinical trial of patients without mechanical ventilation for 60 years. Patients were assigned to a control group that received standard strategies of prevention (n=70) or to an experimental group that received standard strategies plus occupational therapy twice a day for 5 days (n=70). Delirium was valued with Confusion Assessment Method and Delirium Rating Scale, and functional outcomes at discharge with Functional Independence Measure, Hand Dynamometer, and Mini-Mental State Examination. RESULTS: A total of 140 participants were recruited. The experimental group had lower duration (risk incidence ratios, 0.15 [P=.000; 95% confidence interval, 0.12-0.19] vs 6.6 [P=.000, 95% confidence interval, 5.23-8.3]) and incidence of delirium (3% vs 20%, P=.001), and had higher scores in Motor Functional Independence Measure (59 vs 40 points, P<.0001), cognitive state (MMSE: 28 vs 26 points, P<.05), and grip strength in the dominant hand (26 vs 18 kg, P<.05), compared with the control group. CONCLUSIONS: Occupational therapy is effective in decreasing duration and incidence of delirium in nonventilated elderly patients in the intensive care unit and improved functionality at discharge.

DEPARTAMENTO DE CIRUGÍA

J CRANIOMAXILLOFAC SURG. 2016 OCT;44(10):1635-1640.

A NEW APPROACH TO NASOSEPTAL FRACTURES: SUBMUCOSAL ENDOSCOPICALLY ASSISTED SEPTOPLASTY AND CLOSED NASAL REDUCTION.

Andrades P, Pereira N, Borel C, Rocha L, Hernández R, Villalobos R.

BACKGROUND: Nasal bone fracture is the most common among facial bone fractures. The prevalence of concomitant septal and nasal bone fractures fluctuates between 34% and 96.2%. An adequate management of such fractures is essential to prevent complications such as post-traumatic nasal obstruction and nasoseptal deformities. The purpose of the present study is to introduce the submucosal endoscopically assisted septoplasty (SEAS) as an alternative approach for acute septal lesions and to report our experience and outcomes. **METHODS:** Retrospective review including patients with nasal fracture in association with septal fracture (nasoseptal fractures) who underwent to submucosal endoscopically assisted septoplasty and closed nasal reduction. The surgical technique is described and a video is presented. **RESULTS:** Ninety patients were included; 23% were female and 77% were male, with a mean age of 40 years. All the cases were workplace accidents or commuting accidents. The mean time elapsed between the accident and surgery was 15 days. There were no technique-related intraoperative complications. Three (3.3%) patients suffered a subsequent nasal obstruction and/or deviation of the nasal axis, requiring subsequent secondary open rhinoseptoplasty. **CONCLUSIONS:** Submucosal endoscopically assisted septoplasty and closed nasal reduction for the treatment of nasoseptal fractures is a novel approach that reduces the rate of secondary rhinoseptoplasty as compared to other authors' reports. The technique described is reproducible, cost-effective and has very encouraging outcomes.

EAT WEIGHT DISORD. 2016 AUG 23.

MEDICAL COMORBIDITY OF BINGE EATING DISORDER.

Olguin P, Fuentes M, Gabler G, Guerdjikova AI, Keck PE Jr, McElroy SL.

PURPOSE: To gain further understanding of the general medical comorbidity of binge eating disorder (BED) beyond its association with obesity. **METHOD:** We reviewed studies of general medical comorbidity in people with BED or clinically significant binge eating behavior beyond obesity. We also reviewed studies of BED in specific medical conditions. **RESULTS:** Three broad study categories of medical comorbidity in BED were found: cross-sectional studies of medical conditions in BED; prospective studies of medical conditions in BED; and studies of BED in specific medical conditions. Cross-sectional epidemiologic data suggest that BED is associated with medical conditions related to obesity, including diabetes, hypertension, dyslipidemias, sleep problems/disorders, and pain conditions, and that BED may be related to these conditions independent of obesity and co-occurring psychiatric disorders. Prospective data suggest that BED may be associated with type 2 diabetes and metabolic syndrome. BED or binge eating behavior is also associated with asthma and gastrointestinal symptoms and disorders, and among women, menstrual dysfunction, pregnancy complications, intracranial hypertension, and polycystic ovary syndrome. **CONCLUSIONS:** BED is associated with substantial medical comorbidity beyond obesity. Further study of the general medical comorbidity of BED and its relationship to obesity and co-occurring psychiatric disorders is greatly needed.

AESTHETIC PLAST SURG. 2016 FEB;40(1):19-29.

INTRODUCING THE BODY-QOL®: A NEW PATIENT-REPORTED OUTCOME INSTRUMENT FOR MEASURING BODY SATISFACTION-RELATED QUALITY OF LIFE IN AESTHETIC AND POST-BARIATRIC BODY CONTOURING PATIENTS.

Danilla S, Cuevas P, Aedo S, Dominguez C, Jara R, Calderón ME, Al-Himdani S, Rios MA, Taladriz C, Rodriguez D, Gonzalez R, Lazo Á, Erazo C, Benitez S, Andrades P, Sepúlveda S.

OBJECTIVE: To develop a new patient-reported outcome instrument (PRO) to measure body-related satisfaction quality of life (QoL). **METHODS:** Standard 3-phase PRO design was followed; in the first phase, a qualitative design was used in 45 patients to develop a conceptual framework and to create preliminary scale domains and items. In phase 2, large-scale population testing on 1340 subjects was performed to reduce items and domains. In phase 3, final testing of the developed instrument on 34 patients was performed. Statistics used include Factor, RASCH, and multivariate regression analysis. Psychometric properties measured were internal reliability, item-rest, item-test, and test-retest correlations. **RESULTS:** The PRO-developed instrument is composed of four domains (satisfaction with the abdomen, sex life, self-esteem and social life, and physical symptoms) and 20 items in total. The score can range from 20 (worst) to 100 (best). Responsiveness was 100 %, internal reliability 93.3 %, and test-retest concordance 97.7 %. Body image-related QoL was superior in men than women ($p < 0.001$) and decreased with increasing age ($p = 0.004$)

and BMI ($p < 0.001$). Post-bariatric body contouring patients score lower than cosmetic patients in all domains of the Body-QoL instrument ($p < 0.001$). After surgery, the score improves by on average 21.9 ± 16.9 (effect size 1.8, $p < 0.001$). CONCLUSIONS: Body satisfaction-related QoL can be measured reliably with the Body-QoL instrument. It can be used to quantify the improvement in cosmetic and post-bariatric patients including non- or minimally invasive procedures, suction assisted lipectomy, abdominoplasty, lipoabdominoplasty, and lower body lift and to give an evidence-based approach to standard practice.

OBES SURG. 2016 JUL;26(7):1622-6.

PATIENTS HAVING BARIATRIC SURGERY: SURGICAL OPTIONS IN MORBIDLY OBESE PATIENTS WITH BARRETT'S ESOPHAGUS.

Braghetto I, Csendes A.

This article summarizes the currently knowledge and results observed in patients with obesity and Barrett's esophagus which were presented and discussed during the IFSO 2014 held in Montreal. In this meeting, the surgical options for the management after bariatric surgery were discussed. For this purpose, a complete revision of the available literature was done including Pubmed, Medline, Scielo database, own experience, and experts opinion. A total of 49 publications were reviewed and included in the present paper. The majority of authors agree that gastric bypass is the procedure of choice. Sleeve gastrectomy is not an absolute contraindication. Up to now, gastric bypass appears to be the best procedure for treatment of obese patients with Barrett's esophagus. Future investigations should give the definitive consensus.

TOXICON. 2016 SEP 1;119:180-5.

GONYAUTOXINS: FIRST EVIDENCE IN PAIN MANAGEMENT IN TOTAL KNEE ARTHROPLASTY.

Hinzpeter J, Barrientos C, Zamorano Á, Martínez Á, Palet M, Wulf R, Barahona M, Sepúlveda JM, Guerra M, Bustamante T, Del Campo M, Tapia E, Lagos N.

Improvements in pain management techniques in the last decade have had a major impact on the practice of total knee arthroplasty (TKA). Gonyautoxin are phycotoxins, whose molecular mechanism of action is a reversible block of the voltage-gated sodium channels at the axonal level, impeding nerve impulse propagation. This study was designed to evaluate the clinical efficacy of Gonyautoxin infiltration, as a long acting pain blocker in TKA. Fifteen patients received a total dose of 40 µg of Gonyautoxin during the TKA operation. Postoperatively, all patients were given a standard painkiller protocol: 100 mg of intravenous ketoprofen and 1000 mg of oral acetaminophen every 8 hours for 3 days. The Visual Analog Scale (VAS) pain score and range of motion were recorded 12, 36, and 60 hours post-surgery. All patients reported pain of 2 or less on the VAS 12 and 36 hours post-surgery. Moreover, all scored were less than 4 at 60 hours post-surgery. All patients achieved full knee extension at all times. No side effects or adverse reactions to Gonyautoxin were detected in the follow-up period. The median hospital stay was 3 days. For the first time, this study has shown the effect of blocking the neuronal transmission of pain by locally infiltrating Gonyautoxin during TKA. All patients successfully responded to the pain control. The Gonyautoxin infiltration was safe and effective, and patients experienced pain relief without the use of opioids.

AESTHETIC PLAST SURG. 2016 FEB;40(1):149-56.

RELIABILITY OF NASOFACIAL ANALYSIS USING RHINOBASE® SOFTWARE.

Meruane M, Ayala MF, García-Huidobro MA, Andrades P.

OBJECTIVE: Rhinoplasty is a constant challenge for the surgeon, where the correct evaluation of facial aesthetic parameters allows harmonic changes appropriate for each patient. The aim of this study was to compare the preoperative and postoperative results of nasofacial analysis, performed by Rhinobase® software (indirect anthropometry) compared with direct anthropometry (caliper), in patients undergoing aesthetic rhinoplasty. METHODS: The authors assessed the reliability of using Rhinobase® software for measuring nasofacial characteristics in 20 individuals (18 F, 2 M). In each patient, the nasofacial analysis was performed before and after surgery. Two raters performed indirect anthropometry on each image on two separate occasions. RESULTS: Intrarater and interrater reliability for most indirect anthropometric measurements had intraclass correlation coefficients greater than 0.8. Regarding intermethod reliability, Pearson correlation coefficients ranged from 0.6 to 0.9 for most measurements. The highest correlation was found in interalar width, chin vertical, and lower facial height. The Cronbach's

α coefficient calculated for all measurements was 0.8. CONCLUSIONS: The Rhinobase® software is an easy and safe method for facial analysis. This study provides evidence of high reliability for several nasofacial measurements. The nasofacial analysis allows an accurate preoperative evaluation, surgical planning, and analysis of outcomes in rhinoplasty and may be a useful tool for both novice and experienced surgeons. LEVEL OF EVIDENCE IV: This journal requires that authors assign a level of evidence to each article.

OBES SURG. 2016 FEB;26(2):361-8.

MICRONUTRIENT DEFICIENCIES IN MORBIDLY OBESE WOMEN PRIOR TO BARIATRIC SURGERY.

Sánchez A, Rojas P, Basfi-Fer K, Carrasco F, Inostroza J, Codoceo J, Valencia A, Papapietro K, Csendes A, Ruz MO.

BACKGROUND: Although morbid obesity is related to excess of energy and macronutrient intake, it does not rule out the presence of micronutrient deficiencies. The aim of this study was to evaluate food intake and the prevalence of micronutrient deficiencies in a group of morbidly obese women seeking bariatric surgery. METHODS: A total of 103 morbidly obese women were studied prior to bariatric surgery. Anthropometry and body composition (dual-energy X-ray absorptiometry, DEXA) were performed on all subjects. Energy and nutrient intake was determined by food frequency questionnaire. Blood tests to assess micronutrients status, including plasma iron, ferritin, transferrin, zinc, copper, calcium, phosphorus, hemoglobin, hematocrit, mean corpuscular volume (MCV), and hair zinc, were performed. Folic acid, vitamin B12, vitamin D, and parathyroid hormone (PTH) were also assessed in 66 subjects. RESULTS: Mean energy intake was 2801 ± 970 kcal/day. Carbohydrate, protein, and lipid intake represented 55 ± 9.1 , 13.9 ± 3.3 , and $32.5 \pm 8.2\%$ of total energy intake, respectively. Iron, calcium, and vitamin D intake was below the recommended dietary allowance. The prevalence of nutritional deficiencies were as follows: plasma iron 12.6%, ferritin 8.7%, transferrin 14.6%, plasma zinc 2.9%, calcium 3.3%, phosphorus 2.3%, hemoglobin 7.7%, hematocrit 13.6%, MCV 6.8%, and hair zinc 15.7%. In the subsample, 10.6% had a vitamin B12 deficiency, 71.7% showed low concentrations of vitamin D, and 66% had high PTH levels. No folic acid or copper deficiencies were detected. CONCLUSIONS: Despite high daily energy intake and adequate macronutrient distribution, morbidly obese Chilean women seeking bariatric surgery present with deficient intake of some micronutrients and a high prevalence of micronutrient deficiencies.

J PLAST RECONSTR AESTHET SURG. 2016 JUN;69(6):848-55.

