El material que se presenta a continuación proviene de los datos proporcionados por la OAIC (Oficina de Apoyo a la Investigación Clínica) de nuestro Hospital, así como de los recolectados por nuestra Revista.

Abstracts de publicaciones internacionales ISI 2017

DEPARTAMENTO DE CIRUGÍA

ARQ BRAS CIR DIG. 2017 OCT-DEC;30(4):267-271.

SINGLE ANASTOMOSIS GASTRIC BYPASS (ONE ANASTOMOSIS GASTRIC BYPASS OR MINI GASTRIC BYPASS): THE EXPERIENCE WITH BILLROTH II MUST BE CONSIDERED AND IS A CHALLENGE FOR THE NEXT YEARS.

Braghetto I, Csendes A.

INTRODUCTION: Single anastomosis gastric bypass (one anastomosis gastric bypass or mini-gastric bypass) has been presented as an option of surgical treatment for obese patients in order to reduce operation time and avoiding eventual postoperative complications after Roux-en-Y gastric bypass.The main late complication could be related to bile reflux. AIM: To report the experiences published after Billroth II anastomosis and its adverse effects regarding symptoms and damage on the gastric and esophageal mucosa. METHOD: For data recollection Medline, Pubmed, Scielo and Cochrane database were accessed, giving a total of 168 papers being chosen 57 of them. RESULTS: According the reported results during open era surgery for peptic disease and more recent results for gastric cancer surgery, bile reflux and its consequences are more frequent after Billroth II operation compared to Roux-en-Y gastrojejunal anastomosis. CONCLUSION: These findings must be considered for the indication of bariatric surgery.

DIS ESOPHAGUS. 2017 NOV 1;11(1):58-61.

ESOPHAGOCARDIOPLASTY, VAGOTOMY-ANTRECTOMY AND ROUX-EN-Y GASTROJEJUNOSTOMY: INDICATION IN CASES WITH SEVERE ESOPHAGEAL MOTOR DISFUNCTION.

Braghetto I, Korn O, Csendes A, Frias JC.

Almost 10% of patients with Crest syndrome associated with severe gastroesophageal reflux and 5-10% of patients with failed cardiomyotomy for achalasia present with cardial or distal esophageal organic stricture. Some of these cases are poor risk patients for surgery and therefore the surgeon must offer a safe procedure with low morbimortality, keeping in mind the pathophysiological motor pattern of these patients.In order to treat the stricture to improve the esophageal transit we treated patients with esophagocardioplasty associated with vagotomy-antrectomy and Roux-en-Y gastrojejunostomy, thereby avoiding the potential acid or biliary reflux in poor risk patients in whom esophagectomy would be a very deleterious procedure. All four patients had a good postoperative evolution and late control demonstrated good esophagogastric transit with no postoperative esophagitis.

AESTHETIC PLAST SURG. 2017 DEC;41(6):1389-1399.

RECTUS ABDOMINIS FAT TRANSFER (RAFT) IN LIPOABDOMINOPLASTY: A NEW TECHNIQUE TO ACHIEVE FITNESS BODY CONTOUR IN PATIENTS THAT REQUIRE TUMMY TUCK.

Danilla S.

OBJECTIVE: To describe a new technique to achieve a fit-look in lipoabdominoplasty patients through liposculpture and rectus abdominis fat transfer (RAFT). METHODS: Patients with a body mass index under 26 and of both genders scheduled for abdominoplasty or body lift were selected for this procedure. Fat was transferred directly to the rectus abdominis muscle after flap elevation during lipoabdominoplasty. RESULTS: A total of 26 patients were operated on with this technique. No complications attributable to the fat grafting were noticed. All patients had a high satisfaction level with the procedure. Demonstrative cases are shown. DISCUSSION: The RAFT technique is a useful and effective technique to improve results in standard lipoabdominoplasty. Its main limitation is the adequate selection of the patient. The RAFT technique can be incorporated easily to common day practice.

ONCOTARGET. 2017 SEP 19;8(48):84006-84018.

DOWNREGULATION OF THE SONIC HEDGEHOG/GLI PATHWAY TRANSCRIPTIONAL TARGET NEOGENIN-1 IS ASSOCIATED WITH BASAL CELL CARCINOMA AGGRESSIVENESS.

Casas BS, Adolphe C, Lois P, Navarrete N, Solís N, Bustamante E, Gac P, Cabané P, Gallegos I, Wainwright BJ, Palma V.

Basal Cell Carcinoma (BCC) is one of the most diagnosed cancers worldwide. It develops due to an unrestrained Sonic Hedgehog (SHH) signaling activity in basal cells of the skin. Certain subtypes of BCC are more aggressive than others, although the molecular basis of this phenomenon remains unknown. We have previously reported that Neogenin-1 (NEO1) is a downstream target gene of the SHH/GLI pathway in neural tissue. Given that SHH participates in epidermal homeostasis, here we analyzed the epidermal expression of NEO1 in order to identify whether it plays a role in adult epidermis or BCC. We describe the mRNA and protein expression profile of NEO1 and its ligands (Netrin-1 and RGMA) in human and mouse control epidermis and in a broad range of human BCCs. We identify in human BCC a significant positive correlation in the levels of *NEO1* receptor, *NTN-1* and *RGMA* ligands with respect to *GLI1*, the main target gene of the canonical SHH pathway. Moreover, we show via cyclopamine inhibition of the SHH/GLI pathway of *ex vivo* cultures that NEO1 likely functions as a downstream target of SHH/GLI signaling in the skin. We also show how *Neo1* expression decreases throughout BCC progression in the K14-Cre: Ptch1lox$^{/lox}$ mouse model and that aggressive subtypes of human BCC exhibit lower levels of NEO1 than non-aggressive BCC samples. Taken together, these data suggest that NEO1 is a SHH/GLI target in epidermis. We propose that NEO1 may be important in tumor onset and is then down-regulated in advanced BCC or aggressive subtypes.

AESTHET SURG J. 2017 JUN 3.

LONG-TERM QUALITY-OF-LIFE OUTCOMES AFTER BODY CONTOURING SURGERY: PHASE IV RESULTS FOR THE BODY-QOL® COHORT.

Suijker J, Troncoso E, Pizarro F, Montecinos S, Villarroel G, Erazo C, Cisternas JP, Andrades P, Benítez S, Sepúlveda S, Danilla S.

BACKGROUND: Body contouring surgery (BCS) is becoming increasing popular for aesthetic and reconstructive purposes, particularly among patients with massive weight loss (MWL). However, data on quality of life (QoL) following the surgery are limited, especially long-term QoL. OBJECTIVES: The authors evaluated the effect of BCS on QoL and the durability of this effect over time. METHODS: QoL was measured with the Body-QoL® instrument at 3 time points among consecutively treated patients: the day before BCS, 1 to 9 months postoperatively (short term), and 1 to 2.7 years postoperatively (long term). Total Body-QoL scores were compiled, as were scores for the instrument's main domains: body satisfaction, sex life, self-esteem and social performance, and physical symptoms. Scores were examined for the entire study population and separately for the cosmetic and MWL cohorts. RESULTS: Fifty-seven of the 112 patients participated in the short-term assessment and 84 in the long-term assessment. Total Body-QoL scores increased significantly ($P < 0.0001$), from 44.0 ± 14.1 preoperatively to 85.5 ± 17.5 short-term postoperatively and to 84.4 ± 12.7 long-term postoperatively. Scores for the 2 postoperative assessments did not differ significantly. Similar results were observed for scores on each separate domain. Although preoperative scores were lower for the MWL cohort than the cosmetic cohort (33.9 ± 15.6 vs 46.1 ± 12.8; $P = 0.0002$), they improved substantially after BCS, approaching scores for the cosmetic cohort. CONCLUSIONS: QoL increases significantly after BCS. This favorable outcome remained stable throughout long-term follow-up and was true for the cosmetic and MWL cohorts.

CRITICAL CARE 2017;21:227.

CURRENT CLINICAL NUTRITION PRACTICES IN CRITICALLY ILL PATIENTS IN LATIN AMERICA: A MULTINATIONAL OBSERVATIONAL STUDY

Karin Papapietro Vallejo, Carolina Méndez Martínez, Alfredo A. Matos Adames, Vanessa Fuchs-Tarlovsky, Guillermo Carlos Contreras Nogales, Roger Enrique Riofrio Paz, Mario Ignacio Perman, Maria Isabel Toulson Davisson CorreiaEmail authorView ORCID ID profile and Dan Linetzky Waitzberg

Background Malnutrition in critically ill adults in the intensive care unit (ICU) is associated with a significantly elevated risk of mortality. Adequate nutrition therapy is crucial to optimise outcomes. Currently, there is a paucity of such data in Latin America. Our aims were to characterise current clinical nutrition practices in the ICU setting in Latin America and evaluate whether current practices meet caloric and protein requirements in critically ill patients receiving nutrition therapy. Methods. We conducted a cross-sectional, retrospective, observational study in eight Latin American countries (Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Panama, and Peru). Eligible patients were critically ill adults hospitalised in the ICU and receiving enteral nutrition (EN) and/or parenteral nutrition (PN) on the Screening Day and the previous day (day –1). Caloric and protein balance on day –1, nutritional status, and prescribed nutrition therapy were recorded. Multivariable logistic regression analysis was performed to identify independent predictors of reaching daily caloric and protein targets. Results. The analysis included 1053 patients from 116 hospitals. Evaluation of nutritional status showed that 74.1% of patients had suspected/moderate or severe malnutrition according to the Subjective Global Assessment. Prescribed nutrition therapy included EN alone (79.9%), PN alone (9.4%), and EN + PN (10.7%). Caloric intake met >90% of the daily target in 59.7% of patients on day –1; a caloric deficit was present in 40.3%, with a mean (±SD) daily caloric deficit of –688.8 ± 455.2 kcal. Multivariable logistic regression analysis showed that combined administration of EN + PN was associated with a statistically significant increase in the probability of meeting >90% of daily caloric and protein targets compared with EN alone (odds ratio, 1.56; 95% confidence interval, 1.02–2.39; p = 0.038). Conclusions.

In the ICU setting in Latin America, malnutrition was highly prevalent and caloric intake failed to meet targeted energy delivery in 40% of critically ill adults receiving nutrition therapy. Supplemental administration of PN was associated with improved energy and protein delivery; however, PN use was low. Collectively, these findings suggest an opportunity for more effective utilization of supplemental PN in critically ill adults who fail to receive adequate nutrition from EN alone.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

FETAL DIAGN THER. 2017;41(3):202-208.

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.

INT UROGYNECOL J. 2017 JUN;28(6):907-911.

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.

STEROIDS 2017; 126: 85-91

ENDOMETRIUM AND STEROIDS, A PATHOLOGIC OVERVIEW AUTHOR LINKS OPEN OVERLAY PANEL

Francisca Plaza-Parrochia, Carmen Romero, Luis Valladares, Margarita Vega

Normal endometrial function requires of cell proliferation and differentiation; therefore, disturbances in these processes could lead to pathological entities such as hyperplasia and endometrial adenocarcinoma, where cell proliferation is increased. The development of these pathologies is highly related to alterations in the levels and/or action of sexual steroids. In the present review, it has been analyzed how steroids, particularly estrogens, androgens and progestagens are involved in the etiopathogenesis of hyperplasia and endometrial endometrioid adenocarcinoma. The emphasis is given on pathological and pharmacological conditions that are presented as risk factors for endometrial pathologies, such as obesity, polycystic ovarian syndrome and hormone replacement postmenopausal women therapy, among others. Steroids alterations may promote changes at molecular level that enhance the development of hyperplasia and endometrioid cancer. In fact, there are solid data that indicate that estrogens stimulate cell-proliferation in this tissue; meanwhile, progestagens are

able to stop cell proliferation and to increase differentiation. Nevertheless, the role of androgens is less clear, since there is contradictory information. It is most likely that the major contribution of steroids to the development of cell proliferation pathologies in endometria would be in early stages, where there is a high sensitivity to these molecules. This phenomenon is present even in stages previous to the occurrence of hyperplasia, like in the condition of polycystic ovarian syndrome, where the endometria have a greater sensitivity to steroids and high expression of cell cycle molecules. These abnormalities would contribute to the pathogenesis of hyperplasia and then in the progression to endometrioid adenocarcinoma.

HISTOL HISTOPATHOL 2017; 32, 1187-1196

EFFECT OF ESTRADIOL ON THE EXPRESSION OF ANGIOGENIC FACTORS IN EPITHELIAL OVARIAN CANCER

Macarena Valladares, Francisca Plaza-Parrochia, Macarena López, Daniela López, Fernando Gabler, Patricio Gayan, Alberto Selman, Margarita Vega and Carmen Romero

Introduction: Ovarian cancer presents a high angiogenesis (formation of new blood vessels) regulated by pro-angiogenic factors, mainly vascular endothelial growth factor (VEGF) and nerve growth factor (NGF). An association between endogenous levels of estrogen and increased risk of developing ovarian cancer has been reported. Estrogen action is mediated by the binding to its specific receptors (ERα and ERβ), altered ERα/ERβ ratio may constitute a marker of ovarian carcinogenesis progression. Objective: To determine the effect of estradiol through ERα on the expression of NGF and VEGF in epithelial ovarian cancer (EOC). Methodology: Levels of phosphorylated estrogen receptor alpha (pERα) were evaluated in well, moderate and poorly differentiated EOC samples (EOC-I, EOC-II, EOC-III). Additionally, ovarian cancer explants were stimulated with NGF (0, 10 and 100 ng/ml) and ERα, ERβ and pERα levels were detected. Finally, human ovarian surface epithelial (HOSE) and epithelial ovarian cancer (A2780) cell lines were stimulated with estradiol, where NGF and VEGF protein levels were evaluated. Results: In tissues, ERs were detected being pERα levels significantly increased in EOC-III samples compared with EOC-I ($p<0.05$). Additionally, ovarian explants treated with NGF increased pERα levels meanwhile total ERα and ERβ levels did not change. Cell lines stimulated with estradiol revealed an increase of NGF and VEGF protein levels ($p<0.05$). Conclusions: Estradiol has a positive effect on pro-angiogenic factors such as NGF and VEGF expression in EOC, probably through the activation of ERα; generating a positive loop induced by NGF increasing pERα levels in epithelial ovarian cells.

REPRODUCTIVE SCIENCES 2017; VOLUME: 24 ISSUE: 7, PAGE(S): 1079-1087

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

Francisca Plaza-Parrochia, Lorena Oróstica, Paula García

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 (ERα) 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 ERα 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.

INT J ONCOL 2017; FEBRUARY 28: 1261-1270

THE NERVE GROWTH FACTOR ALTERS CALRETICULIN TRANSLOCATION FROM THE ENDOPLASMIC RETICULUM TO THE CELL SURFACE AND ITS SIGNALING PATHWAY IN EPITHELIAL OVARIAN CANCER CELLS

Carolina Andrea Vera, Lorena Oróstica, Fernando Gabler, Arturo Ferreira, Alberto Selman, Margarita Vega, Carmen Aurora Romero.

Ovarian cancer is the seventh most common cancer among women worldwide, causing approximately 120,000 deaths every year. Immunotherapy, designed to boost the body's natural defenses against cancer, appears to be a promising option against ovarian cancer. Calreticulin (CRT) is an endoplasmic reticulum (ER) resident chaperone that, translocated to the cell membrane after ER stress, allows cancer cells to be recognized by the immune system. The nerve growth factor (NGF) is a pro-angiogenic molecule overexpressed in this cancer. In the present study, we aimed to determine weather NGF has an effect in CRT translocation induced by cytotoxic and ER stress. We treated A2780 ovarian cancer cells with NGF, thapsigargin (Tg), an ER stress inducer and mitoxantrone (Mtx), a chemotherapeutic drug; CRT subcellular localization was analyzed by immunofluorescence followed by confocal microscopy. In order to determine NGF effect on Mtx and Tg-induced

CRT translocation from the ER to the cell membrane, cells were preincubated with NGF prior to Mtx or Tg treatment and CRT translocation to the cell surface was determined by flow cytometry. In addition, by western blot analyses, we evaluated proteins associated with the CRT translocation pathway, both in A2780 cells and human ovarian samples. We also measured NGF effect on cell apoptosis induced by Mtx. Our results indicate that Mtx and Tg, but not NGF, induce CRT translocation to the cell membrane. NGF, however, inhibited CRT translocation induced by Mtx, while it had no effect on Tg-induced CRT exposure. NGF also diminished cell death induced by Mtx. NGF effect on CRT translocation could have consequences in immunotherapy, potentially lessening the effectiveness of this type of treatment.