THE ACCURACY OF DIFFERENT METHODS FOR DIAGNOSING SEPTAL DEVIATION IN PATIENTS UNDERGOING SEPTORHINOPLASTY: A PROSPECTIVE STUDY.

Andrades P, Cuevas P, Danilla S, Bernales J, Longton C, Borel C, Hernández R, Villalobos R.

OBJECTIVE: This study aimed to determine the diagnostic accuracy of different diagnostic tests in predicting nasal septum deformities during preoperative planning for septorhinoplasty. METHODS: Consecutive patients who underwent septorhinoplasty between June 2011 and August 2012 were included ($n = 30$) and underwent a protocol of diagnostic tests, including nasal speculoscopy, craniofacial computed tomography (CT), three-dimensional (3D) reconstruction of the nasal septum by CT and nasal endoscopy. A modified Guyuron classification of septal deformities was used for classifying the septal deviations. Direct surgical assessment of the nasal septum during open septorhinoplasty was the reference standard with which each of the diagnostic tests was compared. Sensitivity, specificity and predictive values of each test were calculated. RESULTS: The preoperative diagnosis was nasal bone fracture in 11 patients, nasal septal fracture in 15 and post-traumatic nasal deformity in four. For type A deviations (localised), craniofacial CT showed the highest performance with a sensitivity of 100%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 99%. For type B septal deformations (C shape), nasal endoscopy (sensitivity, 100%; specificity, 87.5%; PPV, 87.7%; and NPV, 100%) showed the highest performance. For type C deformities (S shape), nasal endoscopy (sensitivity, 70%; specificity, 100%; PPV, 100%; and NPV, 87%) showed the highest performance. The accuracy for nasal endoscopy was 27/30 (90%), 26/30 (87%) for craniofacial CT, 22/30 (73%) for 3D reconstruction and 10/28 (36%) for speculoscopy. CONCLUSIONS: Nasal endoscopy and craniofacial CT were more accurate and precise than nasal speculoscopy and 3D reconstruction for preoperative evaluation of the nasal septum, thus enabling more appropriate surgical planning for septorhinoplasty.

OAIC

J AM ACAD DERMATOL. 2016 OCT;75(4):760-7.

COLOR DOPPLER ULTRASOUND ASSESSMENT OF MORPHOLOGY AND TYPES OF FISTULOUS TRACTS IN HIDRADENITIS SUPPURATIVA (HS).

Wortsman X, Castro A, Figueroa A.

BACKGROUND: Fistulous tracts in hidradenitis suppurativa (HS) are key signs of severity and their clinical evaluation alone may be limited for assessing their presence and morphology. There is also a need to determine the factors that allow reversibility of the anatomic changes in HS. **OBJECTIVE:** We sought to categorize fistulous tracts in HS. **METHODS:** A retrospective study of color Doppler ultrasound images of cases with positive clinical and sonographic criteria of HS with fistulous tracts was performed. The sonographic staging of HS, location, and anatomic characteristics of the tracts were registered and graded. Statistical analysis for correlating variables was performed using bivariate and multivariate studies. **RESULTS:** In all, 52 patients presenting 96 fistulous tracts met the criteria. Morphology was defined and a sonographic classification into 3 types of fistulae was developed. Type 3 concentrated 71% of the cases presenting communicating tracts, and type 2, 29%. Types 2 and 3 represented 63% of patients with multiple fistulous tracts. Fistulous tracts types 2 and 3 were significantly correlated with age 35 years or older and groin location. **LIMITATIONS:** Ultrasound cannot detect lesions less than 0.1 mm. **CONCLUSION:** Fistulous tracts in HS can be categorized using ultrasound, which may support earlier and more precise management.

UNIDAD DE PACEINTES CRÍTICOS

CRIT CARE. 2016 AUG 2;20(1):234.

EFFECTS OF DEXMEDETOMIDINE AND ESMOLOL ON SYSTEMIC HEMODYNAMICS AND EXOGENOUS LACTATE CLEARANCE IN EARLY EXPERIMENTAL SEPTIC SHOCK.

Hernández G, Tapia P, Alegría L, Soto D, Luengo C, Gomez J, Jarufe N, Achurra P, Rebolledo R, Bruhn A, Castro R, Kattan E, Ospina-Tascón G, Bakker J.

BACKGROUND: Persistent hyperlactatemia during septic shock is multifactorial. Hypoperfusion-related anaerobic production and adrenergic-driven aerobic generation together with impaired lactate clearance have been implicated. An excessive adrenergic response could contribute to persistent hyperlactatemia and adrenergic modulation might be beneficial. We assessed the effects of dexmedetomidine and esmolol on hemodynamics, lactate generation, and exogenous lactate clearance during endotoxin-induced septic shock. **METHODS:** Eighteen anesthetized and mechanically ventilated sheep were subjected to a multimodal hemodynamic/perfusion assessment including hepatic and portal vein catheterizations, total hepatic blood flow, and muscle microdialysis. After monitoring, all received a bolus and continuous infusion of endotoxin. After 1 h they were volume resuscitated, and then randomized to endotoxin-control, endotoxin-dexmedetomidine (sequential doses of 0.5 and 1.0 µg/k/h) or endotoxin-esmolol (titrated to decrease basal heart rate by 20 %) groups. Samples were taken at four time points, and exogenous lactate clearance using an intravenous administration of sodium L-lactate (1 mmol/kg) was performed at the end of the experiments. **RESULTS:** Dexmedetomidine and esmolol were hemodynamically well tolerated. The dexmedetomidine group exhibited lower epinephrine levels, but no difference in muscle lactate. Despite progressive hypotension in all groups, both dexmedetomidine and esmolol were associated with lower arterial and portal vein lactate levels. Exogenous lactate clearance was significantly higher in the dexmedetomidine and esmolol groups. **CONCLUSIONS:** Dexmedetomidine and esmolol were associated with lower arterial and portal lactate levels, and less impairment of exogenous lactate clearance in a model of septic shock. The use of dexmedetomidine and esmolol appears to be associated with beneficial effects on gut lactate generation and lactate clearance and exhibits no negative impact on systemic hemodynamics.

ANATOMÍA PATOLÓGICA

ORAL DIS. 2016 OCT;22(7):703-8.

MTHFR C.677C>T IS A RISK FACTOR FOR NON-SYNDROMIC CLEFT LIP WITH OR WITHOUT CLEFT PALATE IN CHILE.

Ramírez-Chau C, Blanco R, Colombo A, Pardo, Suazo J.

OBJECTIVE: The functional variant within the 5,10-methylenetetrahydrofolate reductase (MTHFR) gene c.677C>T, producing alterations in folate metabolism, has been associated with the risk of non-syndromic cleft lip with or without cleft palate

(NSCL/P). We assessed this association in a Chilean population using a combined analysis of case-control and case-parent trio samples. SUBJECTS AND METHODS: Samples of 165 cases and 291 controls and 121 case-parent trios (sharing the cases) were genotyped. Odds ratio (OR) was estimated for case-control (allele and genotype frequency differences), and this result was confirmed by allele transmission distortion in trios. Due to that these samples are not independent, a combined OR was also computed. Maternal genotype effect was additionally evaluated based on a log-linear method. RESULTS: Borderline but not significant OR (1.28; CI 0.97-1.69) was observed for risk allele (T) in the case-control sample. However, triad sample showed a significant association (OR 1.56; CI 1.09-2.25) which was confirmed by the combined OR (1.37; CI 1.11-1.71). Maternal genotype has been also associated with the phenotype (P = 0.002). CONCLUSIONS: In contrast to previous reports considering Chilean subjects, our results demonstrated that the offspring and maternal genotypes for MTHFR c.677C>T variant are strongly associated with NSCL/P in this Chilean population.

BIRTH DEFECTS RES A CLIN MOL TERATOL. 2016 OCT;106(10):814-830.

INHIBITION OF THE 3-HYDROXY-3-METHYL-GLUTARYL-COA REDUCTASE INDUCES OROFACIAL DEFECTS IN ZEBRAFISH.

Signore IA, Jerez C, Figueroa D, Suazo J, Marcelain K, Cerda O, Colombo Flores A.

BACKGROUND: Orofacial clefts (OFCs) are common birth defects, which include a range of disorders with a complex etiology affecting formation of craniofacial structures. Some forms of syndromic OFCs are produced by defects in the cholesterol pathway. The principal enzyme of the cholesterol pathway is the 3-hydroxy-3-methyl-glutaryl-CoA reductase (HMGCR). Our aim is to study whether defects of HMGCR function would produce orofacial malformation similar to those found in disorders of cholesterol synthesis. METHODS: We used zebrafish *hmgcrb* mutants and HMGCR inhibition assay using atorvastatin during early and late stages of orofacial morphogenesis in zebrafish. To describe craniofacial phenotypes, we stained cartilage and bone and performed in situ hybridization using known craniofacial markers. Also, we visualized neural crest cell migration in a transgenic fish. RESULTS: Our results showed that mutants displayed loss of cartilage and diminished orofacial outgrowth, and in some cases palatal cleft. Late treatments with statin show a similar phenotype. Affected-siblings displayed a moderate phenotype, whereas early-treated embryos had a minor cleft. We found reduced expression of the downstream component of Sonic Hedgehog-signaling *gli1* in ventral brain, oral ectoderm, and pharyngeal endoderm in mutants and in late atorvastatin-treated embryos. CONCLUSION: Our results suggest that HMGCR loss-of-function primarily affects postmigratory cranial neural crest cells through abnormal Sonic Hedgehog signaling, probably induced by reduction in metabolites of the cholesterol pathway. Malformation severity correlates with the grade of HMGCR inhibition, developmental stage of its disruption, and probably with availability of maternal lipids. Together, our results might help to understand the spectrum of orofacial phenotypes found in cholesterol synthesis disorders.

ACTAS UROL ESP. 2016 AUG 2. PII: S0210-4806(16)30111-5.

ADIPOCYTE ACCUMULATION IN CORPUS CAVERNOSUM: FIRST CLINICAL EVIDENCE AND PATHOPHYSIOLOGICAL IMPLICATIONS IN ERECTILE DYSFUNCTION.

Vinay J, Sarquella J, Sanchez J, Algaba F, Gallegos I, Ruiz-Castañe E, Palma C.

OBJECTIVES: Animal models have shown that erectile dysfunction is associated with adipocyte accumulation under tunica albuginea, which could be involved in venous leakage and loss of penile rigidity. In the current study, we compared the histology of the penile sub-albuginean region of drug-refractory erectile dysfunction patients undergoing penile prosthesis implantation with potent patients with Peyronie's disease undergoing curvature correction procedures. MATERIALS AND METHODS: Seventeen refractory erectile dysfunction patients and fourteen potent patients with Peyronie's disease were recruited. Sub-albuginean tissue samples were taken in each surgery. An expert uropathologist analysed each section. A bivariate analysis was performed. Multivariate logistic regression was used to calculate adjusted odds ratios; P value < .05 was considered significant. RESULTS: Eleven patients (11/17) in the case group presented cavernous fat cell accumulation, while only one patient (1/14) in the control group presented this finding (P < .05). Adjusted odds ratio for erectile dysfunction was 40.72; 95% CI 2.28-727.29 (P = .012). CONCLUSIONS: Different studies have shown that androgen disruption could be involved in penile structural changes, leading to trabecular smooth muscle apoptosis and trans or de-differentiation into adipocytes. This is the first prospective study in humans to report an association between erectile dysfunction and sub-albuginean adipocyte accumulation. Venous leakage secondary to this phenomenon could be a factor in the pathophysiology of erectile dysfunction, especially in patients that do not respond to medical therapy.

EMBO J. 2016 APR 15;35(8):845-65.

ALS-LINKED PROTEIN DISULFIDE ISOMERASE VARIANTS CAUSE MOTOR DYSFUNCTION.

Woehlbier U, Colombo A, Saaranen MJ, Pérez V, Ojeda J, Bustos FJ, Andreu CI, Torres M, Valenzuela V, Medinas DB, Rozas P, Vidal RL, Lopez-Gonzalez R, Salameh J, Fernandez-Collemani S, Muñoz N, Matus S, Armisen R, Sagredo A, Palma K, Irrazabal T, Almeida S, Gonzalez-Perez P, Campero M, Gao FB, Henny P, van Zundert B, Ruddock LW, Concha ML, Henriquez JP, Brown RH, Hetz C.

Disturbance of endoplasmic reticulum (ER) proteostasis is a common feature of amyotrophic lateral sclerosis (ALS). Protein disulfide isomerases (PDIs) are ER foldases identified as possible ALS biomarkers, as well as neuroprotective factors. However, no functional studies have addressed their impact on the disease process. Here, we functionally characterized four ALS-linked mutations recently identified in two major PDI genes, PDIA1 and PDIA3/Erp57. Phenotypic screening in zebrafish revealed that the expression of these PDI variants induce motor defects associated with a disruption of motoneuron connectivity. Similarly, the expression of mutant PDIs impaired dendritic outgrowth in motoneuron cell culture models. Cellular and biochemical studies identified distinct molecular defects underlying the pathogenicity of these PDI mutants. Finally, targeting Erp57 in the nervous system led to severe motor dysfunction in mice associated with a loss of neuromuscular synapses. This study identifies ER proteostasis imbalance as a risk factor for ALS, driving initial stages of the disease.

ENDOCRINOLOGÍA

AM J THER. 2016 JAN-FEB;23(1):E159-71.

DIABETES AND QUALITY OF LIFE: INITIAL APPROACH TO DEPRESSION, PHYSICAL ACTIVITY, AND SEXUAL DYSFUNCTION.

Pozzo MJ, Mociulsky J, Martinez ET, Senatore G, Farias JM, Sapetti A, Sanzana MG, Gonzalez P, Cafferata A, Peloché A, Lemme L.

The different aspects that contribute to quality of life in patients with diabetes mellitus, such as mood, are of great importance for the treatment of this disease. These aspects not only influence the well-being of patients but also influence treatment adherence, therefore affecting the course of the disease. A panel of experts from Argentina, Chile, and Uruguay performed a review of the main aspects affecting quality of life in patients with diabetes: physical activity, mood disorders, and sexual activity. The consensus of the panel was that physical activity is important in the treatment of patients with diabetes because it reduces morbidity, mortality, and disease complications, and it should be performed on a regular basis, bearing in mind the patient's characteristics. Increased physical activity is associated with better glycemic control, and in individuals with glucose intolerance, it delays progression toward diabetes. In patients with diabetes, there is a high prevalence of depression, which can influence treatment adherence. Therefore, early detection of depression is essential to improve the course of diabetes. Regarding sexual activity, erectile dysfunction may be a significant sign in the case of suspected diabetes and the early diagnosis of vasculopathy in patients with diabetes. In conclusion, greater emphasis should be placed on improving patient knowledge, early detection, and multidisciplinary approaches to deal with the aspects of diabetes that affect patients' quality of life.

GASTROENTEROLOGÍA

J PEDIATR GASTROENTEROL NUTR. 2016 JUN 24.

PROTEIN MALNUTRITION DURING JUVENILE AGE INCREASES ILEAL AND COLONIC PERMEABILITY IN THE RAT.

Eyzaguirre-Velásquez J, Olavarría-Ramírez L, González-Arancibia C, Díaz-Merino C, Ariz R, López S, Quiroz W, Beltrán CJ, Bravo JA, Julio-Pieper M.

Protein malnutrition can lead to morphological and functional changes in jejunum and ileum, affecting permeability to luminal contents. Regarding the large intestine, data is scarce, especially at juvenile age. We investigated whether low-protein (LP) diet could modify ileal and colonic permeability and epithelial morphology in young rats. Isocaloric diets containing 26% (control diet) or 4% protein were given to male rats between postnatal days 40-60. LP-diet animals failed to gain weight and displayed decreased plasma Zinc levels (a marker of micronutrient deficiency). Additionally, transepithelial electrical resistance and Occludin expression was reduced in their ileum and colon, indicating increased gut permeability. Macromolecule transit was not modified. Finally, LP-diet induced shortening of colonic crypts without affecting muscle thickness. These data show that protein malnutrition increases not only ileum but also colon permeability in juvenile rats. Enhanced exposure to colonic luminal entities may be an additional component in the pathophysiology of protein malnutrition.

MEDIATORS INFLAMM. 2016;2016:1258504.

ATP INDUCES IL-1 β SECRETION IN NEISSERIA GONORRHOEAE-INFECTED HUMAN MACROPHAGES BY A MECHANISM NOT RELATED TO THE NLRP3/ASC/CASPASE-1 AXIS.

García K, Escobar G, Mendoza P, Beltran Z, Perez C, Arancibia S, Vernal R, Rodas PI, Acuña-Castillo C, Escobar A.

Neisseria gonorrhoeae (Ngo) has developed multiple immune evasion mechanisms involving the innate and adaptive immune responses. Recent findings have reported that Ngo reduces the IL-1 β secretion of infected human monocyte-derived macrophages (MDM). Here, we investigate the role of adenosine triphosphate (ATP) in production and release of IL-1 β in Ngo-infected MDM. We found that the exposure of Ngo-infected MDM to ATP increases IL-1 β levels about ten times compared with unexposed Ngo-infected MDM ($P < 0.01$). However, we did not observe any changes in inflammasome transcriptional activation of speck-like protein containing a caspase recruitment domain (CARD) (ASC, $P > 0.05$) and caspase-1 (CASP1, $P > 0.05$). In addition, ATP was not able to modify caspase-1 activity in Ngo-infected MDM but was able to increase pyroptosis ($P > 0.01$). Notably ATP treatment defined an increase of positive staining for IL-1 β with a distinctive intracellular pattern of distribution. Collectively, these data demonstrate that ATP induces IL-1 β secretion by a mechanism not related to the NLRP3/ASC/caspase-1 axis and likely is acting at the level of vesicle trafficking or pore formation.

J NEUROGASTROENTEROL MOTIL. 2016 SEP 26.

CHRONIC INTESTINAL PSEUDO-OBSTRUCTION: CLINICAL AND MANOMETRIC CHARACTERISTICS IN THE CHILEAN POPULATION.

Pérez de Arce E, Landskron G, Hirsch S, Defilippi C, Madrid AM.

BACKGROUND/AIMS: Chronic intestinal pseudo-obstruction (CIPO) is a rare syndrome characterized by a failure of the propulsion of intraluminal content and recurrent symptoms of partial bowel obstruction in the absence of mechanical obstruction. Regional variations of the intestinal compromise have been described. Intestinal manometry can indicate the pathophysiology and prognosis. Our objective is to establish the demographic and clinical characteristics of group Chilean patients and analyze the motility of the small intestine and its prognostic value. **METHODS:** Patients with symptoms of intestinal pseudo-obstruction with dilated bowel loops were included, in all of whom a manometry of the small intestine was performed using perfused catheters. **RESULTS:** Of the 64 patients included, 51 women (average age 41.5 ± 17.6 years), 54 primary and 10 secondary CIPO were included. Dilatation of the small intestine was the only finding in 38 patients; in the remaining, the compromise was associated with other segments, primarily colon. 49 patients underwent 65 surgeries mainly exploratory laparotomies and colectomies. Intestinal manometry was performed on all patients; 4 "patterns" were observed: neuropathic ($n = 26$), myopathic ($n = 3$), mixed ($n = 24$), and a group without motor activity ($n = 11$). The most relevant findings were the complex migrating motor disorders and decreased frequency and propagation of contractions. The 9 patients who died had a severe myopathic compromise. **CONCLUSIONS:** In our series, isolated small bowel compromise was the most common disorder. Neuropathic motor compromise was observed in most of the patients. Mortality was associated with severe myopathic compromise.

LIVER INT. 2016 NOV;36(11):1657-1667.

LIVER TRANSPLANTATION FOR HEPATOCELLULAR CARCINOMA: EVALUATION OF THE ALPHA-FETOPROTEIN MODEL IN A MULTICENTER COHORT FROM LATIN AMERICA.

Piñero F, Tisi Baña M, de Ataide EC, Hoyos Duque S, Marciano S, Varón A, Anders M, Zerega A, Menéndez J, Zapata R, Muñoz L, Padilla Machaca M, Soza A, McCormack L, Poniachik J, Podestá LG, Gadano A, Boin IS, Duvoux C, Silva M; Latin American Liver Research, Education and Awareness Network (LALREAN).

BACKGROUND & AIMS: The French alpha-fetoprotein (AFP) model has recently shown superior results compared to Milan criteria (MC) for prediction of hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) in European populations. The aim of this study was to explore the predictive capacity of the AFP model for HCC recurrence in a Latin-American cohort. **METHODS:** Three hundred twenty-seven patients with HCC were included from a total of 2018 patients transplanted at 15 centres. Serum AFP and imaging data were both recorded at listing. Predictability was assessed by the Net Reclassification Improvement (NRI) method. **RESULTS:** Overall, 82 and 79% of the patients were within MC and the AFP model respectively. NRI showed a superior predictability of the AFP model against MC. Patients with an AFP score >2 points had higher risk of recurrence at 5 years Hazard Ratio (HR) of 3.15 ($P = 0.0001$) and lower patient survival (HR = 1.51; $P = 0.03$). Among patients exceeding MC, a score ≤ 2 points identified a subgroup of patients with lower recurrence (5% vs 42%; $P = 0.013$) and higher survival rates (84% vs 45%; P

= 0.038). In cases treated with bridging procedures, following restaging, a score >2 points identified a higher recurrence (HR 2.2, P = 0.12) and lower survival rate (HR 2.25, P = 0.03). A comparative analysis between HBV and non-HBV patients showed that the AFP model performed better in non-HBV patients. CONCLUSIONS: The AFP model could be useful in Latin-American countries to better select patients for LT in subgroups presenting with extended criteria. However, particular attention should be focused on patients with HBV.

CLIN TRANSL GASTROENTEROL. 2016 APR 7;7:E161.

IMPACT OF DIETARY LIPIDS ON COLONIC FUNCTION AND MICROBIOTA: AN EXPERIMENTAL APPROACH INVOLVING ORLISTAT-INDUCED FAT MALABSORPTION IN HUMAN VOLUNTEERS.

Morales P, Fujio S, Navarrete P, Ugalde JA, Magne F, Carrasco-Pozo C, Tralma K, Quezada M, Hurtado C, Covarrubias N, Brignardello J, Henriquez D, Gotteland M.

OBJECTIVES: High-fat diets alter gut microbiota and barrier function, inducing metabolic endotoxemia and low-grade inflammation. Whether these effects are due to the high dietary lipid content or to the concomitant decrease of carbohydrate intake is unclear. The aim of this study was to determine whether higher amounts of dietary fat reaching the colon (through orlistat administration) affect the colonic ecosystem in healthy volunteers and the effect of the prebiotic oligofructose (OF) in this model. METHODS: Forty-one healthy young subjects were distributed among four groups: Control (C), Prebiotic (P), Orlistat (O), and Orlistat/Prebiotic (OP). They consumed a fat-standardized diet (60 g/day) during Week-1 (baseline) and after 1 week of washout, Week-3. During Week-3, they also received their respective treatment (Orlistat: 2 × 120 mg/day, OF: 16 g/day, and maltodextrin as placebo). A 72-h stool collection was carried out at the end of Week-1 (T0) and Week-3 (T1). Fecal fat, calprotectin, and short-chain fatty acids (SCFAs) as well as the antioxidant activity of fecal waters (ferric-reducing antioxidant power), fecal microbiota composition (by deep sequencing), and gut permeability (Sucralose/Lactulose/Mannitol test) were determined at these times. RESULTS: Fecal fat excretion was higher in the O (P=0.0050) and OP (P=0.0069) groups. This event was accompanied, in the O group, by an increased calprotectin content (P=0.047) and a decreased fecal antioxidant activity (P=0.047). However, these alterations did not alter gut barrier function and the changes observed in the composition of the fecal microbiota only affected bacterial populations with low relative abundance (<0.01%); in consequences, fecal SCFA remained mainly unchanged. Part of the colonic alterations induced by orlistat were prevented by OF administration. CONCLUSIONS: In the context of an equilibrated diet, the acute exposition of the colonic ecosystem to high amounts of dietary lipids is associated with an incremented excretion of fecal calprotectin and pro-oxidant activity of the colonic content, in the absence of significant changes in the microbiota.

ARCH VIROL. 2016 MAR;161(3):583-94.

REPLICATION OF A CHRONIC HEPATITIS B VIRUS GENOTYPE F1b CONSTRUCT.

Hernández S, Jiménez G, Alarcón V, Prieto C, Muñoz F, Riquelme C, Venegas M, Brahm J, Loyola A, Villanueva RA.

Genotype F is one of the less-studied genotypes of human hepatitis B virus, although it is widely distributed in regions of Central and South American. Our previous studies have shown that HBV genotype F is prevalent in Chile, and phylogenetic analysis of its full-length sequence amplified from the sera of chronically infected patients identified it as HBV subgenotype F1b. We have previously reported the full-length sequence of a HBV molecular clone obtained from a patient chronically infected with genotype F1b. In this report, we established a system to study HBV replication based on hepatoma cell lines transfected with full-length monomers of the HBV genome. Culture supernatants were analyzed after transfection and found to contain both HBsAg and HBeAg viral antigens. Consistently, fractionated cell extracts revealed the presence of viral replication, with both cytoplasmic and nuclear DNA intermediates. Analysis of HBV-transfected cells by indirect immunofluorescence or immunoelectron microscopy revealed the expression of viral antigens and cytoplasmic viral particles, respectively. To test the functionality of the ongoing viral replication further at the level of chromatinized cccDNA, transfected cells were treated with a histone deacetylase inhibitor, and this resulted in increased viral replication. This correlated with changes posttranslational modifications of histones at viral promoters. Thus, the development of this viral replication system for HBV genotype F will facilitate studies on the regulation of viral replication and the identification of new antiviral drugs.

NANOMEDICINE (LOND). 2016 MAY;11(10):1237-51.