INT J MOL SCI. 2017 FEB 26;18(3).

ROLE OF NERVE GROWTH FACTOR (NGF) AND MIRNAS IN EPITHELIAL OVARIAN CANCER.

Retamales-Ortega R, Oróstica L, Vera C, Cuevas P, Hernández A, Hurtado I, Vega M, Romero C.

Ovarian cancer is the eighth most common cancer in women worldwide, and epithelial ovarian cancer (EOC) represents 90% of cases. Nerve growth factor (NGF) and its high affinity receptor tyrosine kinase A receptor (TRKA) have been associated with the development of several types of cancer, including EOC; both NGF and TRKA levels are elevated in this pathology. EOC presents high angiogenesis and several molecules have been reported to induce this process. NGF increases angiogenesis through its TRKA receptor on endothelial cells, and by indirectly inducing vascular endothelial growth factor expression. Other molecules controlled by NGF include ciclooxigenase-2, disintegrin and metalloproteinase domain-containing protein 17 (ADAM17) and calreticulin (CRT), proteins involved in crucial processes needed for EOC progression. These molecules could be modified through microRNA regulation, which could be regulated by NGF. MicroRNAs are the widest family of non-coding RNAs; they bind to 3'-UTR of mRNAs to inhibit their translation, to deadenilate or to degraded them. In EOC, a deregulation in microRNA expression has been described, including alterations of miR-200 family, cluster-17-92, and miR-23b, among others. Since the NGF-microRNA relationship in pathologies has not been studied, this review proposes that some microRNAs could be associated with NGF/TRKA activation, modifying protein levels needed for EOC progression.

INT UROGYNECOL J. 2017 SEP 15.

OBESITY: HOW MUCH DOES IT MATTER FOR FEMALE PELVIC ORGAN PROLAPSE?

Young N, Atan IK, Rojas RG, Dietz HP.

INTRODUCTION AND HYPOTHESIS: The objective was to determine the association between body mass index (BMI) and symptoms and signs of female pelvic organ prolapse (POP). METHODS: An observational cross-sectional study of 964 archived datasets of women seen for symptoms and signs of lower urinary tract and pelvic organ dysfunction between September 2011 and February 2014 at a tertiary urogynaecology centre in Australia was carried out. An in-house standardised interview, the International Continence Society Pelvic Organ Prolapse Quantification (ICS POP-Q) and 4-D translabial ultrasound, followed by analysis of ultrasound volumes for pelvic organ descent and hiatal area on Valsalva, were performed, blinded against other data. RESULTS: There is a positive association between BMI and posterior compartment prolapse on clinical examination and ultrasound imaging, but not for the anterior and central compartments. There was no association with prolapse symptom bother and a negative association with symptoms of prolapse. CONCLUSIONS: In this observational study, we found a strong association between all tested measures of posterior compartment descent and BMI, both clinical and on imaging.

ULTRASOUND OBSTET GYNECOL. 2017 AUG 6.

ANAL SPHINCTER DEFECTS AND FAECAL INCONTINENCE 15-24 YEARS AFTER FIRST DELIVERY: A CROSS-SECTIONAL STUDY.

Guzmán Rojas RA, Salvesen KÅ, Volløyhaug I.

OBJECTIVES: To establish the prevalence of external (EAS) and internal anal sphincter (IAS) defects 15-24 years after childbirth in association to mode of delivery and faecal incontinence (FI), and compare the proportion of obstetric anal sphincter injuries (OASIS) reported at delivery with defects on ultrasound. METHODS: This was a cross-sectional study including 563 women, who delivered their first child from 1990-97. Women responded to a validated questionnaire (PFDI) in 2013-14. The proportion of women with FI was recorded. Information about OASIS was obtained from the National Birth Registry. Study participants underwent 4D transperineal ultrasound examination. A defect of the EAS and IAS of ≥30° in ≥4/6 planes on tomographic ultrasound was registered. Multiple logistic regression was used to calculate adjusted odds ratios (aOR) for comparison of prevalence of EAS defects between different modes of delivery and in association to FI. Fisher's exact test was used for IAS defects. RESULTS: Defects of EAS and IAS were found after normal delivery (n = 201): 10% and 1%; forceps (n = 144): 32% and 7%; vacuum (n = 120): 15% and 4%, and no defects after caesarean section (n = 98). Forceps was associated with increased risk of EAS defects compared to normal delivery (aOR 4.1, 95% CI 2.3-7.2) and vacuum (aOR 3.0, 95% CI 1.6-5.6) and increased risk of IAS defects compared to normal delivery (cOR 7.4, 95% CI 1.5-70.5). The difference between vacuum and normal delivery was not significant. FI was indicated by 18% of women with EAS defects, 29% with IAS defects and 8% without sphincter defects. EAS and IAS defects were associated with increased risk of FI (aOR 2.5, 95% CI 1.3-4.9; cOR 4.2, 95% CI 1.1-13.5). 80% of ultrasonographical sphincter defects were not reported as OASIS at first or subsequent deliveries. CONCLUSIONS: Anal sphincter defects visualized by transperineal ultrasound 15-24 years after delivery were associated with forceps and FI. Undetected OASIS was frequent.

ULTRASOUND OBSTET GYNECOL. 2017 APR 28.

PERINATAL OUTCOME AND PLACENTAL APOPTOSIS IN PATIENTS WITH LATE-ONSET PRE-ECLAMPSIA AND ABNORMAL UTERINE ARTERY DOPPLER AT DIAGNOSIS.

Rodríguez M, Couve-Pérez C, San Martín S, Martínez F, Lozano C, Sepúlveda-Martínez A.

OBJECTIVE: To determine the rate of placental apoptosis and adverse perinatal outcome in patients with late pre-eclampsia and altered uterine artery (UtA) Doppler. METHODS: A cohort study was performed. Patients with a diagnosis of late pre-eclampsia (l-PE) were stratified according to the UtA Doppler status at diagnosis (below or above the 95th percentile). A logistic regression analysis was performed to identify the association between an abnormal UtA Doppler and the presence of adverse maternal and perinatal outcomes. In a subset of this cohort, an immunohistochemical analysis of the placenta was performed to identify the rate of apoptosis and the association with the UtA Doppler against normotensive controls. A non-parametric linear trend analysis was performed for the assessment of the apoptosis index. RESULTS: Eighty-six patients were included in the final analysis. The UtA Doppler was above the 95th percentile in 33 (38.4%) patients. Interestingly, the gestational age at diagnosis and delivery were significantly lower in this group compared to the patients with a normal UtA Doppler. An abnormal UtA Doppler was associated with an increased risk of severe PE (OR= 7.5; 95% CI 2.76 - 20.46; $p < 0.001$), late preterm delivery (OR= 13.7; 95% CI 4.53 - 41.46; $p < 0.001$), SGA at birth (OR= 12.3; 95% CI 3.17 - 47.57; $p < 0.001$), and admission to the NICU (OR= 12.8; 95% CI 2.61 - 62.36; $p = 0.002$). Moreover, the UtA z-score demonstrated a significant inverse correlation with the birth weight z-score ($r = -0.34$; $p = 0.0013$). The mean caspase index in the placenta demonstrated an ascending linear trend according to the UtA Doppler assessment ($p = 0.04$). CONCLUSIONS: In patients with l-PE, the UtA Doppler was useful not only for the clinical classification but also for the placental histological findings. The correlation between the UtA Doppler and the apoptosis index provides new evidence of a sub-group of l-PE patients with a placental origin of the disease.

ULTRASOUND OBSTET GYNECOL. 2017 FEB;49(2):252-256.

IS IT NECESSARY TO DIAGNOSE LEVATOR AVULSION ON PELVIC FLOOR MUSCLE CONTRACTION?

Dietz HP, Pattillo Garnham A, Guzmán Rojas R.

OBJECTIVE: Avulsion of the levator ani muscle commonly occurs at vaginal birth. This condition is usually diagnosed by translabial ultrasound (TLUS) during pelvic floor muscle contraction (PFMC). Some patients are unable to achieve a satisfactory PFMC and in these cases avulsion is assessed at rest. The aim of this study was to validate the diagnosis of levator avulsion by means of TLUS at rest. METHODS: This was a retrospective study of 233 women seen at a tertiary urogynecological center. All women underwent four-dimensional TLUS in the supine position and after voiding. Volumes were obtained on maximal PFMC and at rest. Analysis of the volumes was performed with the observer blinded against all clinical data. Avulsion was defined as an abnormal levator ani muscle insertion that was visible in at least three consecutive axial plane slices, at and above the level of minimal hiatal dimensions, at 2.5-mm intervals. We examined the correlation between both assessment methods using Cohen's kappa coefficient and tested the association of each method with female pelvic organ prolapse on clinical examination, organ descent on ultrasound and hiatal ballooning. RESULTS: In total, datasets from 202 women were available for analysis. The correlation between a diagnosis of avulsion in volumes obtained at rest and those on PFMC was moderate, with a kappa value of 0.583 (95% CI, 0.484-0.683). Agreement for defects visualized on single slices was moderate, with a kappa value of 0.556 (95% CI, 0.520-0.591). When avulsion diagnoses at rest and on PFMC were tested against symptoms of prolapse, and prolapse on clinical examination and on ultrasound, neither of the two methods was superior. CONCLUSION: Although tomographic ultrasound imaging during PFMC enhances tissue discrimination, this may not translate to superior diagnostic performance. Hence, volumes obtained at rest may be used in women unable to contract their pelvic floor. The diagnosis of levator avulsion by tomographic pelvic floor ultrasound is equally valid when performed at rest or on PFMC.

MYCOPATHOLOGIA. 2017 APR;182(3-4):339-347.

GENOTYPING AND PERSISTENCE OF CANDIDA ALBICANS FROM PREGNANT WOMEN WITH VULVOVAGINAL CANDIDIASIS.

Tapia CV, Hermosilla G, Fortes P, Alburquenque C, Bucarey S, Salinas H, Rodas PI, Díaz MC, Magne F.

OBJECTIVE: To study Candida albicans genotypes using RAPD and their susceptibility to fluconazole in healthy pregnant women and in vulvovaginal candidiasis (VVC) patients after topical treatment with clotrimazole. METHODS: Vaginal swabs were collected at t = 0 and t = 1 (1 month later) in pregnant women (control group, n = 33), and before (t = 0), at 1 month (t = 1) and at 2 months (t = 2) after clotrimazole treatment in pregnant women with VVC. RESULTS: Candida albicans was isolated in 30% of healthy pregnant women and 80% of patients with VVC. A high genetic heterogeneity was observed in C. albicans genotypes between individuals. In patients with VVC, topical antifungal treatment with clotrimazole was clinically effective, but only in a 62% C. albicans was eradicated. In patients in which C. albicans was not eradicated, this microorganism persisted for 1 or 2 months after the antifungal treatment. The persistent colonies were not associated with a specific genotype, but they were associated with higher MICs in comparison with colonies isolated from the control group. CONCLUSIONS: Therapy with topical clotrimazole, despite a good clinical outcome, could not eradicate completely C. albicans allowing the persistence of genotypes, with higher MICs to fluconazole. More studies with higher number of patients are needed to validate this preliminary finding.

FETAL DIAGN THER. 2017;41(3):220-225.
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.

AM J OBSTET GYNECOL. 2017 AUG;217(2):196.E1-196.E14
PREDICTION OF NEONATAL RESPIRATORY MORBIDITY BY QUANTITATIVE ULTRASOUND LUNG TEXTURE ANALYSIS: A MULTICENTER STUDY.
Palacio M, Bonet-Carne E, Cobo T, Perez-Moreno A, Sabrià J, Richter J, Kacerovsky M, Jacobsson B, García-Posada RA, Bugatto F, Santisteve R, Vives À, Parra-Cordero M, Hernandez-Andrade E, Bartha JL, Carretero-Lucena P, Tan KL, Cruz-Martínez R, Burke M, Vavilala S, Iruretagoyena I, Delgado JL, Schenone M, Vilanova J, Botet F, Yeo GSH, Hyett J, Deprest J, Romero R, Gratacos E; Fetal Lung Texture Team.

BACKGROUND: Prediction of neonatal respiratory morbidity may be useful to plan delivery in complicated pregnancies. The limited predictive performance of the current diagnostic tests together with the risks of an invasive procedure restricts the use of fetal lung maturity assessment. OBJECTIVE: The objective of the study was to evaluate the performance of quantitative ultrasound texture analysis of the fetal lung (quantusFLM) to predict neonatal respiratory morbidity in preterm and early-term (<39.0 weeks) deliveries. STUDY DESIGN: This was a prospective multicenter study conducted in 20 centers worldwide. Fetal lung ultrasound images were obtained at 25.0-38.6 weeks of gestation within 48 hours of delivery, stored in Digital Imaging and Communication in Medicine format, and analyzed with quantusFLM. Physicians were blinded to the analysis. At delivery, perinatal outcomes and the occurrence of neonatal respiratory morbidity, defined as either respiratory distress syndrome or transient tachypnea of the newborn, were registered. The performance of the ultrasound texture analysis test to predict neonatal respiratory morbidity was evaluated. RESULTS: A total of 883 images were collected, but 17.3% were discarded because of poor image quality or exclusion criteria, leaving 730 observations for the final analysis. The prevalence of neonatal respiratory morbidity was 13.8% (101 of 730). The quantusFLM predicted neonatal respiratory morbidity with a sensitivity, specificity, positive and negative predictive values of 74.3% (75 of 101), 88.6% (557 of 629), 51.0% (75 of 147), and 95.5% (557 of 583), respectively. Accuracy was 86.5% (632 of 730) and positive and negative likelihood ratios were 6.5 and 0.3, respectively. CONCLUSION: The quantusFLM predicted neonatal respiratory morbidity with an accuracy similar to that previously reported for other tests with the advantage of being a noninvasive technique.

DEPARTAMENTO DE DERMATOLOGÍA

DERMATOL SURG. 2017 JUN;43(6):817-825.
COLOR DOPPLER ULTRASOUND ASSESSMENT OF ACTIVITY IN KELOIDS.
Lobos N, Wortsman X, Valenzuela F, Alonso F.

BACKGROUND: The assessment of activity in keloids may be critical for defining their management. There is a lack of clinical scorings designed for the evaluation of keloids and biopsies may be contraindicated. OBJECTIVE: To assess the sonographic activity of keloids in comparison with clinical scoring. MATERIALS AND METHODS: A retrospective study of the clinical and color Doppler ultrasound (CDU) images of patients medically derived to CDU with the diagnosis of keloid was performed. Activity was evaluated clinically (modified Seattle Scar Scale) and CDU. Keloids were considered active when CDU detected vascularity within the lesion. Statistical analysis was performed (Wilcoxon-Mann-Whitney, Student t-test, and interobserver agreement). RESULTS: Thirty-five patients with 42 keloids were evaluated. Color Doppler ultrasound provided the diameters, including depth, and vascularity. On CDU, 76% were active and 24% inactive. Clinically, Observer 1 found 55% and Observer 2 found 88% of active keloids. Interobserver agreement between clinical observers was moderate (k = 0.42). Subclinical fistulous tracts, involvement of the hypodermis, muscle, and calcifications were also found on CDU. CONCLUSION: Color Doppler ultrasound can support the assessment of activity in keloids. Clinical evaluation alone can underestimate the activity in keloids. Relevant anatomical and subclinical features can be detected by CDU.