COPPER OXIDE NANOPARTICLES RECRUIT MACROPHAGES AND MODULATE NITRIC OXIDE, PROINFLAMMATORY CYTOKINES AND PGE2 PRODUCTION THROUGH ARGINASE ACTIVATION.

Arancibia S, Barrientos A, Torrejón J, Escobar A, Beltrán CJ5.

AIM: In the present study, we examine the effects of copper oxide nanoparticles (CuNP) on macrophage immune response and the signaling pathways involved. MATERIALS & METHODS: A peritonitis model was used to determine in vivo immune cells recruitment, while primary macrophages were used as an in vitro model for the cellular and molecular analysis. RESULTS: In vivo, CuNP induce significant macrophages recruitment to the site of injection. In vitro, in LPS-stimulated primary macrophages, the co-treatment with CuNP inhibited the production of NO in a dose-dependent manner. The mechanism underlying NO and proinflammatory cytokines inhibition was associated with an increased arginase activity. Macrophage stimulation with CuNP did not provoke any cytokine secretion; however, arginase inhibition promoted TNF α and MIP-1 β production. In addition, CuNP induced the expression of COX-2 and the production of PGE2 through arginase activation. CONCLUSION: Our results demonstrate that CuNP activate arginase and suppress macrophage innate immune response.

J NUTR BIOCHEM. 2016 JAN;27:289-98.

MOLECULAR MECHANISMS OF GASTROINTESTINAL PROTECTION BY QUERCETIN AGAINST INDOMETHACIN-INDUCED DAMAGE: ROLE OF NF- κ B AND NRF2.

Carrasco-Pozo C, Castillo RL, Beltrán C, Miranda A, Fuentes J, Gotteland M.

The aim of this study was to determine the gastrointestinal protection by quercetin against indomethacin-induced oxidative stress and inflammation, with specific interest in studying the underlying molecular mechanisms. We hypothesized that the quercetin-protective effect relies on its antioxidant and antiinflammatory properties. Rats were pretreated with quercetin (50- or 100-mg/kg, ig single dose), 30 min before INDO administration (40-mg/kg ig single dose). Caco-2 cells were treated with INDO (250 and 500 μ M) in the absence or presence of quercetin (10 μ g/ml). Quercetin prevented the decrease in nuclear translocation of Nrf2, a key regulator of the antioxidant response, and the increase in reactive oxygen species levels induced by INDO by inhibiting the enhancement of NADPH oxidase and xanthine oxidase activities as well as the reduction in superoxide dismutase and glutathione peroxidase activities in gastric and ileal tissues. Quercetin also prevented INDO-induced ICAM-1 and P-selectin expressions and the increase of myeloperoxidase activity in gastric and ileal tissues and NF- κ B activation and IL-8 production in Caco-2 cells. Quercetin did not affect the inhibition of TNF α -mediated production of prostaglandin E2 induced by INDO in Caco-2 cells. The protective effects of quercetin observed in the gastric and ileal mucosa of rats as well as in Caco-2 cells relied on the ability of this flavonol to prevent NF- κ B activation and increase Nrf2 translocation. This study supports the concept that quercetin may be useful in the prevention and/or treatment of nonsteroidal antiinflammatory drug-associated side effects, without interfering with their therapeutic efficacy.

GENÉTICA

INT J ORAL MAXILLOFAC SURG. 2016 NOV;45(11):1323-1332.

MATERNAL BIOMARKERS OF METHYLATION STATUS AND NON-SYNDROMIC OROFACIAL CLEFT RISK: A META-ANALYSIS.

Blanco R, Colombo A, Pardo R, Suazo J.

Animal models have shown evidence of the role of maternal methyl donor status and its metabolism (one-carbon metabolism) in normal embryonic maxillofacial development. Nevertheless, studies in humans have shown conflicting results for the association of maternal methylation status biomarkers in the aetiology of the main craniofacial birth defects: non-syndromic orofacial clefts (NSOFCs). The aim of this study was to perform a meta-analysis assessing the relationship between maternal levels of methylation status biomarkers (plasma and erythrocyte folates and plasma vitamin B12 and homocysteine) and the risk of NSOFCs. A literature search of the conventional and grey medical-scientific databases identified 12 studies considering these variables. Based on standardized differences between means among cases and controls (Cohen's d test), evidence was found of an association only with high plasma homocysteine (d=0.37; P=0.026) when single effects were pooled. In addition to its usefulness as a marker of poor methyl-donor intake and/or metabolism, homocysteine appears to have a teratogenic effect. Although the results are based on a relatively small number of reports and/or studies of small sample sizes showing between-study heterogeneity, these problems were resolved by including an additional analysis. Therefore these findings constitute a real contribution towards explaining the complex aetiology of orofacial clefts.

GERIATRÍA

MOL BRAIN. 2016 MAR 15;9:29.

FRIZZLED-1 RECEPTOR REGULATES ADULT HIPPOCAMPAL NEUROGENESIS.

Mardones MD, Andaur GA, Varas-Godoy M, Henriquez JF, Salech F, Behrens MI, Couve A, Inestrosa NC, Varela-Nallar L.

BACKGROUND: In the adult hippocampus new neurons are continuously generated from neural stem cells (NSCs) present at the subgranular zone of the dentate gyrus. This process is controlled by Wnt signaling, which plays a complex role in regulating multiple steps of neurogenesis including maintenance, proliferation and differentiation of progenitor cells and the development of newborn neurons. Differential effects of Wnt signaling during progression of neurogenesis could be mediated by cell-type specific expression of Wnt receptors. Here we studied the potential role of Frizzled-1 (FZD1) receptor in adult hippocampal neurogenesis. **RESULTS:** In the adult dentate gyrus, we determined that FZD1 is highly expressed in NSCs, neural progenitors and immature neurons. Accordingly, FZD1 is expressed in cultured adult hippocampal progenitors isolated from mouse brain. To evaluate the role of this receptor in vivo we targeted FZD1 in newborn cells using retroviral-mediated RNA interference. FZD1 knockdown resulted in a marked decrease in the differentiation of newborn cells into neurons and increased the generation of astrocytes, suggesting a regulatory role for the receptor in cell fate commitment. In addition, FZD1 knockdown induced an extended migration of adult-born neurons within the granule cell layer. However, no differences were observed in total dendritic length and dendritic arbor complexity between control and FZD1-deficient newborn neurons. **CONCLUSIONS:** Our results show that FZD1 regulates specific stages of adult hippocampal neurogenesis, being required for neuronal differentiation and positioning of newborn neurons into the granule cell layer, but not for morphological development of adult-born granule neurons.

HEMATOLOGÍA

ANN HEMATOL. 2017 JAN;96(1):65-72.

OBSERVATIONAL STUDY OF MULTIPLE MYELOMA IN LATIN AMERICA.

Hungria VT, Maiolino A, Martinez G, Duarte GO, Bittencourt R, Peters L, Colleoni G, Hamerschlag N, Flantl D, Navarro JR, Conte G, International Myeloma Working Group Latin America.

Relatively little is known about the outcomes of multiple myeloma in Latin America, a world region where incorporation of novel agents is generally slow. In the current retrospective-prospective study, we aimed to describe the patterns of care and treatment results in five Latin American countries. Between April 2007 and October 2009, patients who had been diagnosed from January 2005 to December 2007 were registered at 23 institutions from Argentina, Brazil, Chile, Mexico, and Peru. We divided patients into two cohorts, according to transplantation eligibility, and analyzed them with regard to first-line treatment and overall survival (OS). We analyzed a total of 852 patients, 46.9 % of whom were female. The median follow-up was 62 months. Among transplantation-ineligible patients (N=461), the mean age was 67.4 years, approximately one third of patients received a thalidomide-based treatment in the first line, and the median OS was 43.0 months. Transplantation-eligible patients (N=391) had a mean age of 54.7 years and a median OS of 73.6 months. Autologous transplantation was performed in 58.6 % of the patients for whom this procedure was initially planned and in only 26.9 % of the overall patients. Our long-term results reflect the contemporary literature for patients with multiple myeloma treated with autologous transplantation and thalidomide-based regimens in clinical trials and observational studies. However, further efforts are needed to approve and incorporate novel agents in Latin American countries, as well as to increase access to transplantation, in order to achieve the expected improvements in patient outcomes.

NEFROLOGÍA

AM J EPIDEMIOL. 2016 JUN 1;183(11):1071-3.

ASSOCIATIONS OF BLOOD PRESSURE WITH GEOGRAPHICAL LATITUDE, SOLAR RADIATION, AND AMBIENT TEMPERATURE: RESULTS FROM THE CHILEAN HEALTH SURVEY, 2009-2010.

Cabrera SE, Mindell JS, Toledo M, Alvo M, Ferro CJ.

Mean blood pressure and the prevalence of hypertension vary widely throughout the world (1). Geographical latitude has been cited as a possible explanation for this variance (2–5), with increasing distance from the equator being associated with higher blood pressures. However, these statements are often not referenced (3) or refer to data from a post-hoc analysis of the International Study of Sodium, Potassium, and Blood Pressure (INTERSALT) (2, 4), which was published as a hypothesis paper in which the

authors did not adequately report the methodology so as to allow others to assess the validity of the results (6). In other studies in which similar findings were reported, the differences observed were either explained by factors such as salt intake (7) or were confounded by other significant differences in characteristics such as renal function, diabetes prevalence, lifestyle, and diet (8–12). Ambient temperature and number of daylight hours have also been reported to affect blood pressure and the prevalence of hypertension (13–15). Chile is the longest country in the world; it runs almost perfectly north to south for 4,250 km (Web Figure 1, available at <http://aje.oxfordjournals.org/>). It also has a genetically homogeneous population. These factors combined make it an ideal country in which to study the associations of latitude, solar radiation, and ambient temperature with blood pressure

AM J MED. 2016 MAR;129(3):263-5.

THE FORTRESS BECOMES A PRISON: CALCIFIED CONSTRICTIVE PERICARDITIS.

Sanhueza ME, Torres R, Segura P, Villalobos A, Segovia E.

PRESENTATION. The pericardium, normally so useful in defending the heart from outside invaders, can perform more like a cage when its flexibility is compromised. We present the case of a 50-year-old man who was admitted to the nephrology unit when severe chronic hypotension led to poor hemodynamic tolerance during hemodialysis. He had a 24-year history of kidney disease of unknown etiology. At debut, he presented with pericardial effusion that required urgent initiation hemodialysis. In 1993, he underwent a kidney transplant. Chronic graft dysfunction evolved, and in 2010, he started hemodialysis again. His medical history included chronic liver damage secondary to venous-occlusive disease induced by azathioprine and mesenteric thrombosis managed with oral anticoagulation. In 2011, he underwent subtotal parathyroidectomy for hyperparathyroidism.

RESPIRATORIO

J MED VIROL. 2016 JUL;88(7):1173-9.

COMPARISON OF LUMINEX XTAG® RVP FAST ASSAY AND REAL TIME RT-PCR FOR THE DETECTION OF RESPIRATORY VIRUSES IN ADULTS WITH COMMUNITY-ACQUIRED PNEUMONIA.

Luchsinger V, Prades Y, Ruiz M, Pizarro R, Rossi P, Lizama L, Garmendia ML, Meza A, Larrañaga C, Avendaño LF.

Community-acquired pneumonia (CAP) is the third cause of death worldwide. Viruses are frequently detected in adult CAP. Highly sensitive diagnostic techniques should be used due to poor viral shedding. Different sampling methods can affect viral detection, being necessary to establish the optimal type of sample for identifying respiratory viruses in adults. The detection rates of respiratory viruses by Luminex xTAG® RVP fast assay, real time RT-PCR (rtRT-PCR) (Sacace®), and immunofluorescence assay (IFA) in adult CAP were performed in nasopharyngeal swabs (NPS) and aspirates (NPA) from 179 hospitalized adults. Positivity was 47.5% for Luminex®, 42.5% for rtRT-PCR ($P=0.3$), and 2.7% for IFA (2.7%) ($P<0.0$). The sensitivity, specificity, and kappa coefficient of xTAG® RVP compared with rtRT-PCR were 84.2%, 79.6%, and 0.62%, respectively. Luminex® and rtRT-PCR detected 65 (58.0%) and 57 (50.9%) viruses in 112 NPA and 35 (34.3%) and 31 (30.4%) in 102 NPS, respectively ($P<0.01$). xTAG® RVP is appropriate for detecting respiratory viruses in CAP adults. Both molecular techniques yielded better results with nasopharyngeal aspirate than swabs.

BANCO DE SANGRE

J ORAL PATHOL MED. 2016 FEB;45(2):127-35.

DENDRITIC CELL CHIMERISM IN ORAL MUCOSA OF TRANSPLANTED PATIENTS AFFECTED BY GRAFT-VERSUS-HOST DISEASE.

Pérez CA, Rabanales R, Rojas-Alcayaga G, Larrondo M, Escobar AF, López MN, Salazar-Onfray F, Alfaro JI, González FE.

OBJECTIVE: Graft-versus-host disease (GVHD) is one of the main complications after haematopoietic stem cell transplantation. Clinical features of GVHD include either an acute (aGVHD) or a chronic (cGVHD) condition that affects locations such as the oral mucosa. While the involvement of the host's dendritic cells (DCs) has been demonstrated in aGVHD, the origin (donor/host) and mechanisms underlying oral cGVHD have not been completely elucidated. In this study, we intend to determine the origin of DCs present in mucosal tissue biopsies from the oral cavity of transplanted patients affected by cGVHD. METHODS: We purified DCs, from oral biopsies of three patients with cGVHD, through immunobeads and subsequently performed DNA extraction. The origin of the obtained DCs was determined by PCR amplification of 13 informative short tandem repeat (STR) alleles. We also characterised the DCs phenotype and the inflammatory infiltrate from biopsies of two patients by immunohistochemistry. RESULTS: Clinical and histological features of the biopsies were concordant with oral cGVHD. We identified CD11c-, CD207- and

CD1a-positive cells in the epithelium and beneath the basal layer. Purification of DCs from the mucosa of patients affected by post-transplantation cGVHD was >95%. PCR-STR data analysis of DCs DNA showed that 100% of analysed cells were of donor origin in all of the evaluated patients. CONCLUSION: Our results demonstrate that resident DCs isolated from the oral tissue of allotransplanted patients affected by cGVHD are originated from the donor. Further research will clarify the role of DCs in the development and/or severity of oral cGVHD.

FRONT IMMUNOL. 2016 OCT 25;7:458. ECOLLECTION 2016.

TREATMENT WITH DEXAMETHASONE AND MONOPHOSPHORYL LIPID A REMOVES DISEASE-ASSOCIATED TRANSCRIPTIONAL SIGNATURES IN MONOCYTE-DERIVED DENDRITIC CELLS FROM RHEUMATOID ARTHRITIS PATIENTS AND CONFERS TOLEROGENTIC FEATURES.

García-González PA, Schinnerling K, Sepúlveda-Gutiérrez A, Maggi J, Hoyos L, Morales RA, Mehdi AM, Nel HJ, Soto L, Pesce B, Molina MC, Cuchacovich M, Larrondo ML, Neira Ó, Catalán DF, Hilkens CM, Thomas R, Verdugo RA, Aguilón JC.

Tolerogenic dendritic cells (ToDCs) are promising tools for therapy of autoimmune diseases, such as rheumatoid arthritis (RA). Here, we characterize monocyte-derived ToDCs from RA patients modulated with dexamethasone and activated with monophosphoryl lipid A (MPLA), referred to as MPLA-tDCs, in terms of gene expression, phenotype, cytokine profile, migratory properties, and T cell-stimulatory capacity in order to explore their suitability for cellular therapy. MPLA-tDCs derived from RA patients displayed an anti-inflammatory profile with reduced expression of co-stimulatory molecules and high IL-10/IL-12 ratio, but were capable of migrating toward the lymphoid chemokines CXCL12 and CCL19. These MPLA-tDCs induced hyporesponsiveness of autologous CD4⁺ T cells specific for synovial antigens in vitro. Global transcriptome analysis confirmed a unique transcriptional profile of MPLA-tDCs and revealed that RA-associated genes, which were upregulated in untreated DCs from RA patients, returned to expression levels of healthy donor-derived DCs after treatment with dexamethasone and MPLA. Thus, monocyte-derived DCs from RA patients have the capacity to develop tolerogenic features at transcriptional as well as at translational level, when modulated with dexamethasone and MPLA, overcoming disease-related effects. Furthermore, the ability of MPLA-tDCs to impair T cell responses to synovial antigens validates their potential as cellular treatment for RA.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

EXP NEUROL. 2016 SEP;283(Pt A):246-54.

DYSFERLIN FUNCTION IN SKELETAL MUSCLE: POSSIBLE PATHOLOGICAL MECHANISMS AND THERAPEUTICAL TARGETS IN DYSFERLINOPATHIES.

Cárdenas AM, González-Jamett AM, Cea LA, Bevilacqua JA, Caviedes P.

Mutations in the dysferlin gene are linked to a group of muscular dystrophies known as dysferlinopathies. These myopathies are characterized by progressive atrophy. Studies in muscle tissue from dysferlinopathy patients or dysferlin-deficient mice point out its importance in membrane repair. However, expression of dysferlin homologous proteins that restore sarcolemma repair function in dysferlinopathy animal models fail to arrest muscle wasting, therefore suggesting that dysferlin plays other critical roles in muscle function. In the present review, we discuss dysferlin functions in the skeletal muscle, as well as pathological mechanisms related to dysferlin mutations. Particular focus is presented related the effect of dysferlin on cell membrane related function, which affect its repair, vesicle trafficking, as well as Ca²⁺ homeostasis. Such mechanisms could provide accessible targets for pharmacological therapies.

BMC CELL BIOL. 2016 MAY 24;17 SUPPL 1:15.

THE ABSENCE OF DYSFERLIN INDUCES THE EXPRESSION OF FUNCTIONAL CONNEXIN-BASED HEMICHANNELS IN HUMAN MYOTUBES.

Cea LA, Bevilacqua JA, Arriagada C, Cárdenas AM, Bigot A, Mouly V, Sáez JC, Caviedes P.

BACKGROUND: Mutations in the gene encoding for dysferlin cause recessive autosomal muscular dystrophies called dysferlinopathies. These mutations induce several alterations in skeletal muscles, including, inflammation, increased membrane permeability and cell death. Despite the fact that the etiology of dysferlinopathies is known, the mechanism that explains the aforementioned alterations is still elusive. Therefore, we have now evaluated the potential involvement of connexin based

hemichannels in the pathophysiology of dysferlinopathies. RESULTS: Human deltoid muscle biopsies of 5 Chilean dysferlinopathy patients exhibited the presence of muscular connexins (Cx40.1, Cx43 and Cx45). The presence of these connexins was also observed in human myotubes derived from immortalized myoblasts derived from other patients with mutated forms of dysferlin. In addition to the aforementioned connexins, these myotubes expressed functional connexin based hemichannels, evaluated by ethidium uptake assays, as opposed to myotubes obtained from a normal human muscle cell line, RCMH. This response was reproduced in a knock-down model of dysferlin, by treating RCMH cell line with small hairpin RNA specific for dysferlin (RCMH-sh Dysferlin). Also, the presence of P2X7 receptor and the transient receptor potential channel, TRPV2, another Ca(2+) permeable channels, was detected in the myotubes expressing mutated dysferlin, and an elevated resting intracellular Ca(2+) level was found in the latter myotubes, which was in turn reduced to control levels in the presence of the molecule D4, a selective Cx HCs inhibitor. CONCLUSIONS: The data suggests that dysferlin deficiency, caused by mutation or downregulation of dysferlin, promotes the expression of Cx HCs. Then, the de novo expression Cx HC causes a dysregulation of intracellular free Ca(2+) levels, which could underlie muscular damage associated to dysferlin mutations. This mechanism could constitute a potential therapeutic target in dysferlinopathies.

J ALZHEIMERS DIS. 2017;55(4):1595-1603.

TAU PLATELETS CORRELATE WITH REGIONAL BRAIN ATROPHY IN PATIENTS WITH ALZHEIMER'S DISEASE.

Slachevsky A, Guzmán-Martínez L, Delgado C, Reyes P, Farías GA, Muñoz-Neira C, Bravo E, Farías M, Flores P, Garrido C, Becker JT, López OL, Maccioni RB.

BACKGROUND: Intracellular neurofibrillary tangles are part of the core pathology of Alzheimer's disease (AD), which are mainly composed of hyperphosphorylated tau protein. OBJECTIVES: The purpose of this study is to determine whether high molecular weight (HMW) or low molecular weight (LMW) tau protein levels, as well as the ratio HMW/LMW, present in platelets correlates with brain magnetic resonance imaging (MRI) structural changes in normal and cognitively impaired subjects. METHODS: We examined 53 AD patients and 37 cognitively normal subjects recruited from two Memory Clinics at the Universidad de Chile. Tau levels in platelets were determined by immunoreactivity and the MRI scans were analyzed using voxel-based morphometry in 41 AD patients. RESULTS: The HMW/LMW tau ratio was statistically different between controls and AD patients, and no associations were noted between HMW or LMW tau and MRI structures. In a multivariate analysis controlled for age and education level, the HMW/LMW tau ratio was associated with reduced volume in the left medial and right anterior cingulate gyri, right cerebellum, right thalamus (pulvinar), left frontal cortex, and right parahippocampal region. CONCLUSIONS: This exploratory study showed that HMW/LMW tau ratio is significantly higher in AD patients than control subjects, and that it is associated with specific brain regions atrophy. Determination of peripheral markers of AD pathology can help understanding the pathophysiology of neurodegeneration in AD.

MUSCLE NERVE. 2016 JAN;53(1):49-57.

TOWARD AN OBJECTIVE MEASURE OF FUNCTIONAL DISABILITY IN DYSFERLINOPATHY.

Woudt L, Di Capua GA, Krahn M, Castiglioni C, Hughes R, Campero M, Tringulao A6, González-Hormazábal P, Godoy-Herrera R, Lévy N, Urtizberea JA, Jara L, Bevilacqua JA.

INTRODUCTION: Understanding the natural history of dysferlinopathy is essential to design and quantify novel therapeutic protocols. Our aim in this study was to assess, clinically and functionally, a cohort of patients with dysferlinopathy, using validated scales. METHODS: Thirty-one patients with genetically confirmed dysferlinopathy were assessed using the motor function measure (MFM), Modified Rankin Scale (MRS), Muscle Research Council (MRC) scale, serum creatine kinase (CK) assessment, baseline spirometry data, and echocardiographic and electrophysiologic studies. RESULTS: MFM and MRC scores showed a significant negative correlation with disease duration and inverse correlation with MRS, but not with onset age, clinical phenotype, or CK levels. Percent forced vital capacity (%FVC) correlated negatively with disease duration and onset age. Eight known pathogenic mutations were identified recurrently, 4 of which accounted for 79% of the total. CONCLUSIONS: The results suggest that MFM is a reliable outcome measure that may be useful for longitudinal follow-up in dysferlinopathy. Recurrent mutations suggest a founder effect in the Chilean population.

ARCH CLIN NEUROPSYCHOL. 2016 MAR;31(2):165-75.

COMPARISON OF THE PSYCHOMETRIC PROPERTIES OF THE "WORD" AND "PICTURE" VERSIONS OF THE FREE AND CUED SELECTIVE REMINDING TEST IN A SPANISH-SPEAKING COHORT OF PATIENTS WITH MILD ALZHEIMER'S DISEASE AND COGNITIVELY HEALTHY CONTROLS.

Delgado C, Muñoz-Neira C, Soto A, Martínez M, Henríquez F, Flores P, Slachevsky A.

The aim of this study was to compare the psychometric properties of the "Word" and "Picture" versions of the Spanish FCSRT across the same sample of mild Alzheimer disease (AD) patients and controls. Mild AD patients (N = 50, 27 CDR = 0.5; 23 CDR = 1) and controls (N = 42, CDR = 0) were assessed with an extensive clinical and neuropsychological evaluation. Psychometric characteristics for both versions of the FCSRT were compared. Free recall (FR) and total recall (TR) across both versions of the FCSRT showed areas under the curve >0.9 and did not significantly differ between them. The scores of both versions were well correlated, although the scores for the Picture version were greater than those for the Word version, particularly for the TR scores of the mild AD group. Both versions of the FCSRT showed an appropriate accuracy to distinguish mild AD patients and controls. Visual cues were easier to recall than verbal cues, especially in the memory impaired patients.

BLOOD COAGUL FIBRINOLYSIS. 2016 MAY 20.

ACUTE ISCHEMIC STROKE AFTER CARDIAC CATHETERIZATION: THE PROTAMINE LOW-DOSE RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR PATHWAY.

Guevara C, Quijada A, Rosas C, Bulatova K, Lara H, Nieto E, Morales M.

Intravenous thrombolysis is the preferred treatment for acute ischemic stroke; however, it remains unestablished in the area of cardiac catheterization. We report three patients with acute ischemic stroke after cardiac catheterization. After reversing the anticoagulant effect of unfractionated heparin with protamine, all of the patients were successfully off-label thrombolized with reduced doses of intravenous recombinant tissue plasminogen activator (0.6mg/kg). This dose was preferred to reduce the risk of symptomatic cerebral or systemic bleeding. The sequential pathway of protamine recombinant tissue plasminogen activator at reduced doses may be safer for reducing intracranial or systemic bleeding events, whereas remaining efficacious for the treatment of acute ischemic stroke after cardiac catheterization.

PARKINSONS DIS. 2016;2016:9631041.

WHOLE-BRAIN ATROPHY RATE IN IDIOPATHIC PARKINSON'S DISEASE, MULTIPLE SYSTEM ATROPHY, AND PROGRESSIVE SUPRANUCLEAR PALSY.

Guevara C, Bulatova K, Barker GJ, Gonzalez G, Crossley N, Kempton MJ.