G ITAL DERMATOL VENEREOL. 2017 DEC;152(6):658-662.
INTRALESIONAL (INCISION) BIOPSY FOR MELANOMA DIAGNOSIS: THE RULES AND THE EXCEPTION.
Moscarella E, Argenziano G, Moreno C, Piana S, Lallas A, Lombardi M, Longo C, Ferrara G.

Intralesional (incision) biopsy for melanoma diagnosis can be warranted for large lesions or for those lesions whose in-toto excision leads to cosmetic and/or functional impairment. However, this diagnostic approach carries a risk of underdiagnosis, if a clinicopathologic diagnostic approach is not implemented. As a rule, in large pigmented lesions from special body areas (scalp and acral skin), clinicodermoscopic differential diagnosis of melanoma includes non-melanocytic skin lesions, traumatic skin changes, and nevi. The unique indication to incision biopsy for the differential diagnosis between nevus and melanoma is a relatively small nodular proliferation developing within a medium-large congenital nevus.

MED CLIN (BARC). 2017 SEP 20;149(6):256-260.
PYODERMA GANGRENOSUM: CLASSIC AND EMERGING THERAPIES.
Soto Vilches F, Vera-Kellet C.

Pyoderma gangrenosum is an ulceronecrotising dermatosis that represents a challenge for any clinician, not only for its ability to mimic other dermatoses but also for its lack of response to treatment. During the past year, there have been new studies about the efficacy of standard therapies, such as cyclosporine and systemic corticosteroids. These studies showed that classic treatment was comparable, but they are insufficient as monotherapy. That being said, new emerging therapies are becoming important, as the use of corticosteroid-sparing agents, tumour necrosis factor inhibitors or even surgery. This review updates the current evidence for the treatment of pyoderma gangrenosum.

MEDWAVE. 2017 APR 4;17(3):E6901.
LINEAR IMMUNOGLOBULIN A DERMATOSIS: A CASE REPORT.
Valenzuela Ahumada F, Bustos Macaya R, Romero Morgado GP, Sánchez Chacón M.

We present the case of a sixty five year old woman with two months history of pruritus and hyperpigmented annular lesions on the trunk, buttocks and upper extremities. In addition, she presents vesicles with healthy skin on the basis, in the flexor aspect of wrists. No evidence of mucosal involvement. Histological study showed subepidermal vesicular dermatitis with inflammatory infiltrate of neutrophils and eosinophils. Direct immunofluorescence evidenced linear and continuous deposition of immunoglobulin A in basement membrane zone, compatible with linear immunoglobulin A disease.

J ULTRASOUND MED. 2017 DEC;36(12):2403-2418.
SONOGRAPHIC COMPARISON OF MORPHOLOGIC CHARACTERISTICS BETWEEN PILONIDAL CYSTS AND HIDRADENITIS SUPPURATIVA.
Wortsman X, Castro A, Morales C, Franco C, Figueroa A.

OBJECTIVES: To compare the sonographic characteristics of pilonidal cysts and hidradenitis suppurativa. METHODS: A retrospective study of sonographic examinations was performed on 2 groups: 1 with pilonidal cysts and the other with hidradenitis suppurativa. The sonographic characteristics of the pilonidal cyst and hidradenitis suppurativa groups were analyzed, compared, and correlated, including an analysis of the histologic findings. For the pilonidal cyst group, the distribution, morphologic characteristics, location, shape, diameter, axis, vascularity, and scarring were also described. Statistical analyses included Spearman, Wilcoxon, Kruskall-Wallis, $\chi 2$, and Fisher tests. RESULTS: The sonographic examinations of 84 patients were reviewed: 43 with pilonidal cysts and 41 with hidradenitis suppurativa. The comparison of the morphologic characteristics of the key lesions between the pilonidal cyst and hidradenitis suppurativa groups showed no statistically significant differences ($P < .05$). Both groups had similar dermal and hypodermal saclike and bandlike structures that communicated with the widened base of the hair follicles. Retained fragments of hair tracts within the lesions were sonographically detected in both pilonidal cysts (100%) and hidradenitis suppurativa (83%) and also found on histologic specimens; however, the density of hair tracts per structure was higher in pilonidal cysts. Sonographic signs of scarring were absent in 63% of pilonidal cysts. Only 2% of pilonidal cysts showed communicating bandlike structures. CONCLUSIONS: Key lesions of pilonidal cysts and hidradenitis suppurativa have similar sonographic morphologic characteristics, which suggests that a pilonidal cyst may be a variant or localized form of hidradenitis suppurativa. The retained fragments of hair tracts frequently detected in both entities may be caused by ectopic production of hair and not by embedding. Common therapeutic strategies and research can be designed for both entities.

SKIN RES TECHNOL. 2017 MAY;23(2):243-248. 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.

SERVICIO TRAUMATOLOGÍA

FOOT ANKLE SURG. 2017 DEC 6. PII: S1268-7731(17)31358-9.

TECHNIQUE TIP: EDL-TO-EHL DOUBLE LOOP TRANSFER FOR EXTENSOR HALLUCIS LONGUS RECONSTRUCTION.

Bastías GF, Cuchacovich N, Schiff A, Carcuro G, Pellegrini MJ.

BACKGROUND: Extensor hallucis longus (EHL) tendon injuries often occur in the setting of lacerations to the dorsum of the foot. End-to-end repair is advocated in acute lacerations, or in chronic cases when the tendon edges are suitable for tension free repair. Reconstruction with allograft or autograft is advocated for cases not amenable to a primary direct repair. This is often seen in cases with tendon retraction and more commonly in the chronic setting. In many countries the use of allograft is very limited or unavailable making reconstruction with autograft and tendon transfers the primary choice of treatment. Tendon diameter mismatch and diminished resistance are common issues in other previously described tendon transfers. METHODS: We present the results of a new technique for reconstruction of non-reparable EHL lacerations in three patients using a dynamic double loop transfer of the extensor digitorum longus (EDL) of the second toe that addresses these issues. RESULTS: At one-year follow up, all patients recovered active/passive hallux extension with good functional (AOFAS Score) and satisfaction results. No reruptures or other complications were reported in this group of patients. No second toe deformities or dysfunction were reported. CONCLUSIONS: Second EDL-to-EHL Double Loop Transfer for Extensor Hallucis Longus reconstruction is a safe, reproducible and low-cost technique to address EHL ruptures when primary repair is not possible.

ACTA ORTOP MEX. 2017 MAY-JUN;31(3):128-133.

[EFFECT OF SPORTS TRAINING IN ANGULAR COMPARTMENT OF THE LOWER LIMBS IN CHILDREN FOOTBALLERS AGED 11 TO 12 YEARS OLD].

Burboa J, Bahamonde M, Inostroza M, Lillo P, Barahona M, Palet M, Hinzpeter J.

Anterior Cruciate Ligament (ACL) injury is an important cause of days lost in athletes. Most ACL injuries are non-contact and are associated with biomechanical risk factors that increase tension in the ACL: increased knee valgus (KV) and hip flexion (HF) and decreased flexion of knee (KF). Muscle around the knee contributes to knee stability, so fatigue produced by exercise could alter knee balance, increasing LCA tension. The aim of the study is to determine the angular behavior before and after a physical load for CF, RR and RV in children born in 2002-2003. A non-randomized clinical trial was conducted. The sample consisted of 50 students from soccer schools born between 2002 and 2003. The angular behavior of CF, RR and VR was compared, before and after performing standardized training. The angular behavior was measured by performing the DJ test with data obtained by inertial sensors. After exercise, the 3 variables increased, but only HF reached significant difference. Other important finding was the difference found in KV between the dominant leg and the support limb, at both times: rest and post exercise. It was concluded that the angular behavior of CF increases significantly in both limbs post-exercise and that preventive measures should be applied for the management of valgus in the supporting limb.

FOOT ANKLE SPEC. 2017 AUG;10(4):333-336.

CEMENT CASTING TO OPTIMIZE RECONSTRUCTION OF CHRONIC OSTEOCHONDRAL LESIONS OF THE TALUS.

Pulgar J, Escudero M, Carcuro G, Schiff A, Pellegrini M.

Few surgical techniques have been described for reconstruction in massive osteochondral lesions of the talus, and there is limited evidence of techniques for accurately reproducing native talar anatomy with bone auto/allograft techniques. In this article, we present a novel technique, which is highly reproducible, using bone cement to restore the congruence and anatomy of the ankle joint.

FOOT ANKLE SPEC. 2017 JUN;10(3):274-277.
MASSIVE CHONDROBLASTOMA OF THE TALUS: TREATMENT WITH EN BLOC TALECTOMY AND TIBIOCALCANEAL ARTHRODESIS: LONG-TERM FOLLOW-UP OF A CASE.
Bahamonde Munoz L, Escudero Heldt M.

Chondroblastomas are benign bone tumors that are usually located at epiphyseal regions of long bones, and are rarely located at the talus. The usual treatment consists of curettage and filling of the bone defect with bone either bone grafts or some other material, such as cement. The authors present a case of a massive chondroblastma of the talus, extending outside of bone boundaries and with a huge soft tissue mass and invasion of the adjacent calcaneus. Management included an en bloc talectomy through a double medial and lateral approach, and curettage and filling with cement of the calcaneal extension. Reconstruction was done by means of a tibiocalcaneal arthrodesis. At 11 years of follow-up, no tumor recurrence has occurred, and the AOFAS functional score is 83 out of 100 points.

DEPARTAMENTO DE MEDICINA

GASTROENTEROLOGÍA

HEPATITIS MONTHLY 2017;17:1-5.
PNPLA3 RS738409 I748M IS ASSOCIATED WITH STEATOHEPATITIS IN 434 NON-OBESE SUBJECTS WITH HEPATITIS C
Urzua, Alvaro; Mezzano, Gabriel; Brahm, Javier; Poniachik, Jaime; Miranda, Julio; Caceres, Dante D.; Carreno, Laura; Venegas.

Background: The polymorphism rs58542926 C > T (E167K) in the gene of transmembrane 6 superfamily member 2 (TM6SF2) has been identified as a determinant of hepatic steatosis and fibrosis in patients with non-alcoholic fatty liver disease. Only limited data have been published on this subject in chronic hepatitis C (CHC). Objectives: This study aimed to evaluate the effect ofTM6SF2 rs58542926 polymorphism on the risk of liver steatosis and fibrosis in Chilean patients with CHC infection. Methods: A total of 153 biopsied CHC patients were genotyped for TM6SF2 rs58542926 using PCR-RFLP methodology. The risk of fatty liver was assessed by comparing absence (< 5%) with presence (≥ 5%) of steatosis. The association with fibrosis was evaluated according to METAVIR score, by comparing patients in stage F0, F1, or F2 with patients in stage F3 or F4. Results: TM6SF2 rs58542926 genotype CC was found in 138 (90.2%) patients, whereas genotypes CTwas found in 15 (9.8%). No association was observed between rs58542926 genotype and risk of steatosis (OR 0.62,95% CI 0.17 - 2.22, P = 0.459) or fibrosis (OR1.07,95% CI 0.29-3.87, P = 0.923). Conclusions: TM6SF2 rs58542926 polymorphism is not associated with the risk of liver steatosis or fibrosis in Chilean patients with CHC

CASE REP GASTROINTEST MED. 2017;2017:8705195.
ASSOCIATION OF CHRONIC PANCREATITIS AND MALIGNANT MAIN DUCT IPMN: A RARE BUT DIFFICULT CLINICAL PROBLEM.
Berger Z, De La Fuente H, Meneses M, Matamala F, Sepúlveda M, Rojas C.

We report the case of a 70-year-old woman who consulted for recurrent short episodes of mild-to-moderate abdominal pain. Dilated main pancreatic duct was seen on CAT scan and magnetic resonance, with multiple calcifications and intraductal stones, typical in CP. However, for a more pronounced cystic dilatation in the pancreatic head, we could not exclude the coexistence of a main duct IPMN. ERCP was performed, with pancreatic sphincterotomy and extraction of pancreatic stones, but, at the same time, mucin extrusion was seen from the dilated duct through the papilla. Pancreatoduodenectomy was performed. Surgery and histology confirmed malignant IPMN with the typical image of chronic pancreatitis and intraductal stones in the vicinity. The patient is doing well 4 years after the surgery, without recurrence of the malignant disease, with changes of chronic pancreatitis in the pancreatic remnant. This paper discusses the possible relationships between the two entities and emphasizes the need of differential diagnosis.

J PEDIATR GASTROENTEROL NUTR. 2017 MAY;64(5):707-712.
PROTEIN MALNUTRITION DURING JUVENILE AGE INCREASES ILEAL AND COLONIC PERMEABILITY IN RATS.
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 are 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 and 60. LP-diet animals failed to gain weight and displayed decreased plasma zinc levels (a marker of micronutrient deficiency). In addition, transepithelial electrical resistance and occludin expression were 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.

FRONT PSYCHOL. 2017 DEC 18;8:2131.

CHILEAN ADAPTATION AND VALIDATION OF THE EARLY ADOLESCENT TEMPERAMENT QUESTIONNAIRE-REVISED VERSION.

Hoffmann M, Pérez JC, García C, Rojas G, Martínez V.

The aim of this study was to develop an adapted version of the Early Adolescent Temperament Questionnaire-Revised (EATQ-R) that would be valid and reliable for assessing temperament and its components in Chileans between 12 and 18 years of age. Originally, Ellis and Rothbart (2001) developed this questionnaire (EATQ-R) to be used in North American adolescents. For the study in Chile, a translation protocol was developed, to maintain the original instrument's cultural and linguistic equivalence in the adapted version. Psychometric properties of the EATQ-R, such as factor structure, internal consistency, and convergent validity, were also assessed. The adaption and validation was carried out in two stages, with two different studies. The first study, which included 612 adolescent students from educational establishments in the cities of Santiago and Concepcion, Chile, developed the Chilean version of the 83-item EATQ-R, which has 13 dimensions, belonging to 4 theoretical factors with adequate internal consistency (Cronbach's alpha = 0.79-0.82). The second study assessed the questionnaire's convergent validity, through its application to 973 adolescent students in Santiago. Results show that the effortful control subscale was significantly inversely related to indicators of adolescent maladjustment, such as substance abuse and behavioral problems. In addition, it was directly associated with indicators of self-concept, including self-esteem and self-efficacy. The opposite pattern was observed when considering negative affect. These findings coincide with current knowledge on the relationship between temperament and adjustment in adolescents.

J NEUROGASTROENTEROL MOTIL. 2017 APR 30;23(2):273-280.

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 contents 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 the colon. Forty-nine 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.

NEFROLOGÍA

SCI REP. 2017 MAR 17;7:44403.

VITAMIN D INHIBITS LYMPHANGIOGENESIS THROUGH VDR-DEPENDENT MECHANISMS.

Yazdani S, Poosti F, Toro L, Wedel J, Mencke R, Mirkovi K, de Borst MH, Alexander JS, Navis G, van Goor H, van den Born J, Hillebrands JL.

Excessive lymphangiogenesis is associated with cancer progression and renal disease. Attenuation of lymphangiogenesis might represent a novel strategy to target disease progression although clinically approved anti-lymphangiogenic drugs are not available yet. VitaminD(VitD)-deficiency is associated with increased cancer risk and chronic kidney disease. Presently, effects of VitD on lymphangiogenesis are unknown. Given the apparently protective effects of VitD and the deleterious associations of lymphangiogenesis with renal disease, we here tested the hypothesis that VitD has direct anti-lymphangiogenic effects in vitro and is able to attenuate lymphangiogenesis in vivo. In vitro cultured mouse lymphatic endothelial cells (LECs) expressed VitD Receptor (VDR), both on mRNA and protein levels. Active VitD (calcitriol) blocked LEC tube formation, reduced LEC proliferation, and induced LEC apoptosis. siRNA-mediated VDR knock-down reversed the inhibitory effect of calcitriol on LEC tube formation, demonstrating how such inhibition is VDR-dependent. In vivo, proteinuric rats were treated with vehicle or paricalcitol for 6 consecutive weeks. Compared with vehicle-treated proteinuric rats, paricalcitol showed markedly reduced renal lymphangiogenesis. In conclusion, our data show that VitD is anti-lymphangiogenic through VDR-dependent anti-proliferative and pro-apoptotic mechanisms. Our findings highlight an important novel function of VitD demonstrating how it may have therapeutic value in diseases accompanied by pathological lymphangiogenesis.

FRONT PHYSIOL. 2017 JUN 13;8:379.

HUMAN PERITONEAL MESOTHELIAL CELL DEATH INDUCED BY HIGH-GLUCOSE HYPERTONIC SOLUTION INVOLVES CA2+ AND NA+ IONS AND OXIDATIVE STRESS WITH THE PARTICIPATION OF PKC/NOX2 AND PI3K/AKT PATHWAYS.

Simon F, Tapia P, Armisen R, Echeverria C, Gatica S, Vallejos A, Pacheco A, Sanhueza ME, Alvo M, Segovia E, Torres R.

Chronic peritoneal dialysis (PD) therapy is equally efficient as hemodialysis while providing greater patient comfort and mobility. Therefore, PD is the treatment of choice for several types of renal patients. During PD, a high-glucose hyperosmotic (HGH) solution is administered into the peritoneal cavity to generate an osmotic gradient that promotes water and solutes transport from peritoneal blood to the dialysis solution. Unfortunately, PD has been associated with a loss of peritoneal viability and function through the generation of a severe inflammatory state that induces human peritoneal mesothelial cell (HPMC) death. Despite this deleterious effect, the precise molecular mechanism of HPMC death as induced by HGH solutions is far from being understood. Therefore, the aim of this study was to explore the pathways involved in HGH solution-induced HPMC death. HGH-induced HPMC death included influxes of intracellular Ca2+ and Na+. Furthermore, HGH-induced HPMC death was inhibited by antioxidant and reducing agents. In line with this, HPMC death was induced solely by increased oxidative stress. In addition to this, the cPKC/NOX2 and PI3K/Akt intracellular signaling pathways also participated in HGH-induced HPMC death. The participation of PI3K/Akt intracellular is in agreement with previously shown in rat PMC apoptosis. These findings contribute toward fully elucidating the underlying molecular mechanism mediating peritoneal mesothelial cell death induced by high-glucose solutions during peritoneal dialysis.

RESPIRATORIO

J AM MED DIR ASSOC. 2017 DEC 1;18(12):1097.E11-1097.E24.

REDEFINING CUT-POINTS FOR HIGH SYMPTOM BURDEN OF THE GLOBAL INITIATIVE FOR CHRONIC OBSTRUCTIVE LUNG DISEASE CLASSIFICATION IN 18,577 PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

Smid DE, Franssen FME, Gonik M, Miravitlles M, Casanova C, Cosio BG, de Lucas-Ramos P, Marin JM, Martinez C, Mir I, Soriano JB, de Torres JP, Agusti A, Atalay NB, Billington J, Boutou AK, Brighenti-Zogg S, Chaplin E, Coster S, Dodd JW, Dürr S, Fernandez-Villar A, Groenen MTJ, Guimarães M, Hejduk K, Higgins V, Hopkinson NS, Horita N, Houben-Wilke S, Janssen DJA, Jehn M, Joerres R, Karch A, Kelly JL, Kim YI, Kimura H, Koblizek V, Kocks JH, Kon SSC, Kwon N, Ladeira I, Lee SD, Leuppi JD, Locantore N, Lopez-Campos JL, D-C Man W, Maricic L, Mendoza L et al.

BACKGROUND: Patients with chronic obstructive pulmonary disease (COPD) can be classified into groups A/C or B/D based on symptom intensity. Different threshold values for symptom questionnaires can result in misclassification and, in turn, different treatment recommendations. The primary aim was to find the best fitting cut-points for Global initiative for chronic Obstructive Lung Disease (GOLD) symptom measures, with an modified Medical Research Council dyspnea grade of 2 or higher as point of reference. METHODS: After a computerized search, data from 41 cohorts and whose authors agreed to provide data were pooled. COPD studies were eligible for analyses if they included, at least age, sex, postbronchodilator spirometry, modified Medical Research Council, and COPD Assessment Test (CAT) total scores. MAIN OUTCOMES: Receiver operating characteristic curves and the Youden index were used to determine the best calibration threshold for CAT, COPD Clinical Questionnaire, and St. Georges Respiratory Questionnaire total scores. Following, GOLD A/B/C/D frequencies were calculated based on current cut-points and the newly derived cut-points. FINDINGS: A total of 18,577 patients with COPD [72.0% male; mean age: 66.3 years (standard deviation 9.6)] were analyzed. Most patients had a moderate or severe degree of airflow limitation (GOLD spirometric grade 1, 10.9%; grade 2, 46.6%; grade 3, 32.4%; and grade 4, 10.3%). The best calibration threshold for CAT total score was 18 points, for COPD Clinical Questionnaire total score 1.9 points, and for St. Georges Respiratory Questionnaire total score 46.0 points. CONCLUSIONS: The application of these new cut-points would reclassify about one-third of the patients with COPD and, thus, would impact on individual disease management. Further validation in prospective studies of these new values are needed.

PLOS ONE. 2017 NOV 15;12(11):E0186777.

ADHERENCE TO INHALED THERAPIES OF COPD PATIENTS FROM SEVEN LATIN AMERICAN COUNTRIES: THE LASSYC STUDY.

Montes de Oca M, Menezes A, Wehrmeister FC, Lopez Varela MV, Casas A, Ugalde L, Ramirez-Venegas A, Mendoza L, López A, Surmont F, Miravitlles M.

BACKGROUND: This study assessed the adherence profiles to inhaled therapies and the agreement between two patient self-report adherence methods in stable COPD lpatients from seven Latin American countries. METHODS: This observational, cross-sectional, multinational, multicenter study involved 795 COPD patients (post-bronchodilator forced expiratory volume in 1 second/forced vital capacity [FEV1/FVC] <0.70). Adherence to inhaled therapy was assessed using the specific Test of Adherence to Inhalers (10-item TAI) and the generic 8-item Morisky Medication Adherence Scale (MMAS-8) questionnaires. The percentage agreement and the kappa index were used to compare findings. RESULTS: 59.6% of patients were male (69.5±8.7 years); post-bronchodilator FEV1 percent predicted was 50.0±18.6%. Mean values for 10-item TAI and MMAS-8 questionnaires were 47.4±4.9 and 6.8±1.6, respectively. Based on the TAI questionnaire, 54.1% of patients had good, 26.5% intermediate, and 19.4% poor adherence. Using the MMAS-8 questionnaire, 51% had high, 29.1% medium, and 19.9% low adherence. According to both questionnaires, patients with poor adherence had lower smoking

history, schooling but higher COPD Assessment Test score, exacerbations in the past-year and post-bronchodilator FEV1. The agreement between 10-item TAI and MMAS-8 questionnaires was moderate (Kappa index: 0.42; agreement: 64.7%). CONCLUSION: Suboptimal adherence to medication was frequent in COPD patients from Latin America. Low adherence was associated with worse health status impairment and more exacerbations. There was inadequate agreement between the two questionnaires. Greater effort should be made to improve COPD patients' adherence to treatment, and assessment of adherence with more specific instruments, such as the TAI questionnaire, would be more convenient in these patients.

CURR INFECT DIS REP. 2017 MAR;19(3):11.
RISK FACTORS FOR DRUG-RESISTANT CAP IN IMMUNOCOMPETENT PATIENTS.
Arancibia F, Ruiz M.

PURPOSE OF REVIEW: The increase in drug-resistant community-acquired pneumonia (CAP) is an important problem all over the world. This article explores the current state of antimicrobial resistance of different bacteria that cause CAP and also assesses risk factors to identify those pathogens. RECENT FINDINGS: In the last two decades, it has been documented that there is a significant increase in drug-resistant Streptococcus pneumoniae and other bacteria causing CAP. The most important risk factors are overuse of antibiotics, prior hospitalization, and lung comorbidities. The direct consequences can be severe, including prolonged stays in hospital, increased costs, and morbi-mortality. However, drug-resistant CAP declined after the introduction of the pneumococcal conjugate vaccine. This review found an increase in resistance to the antibiotics used in CAP, and the risk factor can be used for identifying patients with drug-resistant CAP and initiate appropriate treatment. Judicious use of antibiotics and the development of effective new vaccines are needed.

BMJ OPEN. 2017 AUG 11;7(8):E015731.
THE BOUNDARIES OF MILD CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): DESIGN OF THE SEARCHING CLINICAL COPD ONSET (SOON) STUDY.
Labarca G, Bustamante A, Valdivia G, Díaz R, Huete Á, Mac Nab P, Mendoza L, Leppe J, Lisboa C, Saldías F, Díaz O.

INTRODUCTION: Clinical onset of chronic obstructive pulmonary disease (COPD) is the point at which the disease is first identifiable by physicians. It is a poorly defined stage which seems to include both mild spirometric and non-spirometric disease, and could be described as early grade COPD, for practical purposes. While dyspnoea; chronic bronchitis and CT imaging evidence of emphysema and airway disease may be present very early, the lone significance of dyspnoea, the most relevant symptom in COPD in identifying these individuals, has been scarcely assessed.The Searching Clinical COPD Onset (SOON) Study was designed primarily to detect clinical, physiological and structural differences between dyspnoeic and non-dyspnoeic individuals with early grade COPD. It is hypothesised that presence of dyspnoea in early disease may identify a subtype of individuals with reduced exercise capacity, notwithstanding of their spirometry results. In addition, dyspnoeic individuals will share worse quality of life, lower physical activity, greater lung hyperinflation greater emphysema and airway thickness and reduced peripheral muscle mass than their non-dyspnoeic counterpart. METHODS AND ANALYSIS: SOON is a monocentric study, with a cross sectional design aimed at obtaining representative samples of current or ex-smoker-adults aged ≥45 and ≤80 years. Two hundred and forty participants will be enrolled into four strata, according to normal spirometry or mild spirometric obstruction and presence or not of dyspnoea modified Medical Research Council score ≥1. The primary outcome will be the difference between dyspnoeic and non-dyspnoeic individuals on the 6-min walk test performance, regardless of their spirometry results. To account for the confounding effect of heart failure on dyspnoea, stress echocardiography will be also performed. Secondary outcomes will include clinical (quality of life, physical activity), physiological (exercise testing) and structural characteristics (emphysema, airway disease and peripheral muscle mass by CT imaging). ETHICS AND DISSEMINATION: The Institutional Ethics Committee from Pontificia Universidad Católica de Chile has approved the study protocol and signed informed consent will be obtained from all participants. The findings of the trial will be disseminated through relevant peer-reviewed journals and international conference presentations.

MEDICINA NUCLEAR

SEMIN NUCL MED. 2017 NOV;47(6):687-693.
COMPREHENSIVE AUDITING IN NUCLEAR MEDICINE THROUGH THE INTERNATIONAL ATOMIC ENERGY AGENCY QUALITY MANAGEMENT AUDITS IN NUCLEAR MEDICINE PROGRAM. PART 2: ANALYSIS OF RESULTS.
Dondi M, Torres L, Marengo M, Massardo T, Mishani E, Van Zyl Ellmann A, Solanki K, Bischof Delaloye A, Lobato EE, Miller RN, Ordonez FB, Paez D, Pascual T.

The International Atomic Energy Agency has developed a program, named Quality Management Audits in Nuclear Medicine (QUANUM), to help its Member States to check the status of their nuclear medicine practices and their adherence to international reference standards, covering all aspects of nuclear medicine, including quality assurance/quality control of instrumentation, radiopharmacy (further subdivided into levels 1, 2, and 3, according to complexity of work), radiation safety, clinical applications, as well as managerial aspects. The QUANUM program is based on both internal and external audits and, with specifically developed Excel spreadsheets, it helps assess the level of conformance (LoC)

to those previously defined quality standards. According to their level of implementation, the level of conformance to requested standards; 0 (absent) up to 4 (full conformance). Items scored 0, 1, and 2 are considered non-conformance; items scored 3 and 4 are considered conformance. To assess results of the audit missions performed worldwide over the last 8 years, a retrospective analysis has been run on reports from a total of 42 audit missions in 39 centers, three of which had been re-audited. The analysis of all audit reports has shown an overall LoC of 73.9 ± 8.3% (mean ± standard deviation), ranging between 56.6% and 87.9%. The highest LoC has been found in the area of clinical services (83.7% for imaging and 87.9% for therapy), whereas the lowest levels have been found for Radiopharmacy Level 2 (56.6%); Computer Systems and Data Handling (66.6%); and Evaluation of the Quality Management System (67.6%). Prioritization of non-conformances produced a total of 1687 recommendations in the final audit report. Depending on the impact on safety and daily clinical activities, they were further classified as critical (requiring immediate action; n = 276; 16% of the total); major (requiring action in relatively short time, typically from 3 to 6 months; n = 604; 36%); whereas the remaining 807 (48%) were classified as minor, that is, to be addressed whenever possible. The greatest proportion of recommendations has been found in the category "Managerial, Organization and Documentation" (26%); "Staff Radiation Protection and Safety" (17.3%); "Radiopharmaceuticals Preparation, Dispensing and Handling" (15.8%); and "Quality Assurance/ Quality Control" and "Management of Equipment and Software" (11.4%). The lowest level of recommendations belongs to the item "Human Resources" (4%). The QUANUM program proved applicable to a wide variety of institutions, from small practices to larger centers with PET/ CT and cyclotrons. Clinical services rendered to patients showed a good compliance with international standards, whereas issues related to radiation protection of both staff and patients will require a higher degree of attention. This is a relevant feedback for the International Atomic Energy Agency with regard to the effective translation of safety recommendations into routine practice. Training on drafting and application of standard operating procedures should also be considered a priority.

SEMIN NUCL MED. 2017 NOV;47(6):680-686.

COMPREHENSIVE AUDITING IN NUCLEAR MEDICINE THROUGH THE INTERNATIONAL ATOMIC ENERGY AGENCY QUALITY MANAGEMENT AUDITS IN NUCLEAR MEDICINE (QUANUM) PROGRAM. PART 1: THE QUANUM PROGRAM AND METHODOLOGY.

Dondi M, Torres L, Marengo M, Massardo T, Mishani E, Van Zyl Ellmann A, Solanki K, Bischof Delaloye A, Lobato EE, Miller RN, Paez D, Pascual T.

An effective management system that integrates quality management is essential for a modern nuclear medicine practice. The Nuclear Medicine and Diagnostic Imaging Section of the International Atomic Energy Agency (IAEA) has the mission of supporting nuclear medicine practice in low- and middle-income countries and of helping them introduce it in their health-care system, when not yet present. The experience gathered over several years has shown diversified levels of development and varying degrees of quality of practice, among others because of limited professional networking and limited or no opportunities for exchange of experiences. Those findings triggered the development of a program named Quality Management Audits in Nuclear Medicine (QUANUM), aimed at improving the standards of NM practice in low- and middle-income countries to internationally accepted standards through the introduction of a culture of quality management and systematic auditing programs. QUANUM takes into account the diversity of nuclear medicine services around the world and multidisciplinary contributions to the practice. Those contributions include clinical, technical, radiopharmaceutical, and medical physics procedures. Aspects of radiation safety and patient protection are also integral to the process. Such an approach ensures consistency in providing safe services of superior quality to patients. The level of conformance is assessed using standards based on publications of the IAEA and the International Commission on Radiological Protection, and guidelines from scientific societies such as Society of Nuclear Medicine and Molecular Imaging (SNMMI) and European Association of Nuclear Medicine (EANM). Following QUANUM guidelines and by means of a specific assessment tool developed by the IAEA, auditors, both internal and external, will be able to evaluate the level of conformance. Nonconformances will then be prioritized and recommendations will be provided during an exit briefing. The same tool could then be applied to assess any improvement after corrective actions are taken. This is the first comprehensive audit program in nuclear medicine that helps evaluate managerial aspects, safety of patients and workers, clinical practice, and radiopharmacy, and, above all, keeps them under control all together, with the intention of continuous improvement.