In multiple system atrophy (MSA) and progressive supranuclear palsy (PSP), the absence of surrogate endpoints makes clinical trials long and expensive. We aim to determine annualized whole-brain atrophy rates (a-WBAR) in idiopathic Parkinson's disease (IPD), MSA, and PSP. Ten healthy controls, 20 IPD, 12 PSP, and 8 MSA patients were studied using a volumetric MRI technique (SIENA). In controls, the a-WBAR was $0.37\% \pm 0.28$ (CI 95% 0.17-0.57), while in IPD a-WBAR was $0.54\% \pm 0.38$ (CI 95% 0.32-0.68). The IPD patients did not differ from the controls. In PSP, the a-WBAR was $1.26\% \pm 0.51$ (CI 95%: 0.95-1.58). In MSA, a-WBAR was $1.65\% \pm 1.12$ (CI 95%: 0.71-2.59). MSA did not differ from PSP. The a-WBAR in PSP and MSA were significantly higher than in the IPD group ($p = 0.004$ and $p < 0.001$, resp.). In PSP, the use of a-WBAR required one-half of the patients needed for clinical scales to detect a 50% reduction in their progression. In MSA, one-quarter of the patients would be needed to detect the same effect. a-WBAR is a reasonable candidate to consider as a surrogate endpoint in short clinical trials using smaller sample sizes. The confidence intervals for a-WBAR may add a potential retrospective application for a-WBAR to improve the diagnostic accuracy of MSA and PSP versus IPD.

FRONT AGING NEUROSCI. 2016 SEP 13;8:218.

WHOLE-BRAIN ATROPHY DIFFERENCES BETWEEN PROGRESSIVE SUPRANUCLEAR PALSY AND IDIOPATHIC PARKINSON'S DISEASE.

Guevara C1, Bulatova K, Barker GJ, Gonzalez G, Crossley NA, Kempton MJ.

BACKGROUND: The absence of markers for ante-mortem diagnosis of progressive supranuclear palsy (PSP), results in this disorder being commonly mistaken for other conditions, such as idiopathic Parkinson's disease (IPD). Such mistakes occur particularly in the initial stages, when "plus syndrome" has not yet clinically emerged. OBJECTIVE: To investigate the global brain volume and

tissue loss in patients with PSP relative to patients with IPD and healthy controls and correlations between clinical parameters and magnetic resonance imaging (MRI)-derived brain volume estimates. METHODS: T1-weighted images were obtained from three groups of Chilean Latin American adults: 21 patients with IPD, 18 patients with PSP and 14 healthy controls. We used Structural Imaging Evaluation with Normalization of Atrophy (SIENAX) to assess white matter, gray matter and whole-brain volumes (normalized to cranial volume). Imaging data were used to analyze putative correlations with the clinical status of PSP and IPD patients using the Unified Parkinson's Disease Rating Scale Part III (UPDRS III), Hoehn and Yahr (H&Y), the Clinical Global Impression for Disease Severity Scale (CGI-S) and the Frontal Assessment Battery (FAB). RESULTS: PSP patients had significantly lower whole brain volume than both IPD patients and controls. Whole brain volume reduction in PSP patients was primarily attributable to gray matter volume reduction. We found a significant correlation between brain volume reduction and clinical status in the PSP group. CONCLUSIONS: At the group level, the whole brain and gray matter volumes differentiated patients with PSP from patients with IPD. There was also significant clinical-imaging correlations with motor disturbances in PSP.

DEPARTAMENTO DE DERMATOLOGÍA

PEDIATR DERMATOL. 2016 JUL;33(4):E260-4.

ULTRASOUND DIAGNOSIS AND STAGING IN PEDIATRIC HIDRADENITIS SUPPURATIVA.

Wortsman X, Rodriguez C, Lobos C, Eguiguren G, Molina MT.

Hidradenitis suppurativa (HS) can affect children, and ultrasound has been proven to be useful in diagnosis and staging. The sonographic characteristics of HS in children have not been reported. We studied color Doppler ultrasound images of children (≤ 15 years old; $n = 12$) with clinically and sonographically positive criteria for HS. Sonographic scoring of hidradenitis suppurativa (SOS-HS) was used to stage the cases sonographically. Subclinical pseudocysts were found in 92% of the cases, fluid collections in 83%, and fistulous tracts in 58%. Retained hair tracts in the fluid collections and fistulous tracts were present in 100% of patients; 67% of cases were SOS-HS stage II. In 92% of cases, management was modified after the ultrasound examination. In conclusion, ultrasound can be a reliable and safe imaging tool to support diagnosis and staging and may help in the noninvasive monitoring of treatment in children.

INT J DERMATOL. 2016 JUL;55(7):804-805.

CUTANEOUS GRANULOMAS IN GRISCELLI TYPE 2 SYNDROME.

Navarrete CL, Aranibar L, Mardones F, Avila R, Veloza L.

Griscelli syndrome (GS) is a rare autosomal recessive disease that may compromise the skin, nervous, immune, and lymphoreticular systems as well as solid internal organs. Mutations in genes responsible for cellular membrane trafficking control have been identified. This may explain the dysfunction of melanocytes, neurons, and immune cells.¹ Correlation between genetic defects and clinical manifestations have been reported: neurologic defects are frequent and severe in type 1 GS, milder in type 2, and absent in type 3. Immunological abnormalities such as hypogammaglobulinemia, natural killer cell dysfunction, and infiltration of lymphoid organs are observed only in types 2 and 3.² Type 2 GS has a poor prognosis, with rapid development of hemophagocytic syndrome and death in the absence of bone marrow transplantation. Dermatological signs are usually limited to characteristic silvery scalp hair and eyebrows and skin hypopigmentation.³ Few reports of other cutaneous manifestations in GS have been published. In this case, we describe a child with type 2 GS associated with granulomatous lesions.

J EUR ACAD DERMATOL VENEREOL. 2016 OCT;30(10):1753-1759.

TOFACITINIB VERSUS ETANERCEPT OR PLACEBO IN PATIENTS WITH MODERATE TO SEVERE CHRONIC PLAQUE PSORIASIS: PATIENT-REPORTED OUTCOMES FROM A PHASE 3 STUDY.

Valenzuela F, Paul C, Mallbris L, Tan H, Papacharalambous J, Valdez H, Mamolo C.

BACKGROUND: Tofacitinib is an oral Janus kinase inhibitor that is being investigated for psoriasis. Psoriasis impacts on physical and psychological well-being; improvements in health-related quality of life (HRQoL) with etanercept in psoriasis are well documented. OBJECTIVE: To evaluate HRQoL with tofacitinib, vs. placebo or etanercept, in the Phase 3, randomized, placebo-controlled, non-inferiority, Oral-treatment Psoriasis Trial (OPT) Compare Study (NCT01241591). METHODS: Adults with moderate to severe chronic plaque psoriasis were randomized 3:3:3:1 to tofacitinib 10 or 5 mg twice daily (BID), etanercept 50 mg twice weekly or placebo, for

12 weeks. Patient-reported outcomes (PROs) included Dermatology Life Quality Index (DLQI), Itch Severity Item and Patient Global Assessment of psoriasis. RESULTS: At baseline, 83.4% (911/1092) of patients had a DLQI score ranging between 6 and 30, indicating a substantial burden of disease. By Week 12, 47.3%, 43.6% and 30.9% of patients in the tofacitinib 10 mg BID, etanercept and tofacitinib 5 mg BID groups, respectively, had a DLQI score of 0 or 1 (no effect of psoriasis on QoL) vs. 7.8% for placebo (all $P < 0.0001$). Tofacitinib significantly reduced itch vs. placebo ($P < 0.05$ both doses) and etanercept ($P < 0.0001$ both doses) within 1 day of starting treatment. Furthermore, reductions in itch were greater with tofacitinib 10 mg BID, vs. etanercept, at Weeks 2-12 (all time points $P < 0.05$). At Week 2, an Itch Severity Item score of 'little or no itch' was more frequent with tofacitinib 10 mg (68.6%) vs. etanercept (57.4%) and placebo (12.2%), and the PtGA response rate was significantly greater with tofacitinib 10 mg vs. placebo ($P < 0.05$). CONCLUSION: Oral tofacitinib provided significant improvements across multiple PROs by Week 12. Improvements with tofacitinib 10 mg BID were comparable to etanercept, and improvements in itch were greater and more rapid with tofacitinib 10 mg BID.

ACTA DERM VENEREOL. 2016 AUG 23;96(217):38-46.

PSYCHONEUROIMMUNOLOGY AND THE SKIN.

Honeyman JF

The nervous, immune, endocrine and integumentary systems are closely related and interact in a number of normal and pathological conditions. Nervous system mediators may bring about direct changes to the skin or may induce the release of immunological or hormonal mediators that cause pathological changes to the skin. This article reviews the psychological mechanisms involved in the development of skin diseases.

SKIN RES TECHNOL. 2016 OCT 30.

CLINICAL AND COLOR DOPPLER ULTRASOUND EVALUATION OF POLYACRYLAMIDE INJECTION IN HIV PATIENTS WITH SEVERE FACIAL LIPOATROPHY SECONDARY TO ANTIRETROVIRAL THERAPY.

Faundez E, Vega N, Vera E, Vega P, Sepulveda D, Wortsman X.

BACKGROUND/PURPOSE: Facial lipoatrophy in HIV patients, secondary to antiretroviral therapy (ART) with thymidine analogs, has been related to important psychosocial alterations and poor adherence to treatment. Polyacrylamide gel (PAAG) is a filler that has been used for treating facial lipoatrophy in HIV patients. The aim was to assess the clinical and sonographic anatomical changes after injection of PAAG in HIV patients with facial lipoatrophy secondary to ART. METHODS: HIV patients receiving ART and suffering from severe facial lipoatrophy were recruited and underwent clinical and color Doppler ultrasound evaluation prior to PAAG application (AQUAMID®) and sonographically monitored at 18 months and clinically followed up for 36 months after the procedure. Adverse effects were recorded based on occurrence and complexity. RESULTS: A total of 33 patients were evaluated, 30 men (91%) and 3 women (9%) with an average age of 49.6 years (± 8.4). Clinical improvement assessed by a dermatologist had an average score of 5.9 (± 0.7) on a scale of 1-7. On color Doppler ultrasound there was a significant increase of the thickness of the subcutaneous tissue (SCT) in both nasofold lines when comparing before and after PAAG injection ($P < 0.01$) and no signs of inflammation (hypervascularity). User satisfaction was qualified as excellent or good in all cases. Only two patients experienced adverse effects (hematoma and puncture site infection), which was successfully managed without consequences. CONCLUSION: Treatment of facial lipoatrophy with PAAG seems to be effective in HIV patients and no signs of complications were observed in the monitoring at 36 months after injection. Color Doppler ultrasound can identify the filler deposits and the anatomical changes of the SCT non-invasively.

J AM ACAD DERMATOL. 2016 OCT;75(4):760-7.

COLOR DOPPLER ULTRASOUND ASSESSMENT OF MORPHOLOGY AND TYPES OF FISTULOUS TRACTS IN HIDRADENITIS SUPPURATIVA (HS).

Wortsman X, Castro A, Figueroa A.

BACKGROUND: Fistulous tracts in hidradenitis suppurativa (HS) are key signs of severity and their clinical evaluation alone may be limited for assessing their presence and morphology. There is also a need to determine the factors that allow reversibility of the anatomic changes in HS. OBJECTIVE: We sought to categorize fistulous tracts in HS. METHODS: A retrospective study of color Doppler ultrasound images of cases with positive clinical and sonographic criteria of HS with fistulous tracts was performed. The sonographic staging of HS, location, and anatomic characteristics of the tracts were registered and graded. Statistical analysis for correlating variables was performed using bivariate and multivariate studies. RESULTS: In all, 52 patients presenting 96 fistulous tracts met the criteria. Morphology was defined and a sonographic classification into 3 types of fistulae was developed. Type 3

concentrated 71% of the cases presenting communicating tracts, and type 2, 29%. Types 2 and 3 represented 63% of patients with multiple fistulous tracts. Fistulous tracts types 2 and 3 were significantly correlated with age 35 years or older and groin location. LIMITATIONS: Ultrasound cannot detect lesions less than 0.1 mm. CONCLUSION: Fistulous tracts in HS can be categorized using ultrasound, which may support earlier and more precise management.

J ULTRASOUND MED. 2016 MAR;35(3):577-80.

GUIDELINES FOR PERFORMING DERMATOLOGIC ULTRASOUND EXAMINATIONS BY THE DERMUS GROUP.

Wortsman X, Alfageme F, Roustan G, Arias-Santiago S, Martorell A, Catalano O, Scotto di Santolo M, Zarchi K, Bouer M, Gonzalez C, Bard R, Mandava A, Gaitini D.