REV ESP MED NUCL IMAGEN MOL. 2017 NOV - DEC;36(6):377-387.

RISK STRATIFICATION OF CORONARY ARTERY DISEASE USING RADIONUCLIDES. CURRENT STATUS OF CLINICAL PRACTICE.

Massardo T, Alarcón L, Spuler J.

A discussion is presented on the current use of radioisotopes for evaluation of coronary artery disease in relation to other available techniques. The review is focused on coronary artery disease risk stratification employing single photon emission computed tomography and positron emission tomography, as well as on ischaemic cardiomyopathy and myocardial viability applications. Concepts are presented regarding coronary blood flow reserve, diagnostic and prognostic values, criteria for its appropriate use, as well as current methods to reduce unnecessary patient irradiation, in order to optimise nuclear cardiology practice.

REUMATOLOGÍA

INVEST OPHTHALMOL VIS SCI. 2017 FEB 1;58(2):974-980.

EVALUATION OF THE GLUCOCORTICOID RECEPTOR AS A BIOMARKER OF TREATMENT RESPONSE IN VOGT-KOYANAGI-HARADA DISEASE.
Urzua CA, Guerrero J, Gatica H, Velasquez V, Goecke A.

PURPOSE: This study is aimed to investigate the role of glucocorticoid receptor (GR) isoforms in peripheral blood mononuclear cells (PBMC) as biomarkers of glucocorticoid (GC) resistance and to validate a set of clinical predictive factors in patients with Vogt-Koyanagi-Harada (VKH) disease. METHODS: This was a prospective cohort study that included a total of 21 patients with VKH. A complete ophthalmologic evaluation was carried out at baseline that recorded the presence of any clinical predictive factors (visual acuity ≤ 20/200, tinnitus, chronic disease, and fundus depigmentation). Real-time quantitative PCR was performed to measure the mRNA levels of GR alpha (GRα) and beta (GRβ) isoforms at baseline and at 2 weeks after prednisone therapy initiation. RESULTS: There were no differences between GRα and GRβ levels in GC-sensitive and GC-resistant patients at baseline before treatment initiation. After 2 weeks of prednisone treatment, GC-sensitive patients had a median 5.5-fold increase in levels of GRα, whereas GC-resistant patients had a median 0.7-fold decrease in levels of this isoform (P = 0.003). Similarly, GRβ increased in GC-sensitive patients, in comparison with GR-resistant patients (6.49-fold versus 1.01 fold, respectively, I = 0.04). The mRNA levels of GR isoforms were independent of disease activity. Fundus depigmentation and chronic disease at diagnosis were associated with GC resistance (P = 0.03, odds ratio = 21.0; and P = 0.008, odds ratio = 37.8, respectively). However, associations with visual acuity or tinnitus were not confirmed in this study. CONCLUSIONS: The evaluation of clinical predictive factors and determination of the change in expression of GR isoforms as potential biomarkers can contribute to the early identification of GC-resistant patients with VKH.

REUMATOL CLIN. 2017 JUL - AUG;13(4):201-209.

TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, FOR THE TREATMENT OF LATIN AMERICAN PATIENTS WITH RHEUMATOID ARTHRITIS: POOLED EFFICACY AND SAFETY ANALYSES OF PHASE 3 AND LONG-TERM EXTENSION STUDIES.
Radominski SC, Cardiel MH, Citera G, Goecke A, Jaller JJ, Lomonte ABV, Miranda P, Velez P, Xibillé D, Kwok K, Rojo R, García EG.

OBJECTIVE: Tofacitinib is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA). We assessed tofacitinib efficacy and safety in the Latin American (LA) subpopulation of global Phase 3 and long-term extension (LTE) studies. MATERIALS AND METHODS: Data from LA patients with RA and inadequate response to disease-modifying antirheumatic drugs (DMARDs) were pooled across five Phase 3 studies. Phase 3 patients received tofacitinib 5 or 10mg twice daily (BID), adalimumab or placebo; patients in the single LTE study received tofacitinib 5 or 10mg BID; treatments were administered alone or with conventional synthetic DMARDs. Efficacy was reported up to 12 months (Phase 3) and 36 months (LTE) by American College of Rheumatology (ACR) 20/50/70 response rates, Disease Activity Score (DAS)28-4(erythrocyte sedimentation rate [ESR]) and Health Assessment Questionnaire-Disability Index (HAQ-DI). Incidence rates (IRs; patients with event/100 patient-years) of adverse events (AEs) of special interest were reported. RESULTS: The Phase 3 studies randomized 496 LA patients; the LTE study enrolled 756 LA patients from Phase 2 and Phase 3. In the Phase 3 studies, patients who received tofacitinib 5 and 10mg BID showed improvements vs placebo at Month 3 in ACR20 (68.9% and 75.7% vs 35.6%), ACR50 (45.8% and 49.7% vs 20.7%) and ACR70 (17.5% and 23.1% vs 6.9%) responses, mean change from baseline in HAQ-DI (-0.6 and -0.8 vs -0.3) and DAS28-4(ESR) score (-2.3 and -2.4 vs -1.4). The improvements were sustained up to Month 36 in the LTE study. In the Phase 3 studies, IRs with tofacitinib 5 and 10mg BID and placebo were 7.99, 6.57 and 9.84, respectively, for SAEs, and 3.87, 5.28 and 3.26 for discontinuation due to AEs. IRs of AEs of special interest in tofacitinib-treated LA patients were similar to the global population. CONCLUSION: In Phase 3 and LTE studies in LA patients with RA, tofacitinib demonstrated efficacy up to 36 months with a manageable safety profile up to 60 months, consistent with the overall tofacitinib study population.

LPS REGULATES THE EXPRESSION OF GLUCOCORTICOID RECEPTOR α AND β ISOFORMS AND INDUCES A SELECTIVE GLUCOCORTICOID RESISTANCE IN VITRO
Maria Luisa Molina, Julia Guerrero, John A. Cidlowski, Héctor Gatica, Annelise Goecke.

Background. This study was aimed to evaluate the effect of LPS in glucocorticoid receptor (GR) isoforms expression on different cell lines and PBMC from healthy donors in vitro and glucocorticoid sensitivity of PBMC in vitro. Methods. U-2 OS cell lines expressing GR isoforms, different cell lines (CEM, RAJI, K562 and HeLa) or PBMC from healthy donors, were cultured or not with LPS. The expression of GRα and GRβ was evaluated by Western blot. Glucocorticoid sensitivity was evaluated in PBMC treated with LPS, testing genes which are transactivated or transrepressed by glucocorticoid. For transactivated genes (MKP1, FKBP5) PBMC were treated with Dexamethasone 100 nM for 6 h. The mRNA expression was measured by RT-PCR. For transrepressed genes (IL-8, GM-CSF), PBMC were cultured in Dexamethasone 100 nM and LPS 10 μg/ml for 6 h and protein expression was measure by ELISA. Results. GR isoforms were induced in U-2 OS cells with a greater effect on GRα expression. Both isoforms were also induced in CEM cells with a tendency to a greater effect on GRβ. LPS induced only the expression of GRα in Raji and HeLa cells, and in PBMC, with no effect in K562 cells. LPS induced a loss of glucocorticoid inhibitory effect only on the secretion of GM-CSF. Conclusion. LPS in vitro differentially modulates the expression of GR isoforms in a cell specific manner. In PBMC from healthy donors LPS induces an approximately two times increase in the expression of GRα and a loss of the glucocorticoid inhibitory effect on the secretion of GM-CSF, without affecting other glucocorticoid responses evaluated.

ENDOCRINOLOGÍA

ONCOL LETT. 2017 MAY;13(5):3787-3792.

ASSOCIATION BETWEEN NON-MELANOMA AND MELANOMA SKIN CANCER RATES, VITAMIN D AND LATITUDE.

Rivas M, Rojas E, Calaf GM, Barberán M, Liberman C, Paula Correa M.

Vitamin D synthesis takes place in the skin due to solar ultraviolet-B (UVB) radiation. Several studies have shown the association between low sun exposure, non-melanoma skin cancer (NMSC) and a lack of vitamin D synthesis. Since such synthesis in the body depends on the exposure of the skin to solar UVB radiation (290-320 nm), experimental measurements of this type of solar radiation are important. Tarapaca University in Arica, Chile, established a solar UV radiation laboratory in 2006 and since then this laboratory has performed systematic experimental solar UVB measurements using a calibrated biometer instrument. The results, which are presented in the current study, showed the association between NMSC and MSC rates, and the time required to produce 1,000 IU vitamin D with latitudinal variation. Solar UV index (UVI) levels reported in 6 cities from the north to the south of Chile indicated that the UVI ratio of monthly mean values was 1.8 times higher in Arica than in Punta Arenas in January (summer in Chile), whereas it was 14 times higher in June (winter). This factor is an important consideration, since vitamin D synthesis is directly associated with the exposure of individuals to solar UVB radiation. A similar trend was observed in Antofagasta, Santiago, Concepcion, Valdivia and Punta Arenas. It can be concluded from these data that there is a direct association between NMSC rates and mortality, and UVB radiation, meaning that this type of cancer would not depend on vitamin D synthesis and therefore on calcium uptake. By contrast, MSC rates increased with decreased levels of vitamin D, and thus calcium uptake, in all cities, with the only exception being Punta Arenas.

THYROID. 2017 AUG;27(8):1058-1067.

A 10-GENE CLASSIFIER FOR INDETERMINATE THYROID NODULES: DEVELOPMENT AND MULTICENTER ACCURACY STUDY.

González HE, Martínez JR, Vargas-Salas S, Solar A, Veliz L, Cruz F, Arias T, Loyola S, Horvath E, Tala H, Traipe E, Meneses M, Marín L, Wohllk N, Diaz RE, Véliz J, Pineda P, Arroyo P, Mena N, Bracamonte M, Miranda G, Bruce E, Urra S.

BACKGROUND: In most of the world, diagnostic surgery remains the most frequent approach for indeterminate thyroid cytology. Although several molecular tests are available for testing in centralized commercial laboratories in the United States, there are no available kits for local laboratory testing. The aim of this study was to develop a prototype in vitro diagnostic (IVD) gene classifier for the further characterization of nodules with an indeterminate thyroid cytology. METHODS: In a first stage, the expression of 18 genes was determined by quantitative polymerase chain reaction (qPCR) in a broad histopathological spectrum of 114 fresh-tissue biopsies. Expression data were used to train several classifiers by supervised machine learning approaches. Classifiers were tested in an independent set of 139 samples. In a second stage, the best classifier was chosen as a model to develop a multiplexed-qPCR IVD prototype assay, which was tested in a prospective multicenter cohort of fine-needle aspiration biopsies. RESULTS: In tissue biopsies, the best classifier, using only 10 genes, reached an optimal and consistent performance in the ninefold cross-validated testing set (sensitivity 93% and specificity 81%). In the multicenter cohort of fine-needle aspiration biopsy samples, the 10-gene signature, built into a multiplexed-qPCR IVD prototype, showed an area under the curve of 0.97, a positive predictive value of 78%, and a negative predictive value of 98%. By Bayes' theorem, the IVD prototype is expected to achieve a positive predictive value of 64-82% and a negative predictive value of 97-99% in patients with a cancer prevalence range of 20-40%. CONCLUSIONS: A new multiplexed-qPCR IVD prototype is reported that accurately classifies thyroid nodules and may provide a future solution suitable for local reference laboratory testing.

ONCOLOGÍA

PLOS GENET. 2017 MAY 25;13(5):E1006756.

SUBTYPES OF NATIVE AMERICAN ANCESTRY AND LEADING CAUSES OF DEATH: MAPUCHE ANCESTRY-SPECIFIC ASSOCIATIONS WITH GALLBLADDER CANCER RISK IN CHILE

Justo Lorenzo Bermejo, Felix Boekstegers, Rosa González Silos, Katherine Marcelain, Pablo Baez Benavides, Carol Barahona Ponce, Bettina Müller, Catterina Ferreccio, Jill Koshiol, Christine Fischer, Barbara Peil, Janet Sinsheimer, Macarena Fuentes Guajardo, Olga Barajas, Rolando Gonzalez-Jose, Gabriel Bedoya, Maria Cátira Bortolini, Samuel Canizales-Quinteros, Carla Gallo, Andres Ruiz Linares, Francisco Rothhammer.

Latin Americans are highly heterogeneous regarding the type of Native American ancestry. Consideration of specific associations with common diseases may lead to substantial advances in unraveling of disease etiology and disease prevention. Here we investigate possible associations between the type of Native American ancestry and leading causes of death. After an aggregate-data study based on genome-wide genotype data from 1805 admixed Chileans and 639,789 deaths, we validate an identified association with gallbladder cancer relying on individual data from 64 gallbladder cancer patients, with and without a family history, and 170 healthy controls. Native American proportions were markedly underestimated when the two main types of Native American ancestry in Chile, originated from the Mapuche and Aymara indigenous peoples, were combined together. Consideration of the type of Native American ancestry was crucial to identify disease associations. Native American ancestry showed no association with gallbladder cancer mortality (P = 0.26). By contrast, each 1%

increase in the Mapuche proportion represented a 3.7% increased mortality risk by gallbladder cancer (95%CI 3.1–4.3%, P = 6×10–27). Individual-data results and extensive sensitivity analyses confirmed the association between Mapuche ancestry and gallbladder cancer. Increasing Mapuche proportions were also associated with an increased mortality due to asthma and, interestingly, with a decreased mortality by diabetes. The mortality due to skin, bladder, larynx, bronchus and lung cancers increased with increasing Aymara proportions. Described methods should be considered in future studies on human population genetics and human health. Complementary individual-based studies are needed to apportion the genetic and non-genetic components of associations identified relying on aggregate-data.

FUTURE ONCOL. 2017 NOV;13(27):2455-2472.

CANCER PAIN MANAGEMENT: RECOMMENDATIONS FROM A LATIN-AMERICAN EXPERTS PANEL.

Escobar Alvarez Y, Agamez Insignares C, Ahumada Olea M, Barajas O, Calderillo G, Calvache Guamán JC, Caponero R, Cavenago Salazar BA, Del Giglio A, Pupo Araya AR, Villalobos-Valencia R, Yepes Pérez A, Zumelzu Delgado N.

Generating a consensus in the Latin-American region on cancer pain management is a current need. Thus a panel of Latin-American experts met in Madrid in March 2017 in order to review the published literature, discuss the best approach for cancer pain classification and evaluation and also make recommendations of pharmacological and nonpharmacological therapies for cancer pain management improvement in Latin-American countries. The result of that meeting is presented in this document. The experts participating were from Costa Rica, Mexico, Chile, Colombia, Peru, Brazil and Ecuador, and the project coordinator was from Spain.

J MINIM INVASIVE GYNECOL. 2017 MAR - APR;24(3):466-472.

LAPAROSCOPIC MANAGEMENT OF URETERAL ENDOMETRIOSIS AND HYDRONEPHROSIS ASSOCIATED WITH ENDOMETRIOSIS.

Alves J, Puga M, Fernandes R, Pinton A, Miranda I, Kovoor E, Wattiez A.

STUDY OBJECTIVE: To evaluate if laparoscopic treatment of ureteral endometriosis is feasible, safe, and effective and to determine if ureteral dilatation and/or the number of incisions increases complications. DESIGN: An institutional review board-approved retrospective cohort study of consecutive patients who underwent surgery for deep infiltrating endometriosis involving the ureter with hydronephrosis (Canadian Task Force classification III). SETTING: A university hospital. PATIENTS: Of 658 patients who had surgery for deep infiltrating endometriosis between November 2004 and December 2013, 198 of the 658 patients had ureteral endometriosis and required ureterolysis, and 28 of the 198 patients were identified with ureteral dilatation and hydronephrosis associated with endometriosis. INTERVENTIONS: Of these 28 cases, 15 ureterolyses, 12 reanastomoses, and 1 reimplantation were performed. MEASUREMENTS AND MAIN RESULTS: Medical, operative, and pathological data on the evolution of pain, urinary complaints, fertility, complications, and recurrences were collected from clinical records. Additionally, telephone interviews were performed for the follow-up of long-term outcomes. All 28 patients had concomitant surgical procedures because of endometriosis elsewhere in the pelvis or abdomen; 12 (42.9%) underwent surgery of the bowel, whereas 5 (17.9%) had bladder surgery. The evolution of pain after surgery showed a positive response (mean dysmenorrhea evaluation measured by the Numeric Pain Rating Scale from 0-10 preoperatively at the short-term follow-up and the long-term follow-up: 7.25-1.73 and 0.25, respectively). Three complications were noted in the group of 28 patients with ureterohydronephrosis; 1 required surgical reintervention. Logistic regression analyses found vaginal incision (odds ratio = 2.08; 95% CI 0.92-4.73), bladder incision (odds ratio = 8.77; 95% CI 3.25-23.63), number of incisions (odds ratio = 2.12; 95% CI 1.29-3.47), and number of previous surgeries (odds ratio = 1.26; 95% CI 0.93-1.71) as independent risk factors for complications in the group of 198 patients. Three patients underwent reoperation in the group of 28 patients: 1 for ureterovaginal fistula, 1 for persistent ureter dilatation and hydronephrosis, and 1 for persistent pain. CONCLUSION: Laparoscopically assisted ureterolyses, ureteral reanastomoses, and ureteral reimplantation are feasible, safe, and effective treatments for ureteral endometriosis. Complete laparoscopic excision is possible with minimal complications, which seem to be associated with the number of incisions. Ureteral endometriosis should be suspected in all cases of deep infiltrating endometriosis.

GERIATRÍA

J GERONTOL A BIOL SCI MED SCI. 2017 DEC 30.

LOCAL KLOTHO ENHANCES NEURONAL PROGENITOR PROLIFERATION IN THE ADULT HIPPOCAMPUS.

Salech F, Varela-Nallar L, Arredondo SB, Bustamante DB, Andaur GA, Cisneros R, Ponce DP, Ayala P, Inestrosa NC, Valdés JL, Behrens MI, Couve A.

Klotho is an aging-related protein associated with hippocampal cognitive performance in mammals. Klotho regulates progenitor cell proliferation in non-neuronal tissues, but its role in adult hippocampal neurogenesis (AHN) has not been explored. Klotho expression in the adult mouse hippocampus was examined by immunofluorescence and PCR. AHN was evaluated in the hippocampus of klotho knock-out mice (KO), klotho KO/vitamin D-receptor mutant mice, and in a model of local klotho hippocampal knockdown. The recombinant Klotho effect on proliferation was measured in mouse-derived hippocampal neural progenitor cells. Hippocampal-dependent memory was assessed by a dry-land version of the Morris water maze. Klotho was expressed in the granular cell layer of the adult Dentate Gyrus. AHN was increased in klotho KO mice, but not in klotho KO/vitamin D-receptor mutant mice. Inversely, local downregulation of hippocampal

Klotho diminished AHN. Recombinant Klotho increased the proliferation rate of neural progenitors. Downregulation of hippocampal Klotho correlated with a decreased performance in hippocampal dependent memory. These results suggest that Klotho directly participates in regulating AHN. Our observations indicate that Klotho promotes proliferation, AHN and hippocampal dependent cognition. Increased neurogenesis in klotho KO mice may be secondary to the activation of other pathways altered in the model, such as vitamin D.

CLIN INTERV AGING. 2017 JUN 26;12:995-1001.

FREQUENCY OF FRAILTY AND ITS ASSOCIATION WITH COGNITIVE STATUS AND SURVIVAL IN OLDER CHILEANS.

Albala C, Lera L, Sanchez H, Angel B, Márquez C, Arroyo P, Fuentes P.

BACKGROUND: Age-associated brain physiologic decline and reduced mobility are key elements of increased age-associated vulnerability. OBJECTIVE: To study the frequency of frailty phenotype and its association with mental health and survival in older Chileans. METHODS: Follow-up of ALEXANDROS cohorts designed to study disability associated with obesity in community-dwelling people 60 years and older living in Santiago, Chile. At baseline, 2,098 (67% women) of 2,372 participants were identified as having the frailty phenotype: weak handgrip dynamometry, unintentional weight loss, fatigue/exhaustion, five chair-stands/slow walking speed and difficulty walking (low physical activity). After 10-15 years, 1,298 people were evaluated and 373 had died. Information regarding deaths was available for the whole sample. RESULTS: The prevalence of frailty at baseline (≥3 criteria) in the whole sample was 13.9% (women 16.4%; men 8.7%) and the pre-frailty prevalence (1-2 criteria) was 63.8% (65.0% vs 61.4%), respectively. Frailty was associated with cognitive impairment (frail 48.1%; pre-frail 21.7%; nonfrail 20.5%, P<0.001) and depression (frail 55.1%; pre-frail 27.3%; nonfrail 18.8%, P<0.001). Logistic regression models for frailty adjusted for sex and age showed a strong association between frailty and mild cognitive impairment (MCI) (odds ratio [OR] =3.93; 95% CI: 1.41-10.92). Furthermore, an important association was found for depression and frailty (OR =2.36; 95% CI 1.82-3.06). Age- and sex-adjusted hazard ratios (HRs) for death showed an increased risk with increasing frailty: pre-frail HR =1.56 (95% CI: 1.07-2.29), frail HR =1.91 (95% CI: 1.15-3.19); after adjustment by age and sex, a higher risk of death was observed for people identified as frail (HR =1.56, P=0.014) and pre-frail (HR =1.30, P=0.065). MCI and dementia were also risk factors for death (MCI: HR =1.69, P<0.027; dementia: HR =1.66, P=0.016). CONCLUSION: Frailty is highly prevalent and strongly associated with cognitive impairment and depression in older Chileans. The risk for death was higher for frail people, but underlying cognitive impairment is a key component of the lower survival rate.

MEDICINA INTERNA

CRITICAL CARE AND SHOCK 20(2):21-23

THREE YEARS AFTER THE REDOXS STUDY: WHAT WE HAVE LEARNED IN THE USE OF GLUTAMINE IN ICU PATIENTS?

Alberto Leguina-Ruzzi, Marcial Emilio Cariqueo, Luis Ricardo Galvez Arevalo

Critical illness has been associated with gluta-mine (Gln) plasma levels depletion and its sup-plementation is related with better outcomes. In 2013 the Reducing Deaths due to Oxidative Stress (REDOXS) study, showed that the sup-plementation of Gln to total parenteral nutrition was associated with higher mortality without conferring beneficial effects. These conclusions had a high impact in the clinical field: two of the main guidelines downgraded its recommendation. However, recent studies are answering ng questions regarding the safety use of this amino acid use and even suggesting new potential beneficial effects. It is important to understand the main lessons learned of the REDOXS study related to the correct use of Gln intra venous and do not rule out its use for the intensive care unit patients. The scientific community is actively working in the field and we expect to have more evidence to guide the correct of this amino acid in parenter-al nutrition.

REV BRAS ANESTESIOL. 2017 DEC 26. PII: S0034-7094(16)30212-4.

[IMPACT OF HYPOTENSION AND GLOBAL HYPOPERFUSION IN POSTOPERATIVE DELIRIUM: A PILOT STUDY IN OLDER ADULTS UNDERGOING OPEN COLON SURGERY].

Tobar E, Abedrapo MA, Godoy JA, Llanos JL, Díaz MJ, Azolas R, Bocic GR, Escobar JA, Cornejo RA, Romero CM.

BACKGROUND: Post-operative delirium is a serious complication in patients undergoing major abdominal surgery. It remains unclear whether peri-operative hemodynamic and perfusion variables affect the risk for postoperative delirium. The objective of this pilot study was to evaluate the association between perfusion and hemodynamics peri-operative with the appearance of post-operative delirium. METHODS: Prospective cohort study of adults 60 years or older undergoing elective open colon surgery. Multimodal hemodynamic and perfusion variables were monitored, including central venous oxygenation ($ScvO_2$), lactate levels, and non-invasive cerebral oxygenation (rSO_2), according to a standard anesthesia protocol. Fisher's exact test or Student's t-test were used to compare patients who developed post-operative delirium with those who did not (p<0.05). RESULTS: We studied 28 patients, age 73±7 years, 60.7% female. Two patients developed post-operative delirium (7.1%). These two patients had fewer years of education than those without delirium (p=0.031). None of the peri-operative blood pressure variables were associated with incidence of post-operative delirium. In terms of perfusion parameters, postoperative $ScvO_2$ was lower in the delirium than the non-delirium group, without reaching statistical significance (65±10% vs. 74±5%; p=0.08), but the delta-$ScvO_2$ (the difference between means post-operative and intra-operative) was associated with post-operative delirium (p=0.043). Post-operative lactate and rSO_2 variables were not associated with delirium. CONCLUSIONS: Our pilot study suggests

an association between delta $ScvO_2$ and post-operative delirium, and a tendency to lower post-operative $ScvO_2$ in patients who developed delirium. Further studies are necessary to elucidate this association.

INMUNOLOGÍA

CLIN EXP IMMUNOL. 2017 JUL;189(1):12-20.

THE ROLE OF INTERLEUKIN-6 SIGNALLING AND ITS THERAPEUTIC BLOCKAGE IN SKEWING THE T CELL BALANCE IN RHEUMATOID ARTHRITIS.

Schinnerling K, Aguillón JC, Catalán D, Soto L.

Therapeutic blockage of cytokine signalling in autoimmune diseases has improved our understanding of the role of these cytokines in triggering, shaping and perpetuating autoimmune responses. In rheumatoid arthritis (RA), immunopathology is driven by a predominance of arthritogenic T helper cells secreting interferon-γ [T helper type 1 (Th1)] and interleukin (IL)-17 (Th17) over regulatory T cells (T_{reg}). The pleiotropic cytokine IL-6 is crucial to the differentiation of Th17 cells and the balance between pathogenic Th17 and protective T_{reg} . Targeting the IL-6 receptor (IL-6R) by humanized antibodies improves signs and symptoms of RA, and has provided new insights into the mechanisms of inflammation and immune regulation. Here we review current evidence on the role of IL-6 in the pathogenesis of RA and the molecular consequences of IL-6R blockage in disease, with special focus on the Th17/T_{reg} balance and plasticity.

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, Oliveira LC, Crusoé E, Coelho ÉO, Pasquini R, Magalhães SM, Nunes R, Neto JV, Faria RM, Souza M, Hamerschlak N, Flantl D, Navarro JR, Conte G, Gomez-Almaguer D, Ruiz-Argüelles G, Durie BG; 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.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

PLOS ONE. 2017 MAR 7;12(3):E0172204.

THE COST OF DEMENTIA IN AN UNEQUAL COUNTRY: THE CASE OF CHILE.

Hojman DA, Duarte F, Ruiz-Tagle J, Budnich M, Delgado C, Slachevsky A.

We study the economic cost of dementia in Chile, and its variation according to socioeconomic status (SES). We use primary data from a survey of 330 informal primary caregivers who completed both a RUD-Lite and a socio-demographic questionnaire to evaluate the severity of dementia and caregiver's burden. The costs of dementia are broken into three components: direct medical costs (medical care, drugs, tests); direct social costs (social service, daycare); and indirect costs (mostly associated to informal care). The average monthly cost per patient is estimated at US$ 1,463. Direct medical costs account for 20 per cent, direct social costs for 5 per cent and indirect costs for 75 per cent of the total cost. The mean monthly cost is found to be inversely related to SES, a pattern largely driven by indirect costs. The monthly cost for high SES is US$ 1,083 and US$ 1,588 for low SES. A multivariate regression analysis suggests that severity of dementia and caregiver's burden account for between 49 and 70 per cent of the difference in the indirect cost across SES. However, between one-third and one-half of the variation across SES is not due to gradient in severity of dementia. Direct medical costs increase in higher SES, reflecting differences in purchasing power, while indirect costs are inversely related to SES and more than compensate differences in medical costs. Moreover, in lower SES groups, female caregivers, typically family members who are inactive in the labor market, mostly provide informal care. The average annual cost of dementia in Chile (US$ 17,559) is lower in

comparison to high-income countries (US$ 39,595) and the proportion of cost related to informal cost is higher (74 per cent compared to 40 per cent). SES is a key determinant in the cost of dementia. In the absence of universal access to treatment, part of the social cost of dementia potentially preserves or increases income and gender inequality.

CURR ALZHEIMER RES. 2017 DEC 27.

VITAMIN D INCREASES Aβ140 PLASMA LEVELS AND PROTECTS LYMPHOCYTES FROM OXIDATIVE DEATH IN MILD COGNITIVE IMPAIRMENT PATIENTS.

San Martín CD, Henriquez M, Chacon C, Ponce DP, Salech F, Rogers N, Behrens MI.

BACKGROUND: Mild cognitive impairment (MCI) has an increased rate of progression to dementia. Alterations of some metabolic factors, such as deficiency of vitamin D, are a risk factor for cognitive deterioration. Vitamin D is involved in the clearance of β-amyloid (Aβ) from the brain. We have reported that lymphocytes from Alzheimer's disease (AD) patients have an increased susceptibility to oxidative death by H2O2 exposure, but currently it is unknown if this characteristic is modifiable in vivo. OBJECTIVE: To determine if correction of low vitamin D levels protects lymphocytes from oxidative death and increases Aβ1-40 plasma levels in MCI and very early AD (VEAD) patients. METHOD: Sixteen MCI, 11 VEAD and 25 healthy control (HC) voluntaries were evaluated with the Clinical Dementia Rating (CDR), Montreal Cognitive assessment (MoCA), and Memory Index score (MIS). Lymphocyte death was measured by flow cytometry after 20h exposure to H2O2. In patients with low levels of vitamin D -11 MCI, 9 VEAD and 20 HC- lymphocyte H2O2-death, plasma Aβ1-40 levels and cognitive status were evaluated pre- and post-vitamin D supplementation for 6 months. RESULTS: Lymphocytes from MCI and VEAD patients showed increased susceptibility to oxidative death at study entry. In MCI, but not VEAD patients, lymphocyte susceptibility to death and Aβ1-40 levels plasma levels improved after 6 months of vitamin D supplementation. In addition, cognitive status on follow-up (18 months) improved in MCI patients after vitamin D supplementation. CONCLUSION: Vitamin D supplementation may be beneficial in MCI. The lack of effect in VEAD may be due to a more advanced stage or different characteristics of the neurodegenerative process.

DEMENT NEUROPSYCHOL. 2017 APR-JUN;11(2):129-136.

UTILITY OF THE NEUROPSYCHIATRIC INVENTORY QUESTIONNAIRE (NPI-Q) IN THE ASSESSMENT OF A SAMPLE OF PATIENTS WITH ALZHEIMER'S DISEASE IN CHILE.