OBJECTIVES: To support standardization for performing dermatologic ultrasound examinations. METHODS: An international working group, called DERMUS (Dermatologic Ultrasound), was formed, composed of physicians who have been working on a regular basis and publishing in peer-reviewed articles on dermatologic ultrasound. A questionnaire on 5 critical issues about performance of the examinations was prepared and distributed by e-mail. The areas of discussion included technical aspects, main areas of application, minimum number of examinations per year required for assessing competence, qualifications of the personnel in charge of the examination, and organization of courses. Final recommendations were approved on the basis of the agreement of more than 50% of the members. RESULTS: The minimum frequency recommended for performing dermatologic examinations was 15 MHz. Routine use of color Doppler ultrasound and the performance of spectral curve analysis for assessing the main vascularity of lesions were suggested. Three-dimensional reconstructions were considered optional. The main dermatologic applications were benign tumors, skin cancer, vascular anomalies, cosmetic field, nail disorders, and inflammatory diseases. The minimum number of examinations per year suggested by the group for assessing competence was 300. A physician and not a sonographer was recommended to be the person in charge of performing the examination. On course organization, a minimum of 2 levels of complexity (basic and advanced) was suggested. CONCLUSIONS: There is a need to standardize the performance and quality of dermatologic ultrasound examinations. The present guidelines written by an international group of specialists in the field may support this objective.

J COSMET DERMATOL. 2016 SEP;15(3):238-44.

COMPARISON OF CLINICAL MARKING AND ULTRASOUND-GUIDED INJECTION OF BOTULINUM TYPE A TOXIN INTO THE MASSETER MUSCLES FOR TREATING BRUXISM AND ITS COSMETIC EFFECTS.

Quezada-Gaon N, Wortsman X, Peñaloza O, Carrasco JE.

BACKGROUND: Botulinum toxin type A has been used for treating the hypertrophy of the masseter muscles and its cosmetic effects. Ultrasound is increasingly used in dermatology, along with the guidance of mini-invasive procedures. AIMS: To evaluate the role of ultrasound for guiding the application of Botulinum A toxin in patients with cosmetic alterations due to bruxism, correlate the clinical landmarks with the ultrasound findings, and study the effect on the symptoms, cosmetics, and quality of life. PATIENTS/METHODS: Twenty individuals with bruxism and cosmetic alterations underwent an ultrasound-guided injection of Botulinum toxin type A in each masseter muscle. Clinical and ultrasound marking of the procedure was compared. Clinical and sonographic evaluation was performed at the time of injection and 3 months later. Ten normal individuals underwent ultrasound of the masseter muscles as a control group. RESULTS: Up to 65% of individuals showed anatomical variants of the salivary glands. The method for clinically marking the skin showed a frequently erroneous location of the anterior point (up to 40% of cases) that was proven by ultrasound to be out of the muscle. In 20% of cases, ultrasound showed that the needle should be longer to enter the muscle. After injection, most of the patients demonstrated a decrease of the symptoms and cosmetic and quality of life improvements. CONCLUSIONS: Ultrasound can be a potent tool for guiding the injection of Botulinum toxin into the masseter muscles. It may contribute to a more personalized procedure, better cosmetic results, and help to avoid potential complications.

CENTRO DE IMAGENOLÓGÍA

ASIAN PAC J CANCER PREV. 2016;17(3):1485-8.

FREQUENCY OF CHOLELITHIASIS AND BILIARY PATHOLOGY IN THE EASTER ISLAND RAPANUI AND NON-RAPANUI POPULATIONS.

Bravo E, Contardo J, Cea J.

BACKGROUND: Chile is one of the countries with the highest prevalence of cholelithiasis worldwide, considering the Mapuche ethnicity as a risk factor for developing this pathology. Moreover, cholelithiasis is the main risk factor for developing gallbladder cancer, being the fifth cause of cancer death in Chile. The purpose of this study was to compare the frequency of cholelithiasis and

biliary pathology among the population belonging to Rapanui ethnicity and non-Rapanui population living on Easter Island. MATERIALS AND METHODS: In this retrospective case-control study, a total of 609 abdominal ultrasonographs performed consecutively in Hanga Roa Hospital during the period August 2012 to January 2015 were analyzed. Multiple logistic regression was used to obtain odds ratio (OR) and 95% confidence intervals (95% CI) of cholelithiasis and biliary pathology, adjusting for age, gender and referral diagnostic hypothesis. RESULTS: In the Rapanui population the frequency for cholelithiasis and biliary pathology was 6.4% and 13%, meanwhile for the non-Rapanui population it was 13% and 22% respectively. Compared to the non-Rapanui Chilean population, the Rapanui ethnicity presented an OR of 0.53 (95% CI: 0.29-0.95) for cholelithiasis and OR of 0.52 (95% CI: 0.33-0.82) for biliary pathology. CONCLUSIONS: We found statistically significant ethnic differences in the frequency of cholelithiasis and biliary disease among the population of Rapanui and non-Rapanui ethnicity, so that this could be a protective factor for the development of biliary pathology, given the Chilean population context. Other studies including community population to determine the real prevalence of cholelithiasis and analyze the protective role of Rapanui ethnicity on this disease are necessary.

J AFFECT DISORD. 2016 JAN 1;189:207-13.

THE COURSE OF MAJOR DEPRESSION DURING IMPRISONMENT - A ONE YEAR COHORT STUDY.

Baier A, Fritsch R, Ignatyev Y, Priebe S, Mundt AP.

BACKGROUND: First longitudinal studies in prisoners point to improvements of depressive symptoms during imprisonment. The aim of the present study was to assess the course of major depressive disorder during imprisonment and to identify factors influencing remission. METHODS: Prisoners with major depressive disorder in a sample of consecutive admissions to the penal justice system in Santiago de Chile were reassessed after one year of imprisonment. Psychiatric diagnoses were established using the Mini-International Neuropsychiatric Interview; psychological symptoms were assessed with the Symptom-Check-List 90 Revised (SCL-90-R). Mean symptom scores were compared at baseline and follow-up using Student's t-test. Odds ratios (OR) of comorbid disorders and socio-demographic factors at baseline to predict depression at follow-up were calculated. RESULTS: N=79 out of 80 inmates (99%) with major depression at baseline were included. Thirty-five prisoners (44%) had major depression at follow-up. The mean global severity score and all mean subscale scores of the SCL-90-R improved. High suicide risk was present in 37 prisoners (47%) at admission and in 11 (14%) at follow-up. The comorbid diagnosis of PTSD (OR 6.3; $p < 0.001$) at admission and having been previously imprisoned (OR 2.5; $p = 0.05$) predicted major depressive disorder at follow-up. LIMITATIONS: The study could not account for temporary improvements between the assessments. CONCLUSION: In spite of important symptom improvements, only about half of the prisoners with major depression at admission remit after one year of imprisonment. New interventions should target people with major depression and comorbid PTSD at admission.

ANN ANAT. 2016 JAN;203:59-68.

THE RELATIONSHIP BETWEEN SKULL MORPHOLOGY, MASTICATORY MUSCLE FORCE AND CRANIAL SKELETAL DEFORMATION DURING BITING.

Toro-Ibacache V, Zapata Muñoz V, O'Higgins P.

The human skull is gracile when compared to many Middle Pleistocene hominins. It has been argued that it is less able to generate and withstand high masticatory forces, and that the morphology of the lower portion of the modern human face correlates most strongly with dietary characteristics. This study uses geometric morphometrics and finite element analysis (FEA) to assess the relationship between skull morphology, muscle force and cranial deformations arising from biting, which is relevant in understanding how skull morphology relates to mastication. The three-dimensional skull anatomies of 20 individuals were reconstructed from medical computed tomograms. Maximal contractile muscle forces were estimated from muscular anatomical cross-sectional areas (CSAs). Fifty-nine landmarks were used to represent skull morphology. A partial least squares analysis was performed to assess the association between skull shape and muscle force, and FEA was used to compare the deformation (strains) generated during incisor and molar bites in two individuals representing extremes of morphological variation in the sample. The results showed that only the proportion of total muscle CSA accounted for by the temporalis appears associated with skull morphology, albeit weakly. However, individuals with a large temporalis tend to possess a relatively wider face, a narrower, more vertically oriented maxilla and a lower positioning of the coronoid process. The FEAs showed that, despite differences in morphology, biting results in similar modes of deformation for both crania, but with localised lower magnitudes of strains arising in the individual with the narrowest, most vertically oriented maxilla. Our results suggest that the morphology of the maxilla modulates the transmission of forces generated during mastication to the rest of the cranium by deforming less in individuals with the ability to generate proportionately larger temporalis muscle forces.

MUSCLE NERVE. 2016 AUG;54(2):203-10.

BROADENING THE IMAGING PHENOTYPE OF DYSFERLINOPATHY AT DIFFERENT DISEASE STAGES.

Díaz J, Woudt L, Suazo L, Garrido C, Caviedes P, CÁrdenas AM, Castiglioni C, Bevilacqua JA.

INTRODUCTION: MRI characterization of dysferlinopathy has been mostly limited to the lower limbs. We aimed to broaden the MRI description of dysferlinopathy and to correlate it with objective measures of motor dysfunction. METHODS: Sequential whole-body axial MRI was performed in 27 patients with genetically confirmed dysferlinopathy classified according to disease duration. Spearman correlations of fatty infiltration scores versus Motor Function Measure (MFM) were calculated. RESULTS: Significant fatty infiltration was symmetrically present in early stages mainly in the posterior compartments of legs and thighs, thigh adductors, pelvic girdle, and some paravertebral muscles and the subscapularis. Later, fatty infiltration involved leg and thigh anterior compartments, arms and forearms, paravertebral, and trunk muscles. MRI infiltration score correlated positively with disease duration and negatively with MFM scale. CONCLUSIONS: We expand MRI characterization of dysferlinopathy and provide evidence for use of MRI scoring combined with motor functional scales to assess the natural course of disease.

DEPARTAMENTO DE OFTALMOLOGÍA

OCUL IMMUNOL INFLAMM. 2016 MAR 4:1-5.

EVALUATION OF THE ACCURACY OF T-SPOT.TB FOR THE DIAGNOSIS OF OCULAR TUBERCULOSIS IN A BCG-VACCINATED, NON-ENDEMIC POPULATION.

Urzua CA, Liberman P, Abuauad S, Sabat P, Castiglione E, Beltran-Videla MA, Aguilera R.

PURPOSE: To determine the performance of T-SPOT.TB, an interferon gamma release assay test, in patients with ocular tuberculosis (TB) in a BCG-vaccinated, non-endemic population. METHODS: We employed a nested case-control design. In total, 45 subjects were enrolled (23 patients with ocular tuberculosis and 22 patients with other causes of uveitis). A blood sample was collected from each subject, and T-SPOT.TB was executed. Laboratory professionals were blinded to the disease status of each subject. RESULTS: Five patients were excluded because of indeterminate results. The calculated sensitivity and specificity were 0.80 and 0.85, respectively. The positive likelihood ratio was 5.33 and the negative likelihood ratio was 0.23. The overall accuracy of the test was 0.83. CONCLUSIONS: T-SPOT.TB adequately diagnosed ocular TB. This technique is particularly useful in populations where BCG vaccinations are still mandatory.

INVEST OPHTHALMOL VIS SCI. 2016 APR;57(4):1765-72.

ELEVATED CD1c+ MYELOID DENDRITIC CELL PROPORTIONS ASSOCIATE WITH CLINICAL ACTIVITY AND PREDICT DISEASE REACTIVATION IN NONINFECTIOUS UVEITIS.

Chen P, Urzua CA, Knickelbein JE, Kim JS, Li Z, Hannes S, Kuo D, Chaigne-Delalande B, Armbrust K, Tucker W, Liu B, Agrón E, Sen HN, Nussenblatt RB.

PURPOSE: To test the association between elevated proportions of CD1c+ myeloid dendritic cells (mDCs) and disease activation/reactivation in noninfectious uveitis. METHODS: Noninfectious uveitis patients (n = 89) and healthy controls (n = 111) were recruited. The proportion of CD1c+ mDCs in the total dendritic cell (DC) population of peripheral blood was measured by flow cytometry (CD1c+ mDCs gated on Lineage 1+HLADR+ DCs). Disease activity was assessed per Standardization of Uveitis Nomenclature criteria. Uveitis reactivation was ascribed to clinically quiescent patients who developed reactivation of intraocular inflammation within 6 months. RESULTS: The proportions of CD1c+ mDCs were increased in noninfectious uveitis patients, especially in active disease, compared to healthy controls. This CD1c+ mDC elevation was not associated with underlying systemic diseases, anatomic locations of uveitis, medications, or demographic factors. Longitudinal data showed that the dynamics of CD1c+ mDC levels were correlated with disease activity. The average proportion of CD1c+ mDCs in active uveitis patients was 60% so we set this as the cutoff between high and low CD1c+ mDC levels. Although 74% of quiescent patients had low proportions of CD1c+ mDCs, 26% still had high proportions. Quiescent patients with high CD1c+ mDC proportions showed increased risk of disease reactivation, compared to quiescent patients with low CD1c+ mDC proportions. CONCLUSIONS: Increased proportions of CD1c+ mDCs were associated with clinical activity, and quiescent patients with elevated CD1c+ mDCs were more likely to undergo reactivation. This suggests that CD1c+ mDC proportion may be a potential biomarker for assessing clinical activation and reactivation in noninfectious uveitis.

STEM CELL RES THER. 2016 MAR 16;7:42.

INTRAVITREAL ADMINISTRATION OF MULTIPOTENT MESENCHYMAL STROMAL CELLS TRIGGERS A CYTOPROTECTIVE MICROENVIRONMENT IN THE RETINA OF DIABETIC MICE.