Musa G, Henríquez F, Muñoz-Neira C, Delgado C, Lillo P, Slachevsky A

The Neuropsychiatric Inventory Questionnaire (NPI-Q) is an informant-based instrument that measures the presence and severity of 12 Neuropsychiatric Symptoms (NPS) in patients with dementia, as well as informant distress. OBJECTIVE: To measure the psychometric properties of the NPI-Q and the prevalence of NPS in patients with Alzheimer's disease (AD) in Chile. METHODS: 53 patients with AD were assessed. Subjects were divided into two different groups: mild AD (n=26) and moderate AD (n=27). Convergent validity was estimated by correlating the outcomes of the NPI-Q with Neuropsychiatric Inventory (NPI) scores and with a global cognitive efficiency test (Addenbrooke's Cognitive Examination - Revised - ACE-R). Reliability of the NPI-Q was analysed by calculating its internal consistency. Prevalence of NPS was estimated with both the NPI and NPI-Q. RESULTS: Positive and significant correlations were observed between the NPI-Q, the NPI, and the ACE-R ($r=0.730$; $p<0.01$ and 0.315; $p<0.05$ respectively). The instrument displayed an adequate level of reliability (Cronbach's alpha=0.783). The most prevalent NPS were apathy/indifference (62.3%) and dysphoria/depression (58.5%). CONCLUSION: The NPI-Q exhibited acceptable validity and reliability indicators for patients with AD in Chile, indicating that it is a suitable instrument for the routine assessment of NPS in clinical practice.

SCI REP. 2017 JUL 4;7(1):4580.

DYNAMIN-2 MUTATIONS LINKED TO CENTRONUCLEAR MYOPATHY IMPAIR ACTIN-DEPENDENT TRAFFICKING IN MUSCLE CELLS.

González-Jamett AM, Baez-Matus X, Olivares MJ, Hinostroza F, Guerra-Fernández MJ, Vasquez-Navarrete J, Bui MT, Guicheney P, Romero NB, Bevilacqua JA, Bitoun M, Caviedes P, Cárdenas AM.

Dynamin-2 is a ubiquitously expressed GTP-ase that mediates membrane remodeling. Recent findings indicate that dynamin-2 also regulates actin dynamics. Mutations in dynamin-2 cause dominant centronuclear myopathy (CNM), a congenital myopathy characterized by progressive weakness and atrophy of skeletal muscles. However, the muscle-specific roles of dynamin-2 affected by these mutations remain elusive. Here we show that, in muscle cells, the GTP-ase activity of dynamin-2 is involved in de novo actin polymerization as well as in actin-mediated trafficking of the glucose transporter GLUT4. Expression of dynamin-2 constructs carrying CNM-linked mutations disrupted the formation of new actin filaments as well as the stimulus-induced translocation of GLUT4 to the plasma membrane. Similarly, mature muscle fibers isolated from heterozygous knock-in mice that harbor the dynamin-2 mutation p.R465W, an animal model of CNM, exhibited altered actin organization, reduced actin polymerization and impaired insulin-induced translocation of GLUT4 to the sarcolemma. Moreover, GLUT4 displayed aberrant perinuclear accumulation in biopsies from CNM patients carrying dynamin-2 mutations, further suggesting trafficking defects. These results suggest that dynamin-2 is a key regulator of actin dynamics and GLUT4 trafficking in muscle cells. Our findings also support a model in which impairment of actin-dependent trafficking contributes to the pathological mechanism in dynamin-2-associated CNM.

FRONT NEUROL. 2017 JUN 9;8:245.

NOTCH 1 MUTATION IN A PATIENT WITH SPONTANEOUS AND RECURRENT DISSECTIONS OF EXTRACRANIAL ARTERIES.

Guevara C, Farias G, Bulatova K, Alarcón P, Soruco W, Robles C, Morales M.

Dissections of extracranial arteries are estimated to account for only 2% of all ischemic strokes but for approximately 20% of strokes in patients younger than 45 years old. Most dissections of extracranial arteries involve some trauma stretch, mechanical stress, or connective tissue abnormalities. In the absence of these disorders, determining the etiology of recurrent extracranial dissections is quite challenging because the underlying nature of these cases is poorly understood. We report the case of a 44-year-old female with recurrent dissections of the vertebral and carotid arteries associated with a heterozygous mutation p.Pro2122Leu in the NOTCH 1 gene. Her mother with a thoracic aortic aneurysm was also positive for this variant.

NEUROMUSCUL DISORD. 2017 SEP;27(9):836-842.

INSIGHTS FROM GENOTYPE-PHENOTYPE CORRELATIONS BY NOVEL SPEG MUTATIONS CAUSING CENTRONUCLEAR MYOPATHY.

Wang H, Castiglioni C, Kaçar Bayram A, Fattori F, Pekuz S, Araneda D, Per H, Erazo R, Gümü H, Zorludemir S, Becker K, Ortega X, Bevilacqua JA, Bertini E, Cirak S.

Centronuclear myopathies (CNM) are a clinically and genetically heterogeneous group of congenital myopathies, defined histologically by increased number of fibres with centrally located nuclei, and type I fibre predominance in muscle biopsy. Myotubular myopathy, the X-linked form of CNM caused by mutations in the phosphoinositide phosphatase MTM1, is histologically characteristic since muscle fibres resemble myotubes. Here we present two unrelated patients with CNM and typical myotubular fibres in the muscle biopsy caused by mutations in striated muscle preferentially expressed protein kinase (SPEG). Next generation sequencing revealed novel biallelic homozygous mutations in SPEG in both cases. Patient 1 showed the c.1627_1628insA (p.Thr544Aspfs*48) mutation and patient 2 the c.9586C>T (p.Arg3196*) mutation. The clinical phenotype was distinctive in the two patients since patient 2 developed a dilated cardiomyopathy with milder myopathy features, while patient 1 showed only myopathic features without cardiac involvement. These findings expand the genotype-phenotype correlations after the initial report. Additionally, we describe whole body muscle MRI of patient 2 and we argue on the different SPEG isoforms in skeletal muscle and heart as the possible explanation leading to variable phenotypes of SPEG mutations.

NEUROLOGIA. 2017 MAR 30. PII: S0213-4853(17)30102-0.

VALIDATION OF THE SPANISH-LANGUAGE VERSION OF THE MONTREAL COGNITIVE ASSESSMENT TEST IN ADULTS OLDER THAN 60 YEARS.

Delgado C, Araneda A, Behrens MI.

INTRODUCTION: Few studies have validated the Spanish-language version of the Montreal Cognitive Assessment (MoCA-S) test in Latin American populations. OBJETIVE: To evaluate the psychometric properties and discriminant validity of the MoCA-S in elderly patients in Santiago de Chile. METHODS: 172 individuals were grouped according to their clinical diagnosis based on the Clinical Dementia Rating (CDR) scale as follows: amnestic mild cognitive impairment (aMCI; n±24), non-amnestic MCI (naMCI; n±24), mild dementia (n±20), and cognitively normal (n±104). Participants were evaluated with both the MoCA-S and the Mini-Mental State Examination (MMSE) to determine the discriminant validity of the MoCA-S. RESULTS: Mean age and years of schooling were 73±6 and 11±4 years, respectively, with no significant intergroup differences. The MoCA-S displayed good internal consistency (Cronbach's α: 0.772), high inter-rater reliability (Spearman correlation coefficient: 0.846; P<.01), and high intra-rater reliability (test-retest reliability coefficient: 0.922; P<.001). The MoCA-S was found to be an effective and valid test for detecting aMCI (AUC±0.903) and mild dementia (AUC±0.957); its effectiveness for detecting naMCI was lower (AUC±0.629). The optimal cut-off points for aMCI and mild dementia were<21 and<20, respectively, with sensitivity and specificity rates of 75% and 82% for aMCI and 90% and 86% for mild dementia. The level of education had a great impact on scores: as a result, 2 points were added for patients with less than 8 years of schooling and one point for patients with 8-12 years of schooling (MoCA-S1-2). The MoCA-S1-2 showed significantly greater discriminant validity than the MMSE for differentiating aMCI from dementia. CONCLUSIONS: The MoCA-S1-2 is a short, easy-to-use, and useful test for diagnosing aMCI and mild dementia.

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.

NEUROTOX RES. 2017 AUG;32(2):172-174.

ON THE ROLE OF MINING EXPOSURE IN EPIGENETIC EFFECTS IN PARKINSON'S DISEASE.

Castillo S, Muñoz P, Behrens MI, Diaz-Grez F, Segura-Aguilar J.

To explore the possible influence of heavy metal mining on incidence of Parkinson's disease (PD), global DNA methylation was assessed in blood samples from a population of PD patients (n = 45) and control subjects (n = 52) in Antofagasta neighborhood, a Chilean city built for exclusive use of mining companies. Comparisons were made with PD subjects (n = 52) and control subjects (n = 59) from Santiago Chile, a city having little association with mining. All subjects were assessed by two neurologists and PD diagnosis was based on UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria. From blood samples obtained from each individual, a decrease in global DNA methylation was observed in PD patients either exposed (49% of control, $P < 0.001$) or not exposed (47% of control, $P < 0.001$) to mining activity. Although there was no difference in levels of DNA methylation between PD patients from the two cities, there was a lower level of DNA methylation in control subjects from Santiago versus Antofagasta.

FRONT NEUROSCI. 2017 OCT 6;11:553.

MITOCHONDRIAL BIOENERGETICS IS ALTERED IN FIBROBLASTS FROM PATIENTS WITH SPORADIC ALZHEIMER'S DISEASE.

Pérez MJ, Ponce DP, Osorio-Fuentealba C, Behrens MI, Quintanilla RA.

The identification of an early biomarker to diagnose Alzheimer's disease (AD) remains a challenge. Neuropathological studies in animal and AD patients have shown that mitochondrial dysfunction is a hallmark of the development of the disease. Current studies suggest the use of peripheral tissues, like skin fibroblasts as a possibility to detect the early pathological alterations present in the AD brain. In this context, we studied mitochondrial function properties (bioenergetics and morphology) in cultured fibroblasts obtained from AD, aged-match and young healthy patients. We observed that AD fibroblasts presented a significant reduction in mitochondrial length with important changes in the expression of proteins that control mitochondrial fusion. Moreover, AD fibroblasts showed a distinct alteration in proteolytic processing of OPA1, a master regulator of mitochondrial fusion, compared to control fibroblasts. Complementary to these changes AD fibroblasts showed a dysfunctional mitochondrial bioenergetics profile that differentiates these cells from aged-matched and young patient fibroblasts. Our findings suggest that the human skin fibroblasts obtained from AD patients could replicate mitochondrial impairment observed in the AD brain. These promising observations suggest that the analysis of mitochondrial bioenergetics could represent a promising strategy to develop new diagnostic methods in peripheral tissues of AD patients.

FRONT AGING NEUROSCI. 2017 OCT 5;9:310.

PARP-1 AND P53 REGULATE THE INCREASED SUSCEPTIBILITY TO OXIDATIVE DEATH OF LYMPHOCYTES FROM MCI AND AD PATIENTS.

Salech F, Ponce DP, SanMartín CD, Rogers NK, Chacón C, Henríquez M, Behrens MI.

Mild cognitive impairment (MCI) is a clinically detectable initial stage of cognitive deterioration with a high conversion rate to dementia. There is increasing evidence that some of the cerebral alterations present in Alzheimer type dementia can be found in peripheral tissues. We have previously shown that lymphocytes from Alzheimer's disease (AD) patients have increased susceptibility to hydrogen peroxide (H_2O_2)-induced death that depends on dementia severity. We here investigated whether lymphocytes from MCI patients show increased vulnerability to death, and explored the involvement of Poly [ADP-ribose] polymerase (PARP-1) and p53 in the regulation of this process. Lymphocytes from 16 MCI and 10 AD patients, and 15 healthy controls (HCs) were submitted to increasing concentrations of H_2O_2 for 20 h. Cell death was determined by flow cytometry, in the presence or absence of PARP-1 inhibitors (3-aminobenzamide (3-ABA) or Nicotinamide (NAM)), or the p53 inhibitor (nutlin-3) or stabilizer (pifithrin-α). PARP-1 and p53 mRNA levels were determined by quantitative PCR (qPCR). Lymphocytes from MCI patients showed increased susceptibility to death, attaining intermediate values between AD and controls. PARP inhibitors -3-ABA and NAM- markedly protected from H_2O_2-induced death, making the difference between MCI and controls disappear, but not the difference between AD and controls. PARP-1 mRNA expression was increased in MCI lymphocytes. Modulation of p53 with Nutlin-3 or pifithrin-α did not modify the H_2O_2-induced death of lymphocytes from MCI or AD patients, but augmented the death in control lymphocytes attaining levels similar to MCI and AD. Accordingly, p53 mRNA expression was increased in AD and MCI lymphocytes compared to controls. In all, these results show that increased oxidative death is present in lymphocytes at the MCI stage. PARP-1 has a preponderant role, with complete death protection achieved with PARP inhibition in MCI lymphocytes, but not in AD, suggesting that PARP-1 might have a protective role. In addition, deregulations of the p53 pathway seem to contribute to the H_2O_2-induced death in MCI and AD lymphocytes, which show increased p53 expression. The results showing a prominent protective role of PARP inhibitors opens the door to study the use of these agents to prevent oxidative death in MCI patients.

FRONT AGING NEUROSCI. 2017 MAY 19;9:149.

MUSIC TRAINING AND EDUCATION SLOW THE DETERIORATION OF MUSIC PERCEPTION PRODUCED BY PRESBYCUSIS IN THE ELDERLY.

Moreno-Gómez FN, Véliz G, Rojas M, Martínez C, Olmedo R, Panussis F, Dagnino-Subiabre A, Delgado C, Delano PH.

The perception of music depends on the normal function of the peripheral and central auditory system. Aged subjects without hearing loss have altered music perception, including pitch and temporal features. Presbycusis or age-related hearing loss is a frequent condition in elderly people, produced by neurodegenerative processes that affect the cochlear receptor cells and brain circuits involved in auditory perception. Clinically, presbycusis patients have bilateral high-frequency hearing loss and deteriorated speech intelligibility. Music impairments in presbycusis subjects can be attributed to the normal aging processes and to presbycusis neuropathological changes. However, whether presbycusis further impairs music perception remains controversial. Here, we developed a computerized version of the Montreal battery of evaluation of amusia (MBEA) and assessed music perception in 175 Chilean adults aged between 18 and 90 years without hearing complaints and in symptomatic presbycusis patients. We give normative data for MBEA performance in a Latin-American population, showing age and educational effects. In addition, we found that symptomatic presbycusis was the most relevant factor determining global MBEA accuracy in aged subjects. Moreover, we show that melodic impairments in presbycusis individuals were diminished by music training, while the performance in temporal tasks were affected by the educational level and music training. We conclude that music training and education are important factors as they can slow the deterioration of music perception produced by age-related hearing loss.

SCI REP. 2017 JUL 4;7(1):4580.

DYNAMIN-2 MUTATIONS LINKED TO CENTRONUCLEAR MYOPATHY IMPAIR ACTIN-DEPENDENT TRAFFICKING IN MUSCLE CELLS.

González-Jamett AM, Baez-Matus X, Olivares MJ, Hinostroza F, Guerra-Fernández MJ, Vasquez-Navarrete J, Bui MT, Guicheney P, Romero NB, Bevilacqua JA, Bitoun M, Caviedes P, Cárdenas AM.

Dynamin-2 is a ubiquitously expressed GTP-ase that mediates membrane remodeling. Recent findings indicate that dynamin-2 also regulates actin dynamics. Mutations in dynamin-2 cause dominant centronuclear myopathy (CNM), a congenital myopathy characterized by progressive weakness and atrophy of skeletal muscles. However, the muscle-specific roles of dynamin-2 affected by these mutations remain elusive. Here we show that, in muscle cells, the GTP-ase activity of dynamin-2 is involved in de novo actin polymerization as well as in actin-mediated trafficking of the glucose transporter GLUT4. Expression of dynamin-2 constructs carrying CNM-linked mutations disrupted the formation of new actin filaments as well as the stimulus-induced translocation of GLUT4 to the plasma membrane. Similarly, mature muscle fibers isolated from heterozygous knock-in mice that harbor the dynamin-2 mutation p.R465W, an animal model of CNM, exhibited altered actin organization, reduced actin polymerization and impaired insulin-induced translocation of GLUT4 to the sarcolemma. Moreover, GLUT4 displayed aberrant perinuclear accumulation in biopsies from CNM patients carrying dynamin-2 mutations, further suggesting trafficking defects. These results suggest that dynamin-2 is a key regulator of actin dynamics and GLUT4 trafficking in muscle cells. Our findings also support a model in which impairment of actin-dependent trafficking contributes to the pathological mechanism in dynamin-2-associated CNM.