Ezquer M, Urzua CA, Montecino S, Leal K, Conget P, Ezquer F.

BACKGROUND: Diabetic retinopathy is a common complication of diabetes and the leading cause of irreversible vision loss in the Western world. The reduction in color/contrast sensitivity due to the loss of neural cells in the ganglion cell layer of the retina is an early event in the onset of diabetic retinopathy. Multipotent mesenchymal stromal cells (MSCs) are an attractive tool for the treatment of neurodegenerative diseases, since they could differentiate into neuronal cells, produce high levels of neurotrophic factors and reduce oxidative stress. Our aim was to determine whether the intravitreal administration of adipose-derived MSCs was able to prevent the loss of retinal ganglion cells in diabetic mice. **METHODS:** Diabetes was induced in C57BL6 mice by the administration of streptozotocin. When retinal pro-damage mechanisms were present, animals received a single intravitreal dose of 2×10^5 adipose-derived MSCs or the vehicle. Four and 12 weeks later we evaluated: (a) retinal ganglion cell number (immunofluorescence); (b) neurotrophic factor levels (real-time quantitative polymerase chain reaction (RT-qPCR) and enzyme-linked immunosorbent assay (ELISA)); (c) retinal apoptotic rate (TUNEL); (d) retinal levels of reactive oxygen species and oxidative damage (ELISA); (e) electrical response of the retina (electroretinography); (f) pro-angiogenic and anti-angiogenic factor levels (RT-qPCR and ELISA); and (g) retinal blood vessels (angiography). Furthermore, 1, 4, 8 and 12 weeks post-MSC administration, the presence of donor cells in the retina and their differentiation into neural and perivascular-like cells were assessed (immunofluorescence and flow cytometry). **RESULTS:** MSC administration completely prevented retinal ganglion cell loss. Donor cells remained in the vitreous cavity and did not differentiate into neural or perivascular-like cells. Nevertheless, they increased the intraocular levels of several potent neurotrophic factors (nerve growth factor, basic fibroblast growth factor and glial cell line-derived neurotrophic factor) and reduced the oxidative damage in the retina. Additionally, MSC administration has a neutral effect on the electrical response of the retina and did not result in a pathological neovascularization. **CONCLUSIONS:** Intravitreal administration of adipose-derived MSCs triggers an effective cytoprotective microenvironment in the retina of diabetic mice. Thus, MSCs represent an interesting tool in order to prevent diabetic retinopathy.

DEPARTAMENTO DE UROLOGÍA

ANDROLOGY. 2017 JAN;5(1):41-48.

OVEREXPRESSION OF CYP19A1 AROMATASE IN LEYDIG CELLS IS ASSOCIATED WITH STEROIDOGENIC DYSFUNCTION IN SUBJECTS WITH SERTOLI CELL-ONLY SYNDROME.

Lardone MC, Argandoña F, Flórez M, Parada-Bustamante A, Ebensperger M, Palma C, Piottante A, Castro A.

Several observational studies have showed a combination of lower testosterone (T) to LH ratio and higher estradiol (E2) to T ratio in secretory infertile men compared to men with normal spermatogenesis, suggesting a steroidogenic dysfunction of Leydig cells (Lc) that may involve increased aromatase activity. Low T/LH ratio is associated with Lc hyperplasia, which together with LH hyperstimulation may represent compensation for impaired T production. Aromatase expression and oestrogen production are mainly detected in Lc of the testis, although Sertoli and germ cells also contribute to testicular aromatase activity. The aim of this study was to assess the transcriptional expression of CYP19A1 (aromatase) in isolated Lc of subjects with Sertoli cell-only syndrome (SCOS) and signs of Lc impairment. Nineteen patients with SCOS and 10 controls with normal spermatogenesis who had medical indication of testicular biopsy for sperm retrieval were studied. Leydig cells were isolated by Laser Capture Microdissection (LCM) and CYP19A1 mRNA expression was quantified by SYBR® Green-based qPCR. In addition, testicular T and E2 and serum hormonal levels were measured. Relative to control group, CYP19A1 was overexpressed more than twofold in 10/19 cases (2.3-12.2-fold increase), showing a significant increment in cases with low T/LH ratio ($T/LH < 2$) compared to cases with $T/LH \geq 2$ ($p = 0.038$, REST®). Moreover, Rq data for CYP19A1 had a direct correlation with testicular levels of E2 and the E2/T ratio ($r = 0.869$; $p < 0.001$ and $r = 0.633$; $p = 0.005$). In summary, Lc from infertile patients with signs of Lc dysfunction overexpressed aromatase and showed an increment of testicular E2. Our results suggest that increased expression of aromatase in Lc leads to higher E2 production and may account for the functional impairment of the Lc in patients with SCOS.

DEPARTAMENTO DE TRAUMATOLOGÍA

FOOT ANKLE INT. 2016 AUG;37(8):803-8.

EFFECTIVENESS OF ALLOGRAFT RECONSTRUCTION VS TENODESIS FOR IRREPARABLE PERONEUS BREVIS TEARS: A CADAVERIC MODEL.

Pellegrini MJ, Glisson RR, Matsumoto T, Schiff A, Laver L, Easley ME, Nunley JA.

BACKGROUND: Irreparable peroneus brevis tendon tears are uncommon, and there is scant evidence on which to base operative treatment. Options include tendon transfer, segmental resection with tenodesis to the peroneus longus tendon, and allograft reconstruction. However, the relative effectiveness of the latter 2 procedures in restoring peroneus brevis function has not been established. **METHODS:** Custom-made strain gage-based tension transducers were implanted into the peroneus longus and brevis tendons near their distal insertions in 10 fresh-frozen cadaver feet. Axial load was applied to the foot, and the peroneal tendons and antagonistic tibialis anterior and posterior tendons were tensioned to 50% and 100% of physiologic load. Distal tendon tension was recorded in this normal condition and after sequential peroneus brevis-to-longus tenodesis and peroneus brevis allograft reconstruction. Measurements were made in 5 foot inversion/eversion and plantarflexion/dorsiflexion positions. **RESULTS:** Distal peroneus brevis tendon tension after allograft reconstruction significantly exceeded that measured after tenodesis in all tested loading conditions ($P \leq 0.022$). With 50% of physiologic load applied, peroneus brevis tension was 1% to 28% of normal (depending on foot position) after tenodesis and 73% to 101% of normal after allograft reconstruction. Under the 100% loading condition, peroneus brevis tension was 6% to 43% of normal after tenodesis and 88% to 99% of normal after reconstruction with allograft. Distal peroneus longus tension remained within 20% of normal under all operative and loading conditions. **CONCLUSION:** Allograft reconstruction of a peroneus brevis tendon tear in this model substantially restored distal tension when the peroneal tendons and their antagonists were loaded to 50% and 100% of physiologic load. Tenodesis to the peroneus longus tendon did not effectively restore peroneus brevis tension under the tested conditions. **CLINICAL RELEVANCE:** Because tenodesis was demonstrated to be ineffective for restoration of peroneus brevis function, this procedure may result in an imbalanced foot clinically.

J BONE JOINT SURG AM. 2016 MAY 18;98(10):842-8.

SYSTEMATIC QUANTIFICATION OF STABILIZING EFFECTS OF SUBTALAR JOINT SOFT-TISSUE CONSTRAINTS IN A NOVEL CADAVERIC MODEL.

Pellegrini MJ, Glisson RR, Wurm M, Ousema PH, Romash MM, Nunley JA 2nd, Easley ME.

BACKGROUND: Distinguishing between ankle instability and subtalar joint instability is challenging because the contributions of the subtalar joint's soft-tissue constraints are poorly understood. This study quantified the effects on joint stability of systematic sectioning of these constraints followed by application of torsional and drawer loads simulating a manual clinical examination. **METHODS:** Subtalar joint motion in response to carefully controlled inversion, eversion, internal rotation, and external rotation moments and multidirectional drawer forces was quantified in fresh-frozen cadaver limbs. Sequential measurements were obtained under axial load approximating a non-weight-bearing clinical setting with the foot in neutral, 10° of dorsiflexion, and 10° and 20° of plantar flexion. The contributions of the components of the inferior extensor retinaculum were documented after incremental sectioning. The calcaneofibular, cervical, and interosseous talocalcaneal ligaments were then sectioned sequentially, in two different orders, to produce five different ligament-insufficiency scenarios. **RESULTS:** Incremental detachment of the components of the inferior extensor retinaculum had no effect on subtalar motion independent of foot position. Regardless of the subsequent ligament-sectioning order, significant motion increases relative to the intact condition occurred only after transection of the calcaneofibular ligament. Sectioning of this ligament produced increased inversion and external rotation, which was most evident with the foot dorsiflexed. **CONCLUSIONS:** Calcaneofibular ligament disruption results in increases in subtalar inversion and external rotation that might be detectable during a manual examination. Insufficiency of other subtalar joint constraints may result in motion increases that are too subtle to be perceptible. **CLINICAL RELEVANCE:** If calcaneofibular ligament insufficiency is established, its reconstruction or repair should receive priority over that of other ankle or subtalar periarticular soft-tissue structures.

CLÍNICA QUILÍN

FOOT ANKLE INT. 2016 MAR;37(3):312-9.

OUTCOMES OF TIBIOTALOCALCANEAL ARTHRODESIS THROUGH A POSTERIOR ACHILLES TENDON-SPLITTING APPROACH.

Pellegrini MJ, Schiff AP, Adams SB Jr, DeOrio JK, Easley ME, Nunley JA 2nd.

BACKGROUND: A number of operative approaches have been described to perform a tibiotalocalcaneal (TTC) arthrodesis. Here we present the largest reported series of a posterior Achilles tendon-splitting approach for TTC fusion. **METHODS:** With institutional review board approval, a retrospective review of the TTC fusions performed at a single academic institution was carried out. Orthopedic surgeons specializing in foot and ankle surgery performed all procedures. Eligible patients included all those who underwent a TTC fusion via a posterior approach and had at least a 2-year follow-up. Forty-one patients underwent TTC arthrodesis through a posterior Achilles tendon-splitting approach. Mean age at surgery was 56.9 ± 15.0 years. There were 21 female and 20 male patients. Preoperative diagnoses included arthritis ($n = 13$ patients), failed total ankle arthroplasty (9), avascular necrosis of the talus (9), prior nonunion of the ankle and/or subtalar joint (6), Charcot neuro-arthropathy (2), and stage IV flatfoot deformity (2). In 37 patients (90.2%), a hindfoot intramedullary arthrodesis nail was used, with posterior plate or supplemental screw augmentation in 17 patients. Posterior plate stabilization alone was utilized in 4 cases (9.8%). **RESULTS:** The fusion rate was 80.4%. Eight patients developed a nonunion of the subtalar, tibiotalar, or both joints. Complications were observed in 17 patients (41.4%). Of these, ankle nonunion (19.5%), tibial stress fracture (17%), postoperative cellulitis and superficial wound breakdown (9.7%), subtalar nonunion (4.8%), and TTC malunion (2.4%) were the most frequently identified. One patient eventually underwent amputation (2.4%). **CONCLUSION:** We believe that posterior Achilles tendon-splitting approach for tibiotalocalcaneal arthrodesis was a safe and effective method, with similar union and complications rates to some previously described techniques. We believe the posterior approach is advantageous as it provides simultaneous access to both the ankle and subtalar joints and allows for dissection to occur between angiosomes, which may preserve blood supply to the skin.

AESTHET SURG J. 2016 JUN;36(6):697-702.

EFFECTS OF ABDOMINOPLASTY ON INTRA-ABDOMINAL PRESSURE AND PULMONARY FUNCTION.

Pereira N, Sciaraffia C, Danilla S, Parada F, Asfora C, Moral C.

BACKGROUND: Abdominal wall weakness is a consequence of rectus abdominis diastasis and flaccidity of the myofascial component. A degree of plicature of the rectus abdominis generates an increase of intra-abdominal pressure (IAP), which may result in an increase of intrathoracic pressure, thus affecting thoracic hemodynamics and leading to inadequate ventilation. **OBJECTIVES:** To assess changes generated by plicature of the rectus abdominis on IAP and pulmonary function in patients undergoing abdominoplasty. **METHODS:** A total of 10 female patients with abdominal ptosis were included. Chronic smokers and patients with respiratory co-morbidities were excluded. The IAP was measured using a modified Kron's trans-bladder technique. Pulmonary function was assessed by pulmonary compliance (P-Comp) and was calculated with parameters provided by the mechanical ventilator. Both were calculated before and after plicature. **RESULTS:** The mean values for IAP before and after plicature were 6.6 and 9.3 mmHg respectively. Before plicature, the mean P-Comp value was 38.97 mL/cm of water, and after it was 36.54 mL/cm. Both differences were statistically significant. **CONCLUSIONS:** Based on the results obtained, it is possible to conclude that plicature of the rectus abdominis generates significant physiological changes, such as an increase in IAP and a decrease of P-Comp, which do not have a clinically relevant impact on healthy individuals. Measuring IAP with the modified technique and the assessment of pulmonary function using P-Comp are both reliable and provide a more accurate correlation with such physiologic changes. **LEVEL OF EVIDENCE 3:** Therapeutic.