SERVICIO ANATOMÍA PATOLÓGICA

EUR J ORAL SCI. 2017 APR;125(2):102-109.

HAPLOTYPE-BASED GENE-GENE INTERACTION OF BONE MORPHOGENETIC PROTEIN 4 AND INTERFERON REGULATORY FACTOR 6 IN THE ETIOLOGY OF NON-SYNDROMIC CLEFT LIP WITH OR WITHOUT CLEFT PALATE IN A CHILEAN POPULATION.

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

Non-syndromic cleft lip with or without cleft palate (NSCL/P) is the most common craniofacial birth defect in humans, the etiology of which can be dependent on the interactions of multiple genes. We previously reported haplotype associations for polymorphic variants of interferon regulatory factor 6 (IRF6), msh homeobox 1 (MSX1), bone morphogenetic protein 4 (BMP4), and transforming growth factor beta 3 (TGFB3) in Chile. Here, we analyzed the haplotype-based gene-gene interaction for markers of these genes and NSCL/P risk in the Chilean population. We genotyped 15 single nucleoptide polymorphisms (SNPs) in 152 Chilean patients and 164 controls. Linkage disequilibrium (LD) blocks were determined using the Haploview software, and phase reconstruction was performed by the Phase program. Haplotype-based interactions were evaluated using the multifactor dimensionality reduction (MDR) method. We detected two LD blocks composed of two SNPs from BMP4 (Block 1) and three SNPs from IRF6 (Block 2). Although MDR showed no statistical significance for the global interaction model involving these blocks, we found four combinations conferring a statistically significantly increased NSCL/P risk (Block 1-Block 2): T-T/T-G C-G-T/G-A-T; T-T/T-G C-G-C/C-G-C; T-T/T-G G-A-T/G-A-T; and T-T/C-G G-A-T/G-A-T. These findings may reflect the presence of a genomic region containing potential causal variants interacting in the etiology of NSCL/P and may contribute to disentangling the complex etiology of this birth defect.

CLIN EPIGENETICS. 2017 OCT 17;9:114.

MICRORNA-335-5P IS A POTENTIAL SUPPRESSOR OF METASTASIS AND INVASION IN GASTRIC CANCER.

Sandoval-Bórquez A, Polakovicova I, Carrasco-Véliz N, Lobos-González L Riquelme I, Carrasco-Avino G, Bizama C, Norero E, Owen GI, Roa JC, Corvalán AH.

BACKGROUND: Multiple aberrant microRNA expression has been reported in gastric cancer. Among them, microRNA-335-5p (miR-335), a microRNA regulated by DNA methylation, has been reported to possess both tumor suppressor and tumor promoter activities. RESULTS: Herein, we show that miR-335 levels are reduced in gastric cancer and significantly associate with lymph node metastasis, depth of tumor invasion, and ultimately poor patient survival in a cohort of Amerindian/Hispanic patients. In two gastric cancer cell lines AGS and, Hs 746T the exogenous miR-335 decreases migration, invasion, viability, and anchorage-independent cell growth capacities. Performing a PCR array on cells transfected with miR-335, 19 (30.6%) out of 62 genes involved in metastasis and tumor invasion showed decreased transcription levels. Network enrichment analysis narrowed these genes to nine (PLAUR, CDH11, COL4A2, CTGF, CTSK, MMP7, PDGFA, TIMP1, and TIMP2). Elevated levels of PLAUR, a validated target gene, and CDH11 were confirmed in tumors with low expression of miR-335. The 3'UTR of CDH11 was identified to be directly targeted by miR-335. Downregulation of miR-335 was also demonstrated in plasma samples from gastric cancer patients and inversely correlated with DNA methylation of promoter region ($Z = 1.96$, $p = 0.029$). DNA methylation, evaluated by methylation-specific PCR assay, was found in plasma from 23 (56.1%) out of 41 gastric cancer patients but in only 9 (30%) out of 30 healthy donors ($p = 0.029$, Pearson's correlation). Taken in consideration, our results of the association with depth of invasion, lymph node metastasis, and poor prognosis together with functional assays on cell migration, invasion, and tumorigenicity are in accordance with the downregulation of miR-335 in gastric cancer. CONCLUSIONS: Comprehensive evaluation of metastasis and invasion pathway identified a subset of associated genes and confirmed PLAUR and CDH11, both targets of miR-335, to be overexpressed in gastric cancer tissues. DNA methylation of miR-335 may be a promissory strategy for non-invasive approach to gastric cancer.

PLOS ONE. 2017 MAY 31;12(5):E0178274.

REPRIMO TISSUE-SPECIFIC EXPRESSION PATTERN IS CONSERVED BETWEEN ZEBRAFISH AND HUMAN.

Figueroa RJ, Carrasco-Avino G, Wichmann IA, Lange M, Owen GI, Siekmann AF, Corvalán AH, Opazo JC, Amigo JD.

Reprimo (RPRM), a member of the RPRM gene family, is a tumor-suppressor gene involved in the regulation of the p53-mediated cell cycle arrest at G2/M. RPRM has been associated with malignant tumor progression and proposed as a potential biomarker for early cancer detection. However, the expression and role of RPRM, as well as its family, are poorly understood and their physiology is as yet unstudied. In this scenario, a model system like the zebrafish could serve to dissect the role of the RPRM family members in vivo. Phylogenetic analysis reveals that RPRM and RPRML have been differentially retained by most species throughout vertebrate evolution, yet RPRM3 has been retained only in a small group of distantly related species, including zebrafish. Herein, we characterized the spatiotemporal expression of RPRM (present in zebrafish as an infraclass duplication rprma/rprmb), RPRML and RPRM3 in the zebrafish. By whole-mount in situ hybridization (WISH) and fluorescent in situ hybridization (FISH), we demonstrate that rprm (rprma/rprmb) and rprml show a similar spatiotemporal expression profile during zebrafish development. At early developmental stages rprmb is expressed in somites. After one day post-fertilization, rprm (rprma/rprmb) and rprml are expressed in the notochord, brain, blood vessels and digestive tube. On the other hand, rprm3 shows the most unique expression profile, being expressed only in the central nervous system (CNS). We assessed the expression patterns of RPRM gene transcripts in adult zebrafish and human RPRM protein product in tissue samples by RT-qPCR and immunohistochemistry (IHC) staining, respectively. Strikingly, tissue-specific expression patterns of the RPRM transcripts and protein are conserved between zebrafish and humans. We propose the zebrafish as a powerful tool to elucidate the both physiological and pathological roles of the RPRM gene family.

ACTAS UROL ESP. 2017 MAR;41(2):97-102.

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 albugínea, which could be involved in venous leakage and loss of penile rigidity. In the current sudy, 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.

J. CELL. BIOCHEM. 2017; 118: 3662–3674.

WNT/β-CATENIN SIGNALING ACTIVATES EXPRESSION OF THE BONE-RELATED TRANSCRIPTION FACTOR RUNX2 IN SELECT HUMAN OSTEOSARCOMA CELL TYPES

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Osteosarcoma is the most common malignant bone tumor in children and adolescents. Metastasis and poor responsiveness to chemotherapy in osteosarcoma correlates with over-expression of the runt-related transcription factor RUNX2, which normally plays a key role in osteogenic lineage commitment, osteoblast differentiation, and bone formation. Furthermore, WNT/β-catenin signaling is over-activated in osteosarcoma and promotes tumor progression. Importantly, the WNT/β-catenin pathway normally activates RUNX2 gene expression during osteogenic lineage commitment. Therefore, we examined whether the WNT/β-catenin pathway controls the tumor-related elevation of RUNX2 expression in osteosarcoma. We analyzed protein levels and nuclear localization of β-catenin and RUNX2 in a panel of human osteosarcoma cell lines (SAOS, MG63, U2OS, HOS, G292, and 143B). In all six cell lines, β-catenin and RUNX2 are expressed to different degrees and localized in the nucleus and/or cytoplasm. SAOS cells have the highest levels of RUNX2 protein that is localized in the nucleus, while MG63 cells have the lowest RUNX2 levels which is mostly localized in the cytoplasm. Levels of β-catenin and RUNX2 protein are enhanced in HOS, G292, and 143B cells after treatment with the GSK3β inhibitor SB216763. Furthermore, small interfering RNA (siRNA)-mediated depletion of β-catenin inhibits RUNX2 expression in G292 cells. Thus, WNT/β-catenin activation is required for RUNX2 expression in at least some osteosarcoma cell types, where RUNX2 is known to promote expression of metastasis related genes.

CENTRO INVESTIGACIÓN CLÍNICA AVANZADA - CICA

FRONT AGING NEUROSCI. 2017 OCT 5;9:310.

PARP-1 AND P53 REGULATE THE INCREASED SUSCEPTIBILITY TO OXIDATIVE DEATH OF LYMPHOCYTES FROM MCI AND AD PATIENTS.

Salech F, Ponce DP, SanMartín CD, Rogers NK, Chacón C, Henríquez M, Behrens MI.

Mild cognitive impairment (MCI) is a clinically detectable initial stage of cognitive deterioration with a high conversion rate to dementia. There is increasing evidence that some of the cerebral alterations present in Alzheimer type dementia can be found in peripheral tissues. We have previously shown that lymphocytes from Alzheimer's disease (AD) patients have increased susceptibility to hydrogen peroxide (H_2O_2)-induced death that depends on dementia severity. We here investigated whether lymphocytes from MCI patients show increased vulnerability to death, and explored the involvement of Poly [ADP-ribose] polymerase (PARP-1) and p53 in the regulation of this process. Lymphocytes from 16 MCI and 10 AD patients, and 15 healthy controls (HCs) were submitted to increasing concentrations of H_2O_2 for 20 h. Cell death was determined by flow cytometry, in the presence or absence of PARP-1 inhibitors (3-aminobenzamide (3-ABA) or Nicotinamide (NAM)), or the p53 inhibitor (nutlin-3) or stabilizer (pifithrin-α). PARP-1 and p53 mRNA levels were determined by quantitative PCR (qPCR). Lymphocytes from MCI patients showed increased susceptibility to death, attaining intermediate values between AD and controls. PARP inhibitors -3-ABA and NAM- markedly protected from H_2O_2-induced death, making the difference between MCI and controls disappear, but not the difference between AD and controls. PARP-1 mRNA expression was increased in MCI lymphocytes. Modulation of p53 with Nutlin-3 or pifithrin-α did not modify the H_2O_2-induced death of lymphocytes from MCI or AD patients, but augmented the death in control lymphocytes attaining levels similar to MCI and AD. Accordingly, p53 mRNA expression was increased in AD and MCI lymphocytes compared to controls. In all, these results show that increased oxidative death is present in lymphocytes at the MCI stage. PARP-1 has a preponderant role, with complete death protection achieved with PARP inhibition in MCI lymphocytes, but not in AD, suggesting that PARP-1 might have a protective role. In addition, deregulations of the p53 pathway seem to contribute to the H_2O_2-induced death in MCI and AD lymphocytes, which show increased p53 expression. The results showing a prominent protective role of PARP inhibitors opens the door to study the use of these agents to prevent oxidative death in MCI patients.

OSTEOPOROS INT. 2017 JUL;28(7):2187-2193.

TUMOR-INDUCED OSTEOMALACIA: EXPERIENCE FROM A SOUTH AMERICAN ACADEMIC CENTER.

González G, Baudrand R, Sepúlveda MF, Vucetich N, Guarda FJ, Villanueva P, Contreras O, Villa A, Salech F, Toro L, Michea L, Florenzano P.

The majority of tumor-induced osteomalacia cases have been reported in the Northern Hemisphere and Asia. In this first series of South American patients, we show that the clinical presentation and sensitivity of plasmatic fibroblast growth factor 23 and somatostatin analog-based imaging are similar to those described in other populations. INTRODUCTION: Describe the experience of clinical presentation, diagnostic study, and treatment of patients with tumor-induced osteomalacia (TIO) in a South American academic center in comparison to literature. METHODS: Analysis of the records of patients diagnosed with TIO. The clinical presentation, diagnostic studies, and treatment were analyzed. Fibroblast growth factor 23 (FGF23) was measured by ELISA. RESULTS: Six patients were diagnosed with TIO during the studied period. The patients' median age was 53 years (range 22-64). All patients presented with weakness and pain in the extremities.

Four experienced fractures during their evolution. The median time to diagnosis was 4.5 years (1-20). Biochemical studies showed hypophosphatemia, median of 1.4 mg/dL (1.2-1.6), with low maximum rates of tubular reabsorption of phosphate adjusted for glomerular filtration rate. FGF23 was elevated in 4/6 patients and inappropriately normal in the other two. In three patients, the location of the tumor was clinically evident and confirmed with anatomical imaging. In the remaining patients, two tumors were located with ^{68}Ga DOTATATE-PET/CT and one with OctreoScan. The causal tumors were located in the lower extremities in five patients and invading the frontal sinus in one patient. In all patients, tumors were successfully removed. Within 14 days, there was normalization of phosphate and FGF23 levels and resolution of clinical symptoms in all patients. In all cases, the histopathology was compatible with a phosphaturic mesenchymal tumor. CONCLUSIONS: The clinical presentation, delay time to diagnosis, FGF23 diagnostic sensitivity and histopathology in this first series of South American patients is similar to those described in other populations. The success of localization by somatostatin analog-based imaging, suggests this may the optimal imaging modality.

DEPARTAMENTO DE UROLOGÍA

INT UROL NEPHROL. 2017 JAN;49(1):31-35.

CONCORDANCE OF RENAL STONE CULTURE: PMUC, RPUC, RSC AND POST-PCNL SEPSIS-A NON-RANDOMIZED PROSPECTIVE OBSERVATION COHORT STUDY.

Walton-Diaz A, Vinay JI, Barahona J, Daels P, González M, Hidalgo JP, Palma C, Díaz P, Domenech A, Valenzuela R, Marchant F.

INTRODUCTION: Between 5 and 10% of patients undergoing percutaneous nephrolithotomy (PCNL) develop postoperative sepsis 1, 2. Strategies to prevent infectious complications are based on information provided by preoperative midstream urine cultures (PMUC). The aim of this study is to evaluate the concordance of the microbiologic findings of PMUC, cultures of the renal stone (RSC) and urine obtained directly from the renal pelvis (RPUC) in patients undergoing PCNL. MATERIALS AND METHODS: This is a multicenter prospective study. The study included all patients who underwent PCNL from May 2013 to July 2015 in three academic hospitals. All patients underwent a PMUC. Samples for RPUC were obtained by renal puncture for PCNL. Stone fragments extracted during the procedure were sent for culture (RSC). Clinical variables, stone configuration, burden and microbiology reports of cultures were recorded. We analyzed concordance between cultures and association with infectious complications. RESULTS: One hundred and twenty-two patients underwent PCNL. Twenty-four percent had positive culture, 3.2% (4/122) PMUC, 14.7% (18/122) RPUC and 13.9% (17/122) RSC. Positive PMUC demonstrated multidrug-susceptible Escherichia coli and Staphylococcus aureus, while RPUC showed multidrug-resistant pathogens and/or fungus. Seven patients (5.7%) developed postoperative infectious complications prior to discharge. There was a weak correlation between PMUC and intraoperative urine cultures (RPUC and RSC). Concordance rate between RPUC and RSC was 83.3%. The most common isolated pathogens were multidrug-resistant bacteria or fungus. CONCLUSIONS: PMUC did not reflect the microbiological environment found in stones and urine directly obtained from the renal pelvis. Patients with postoperative infectious complications had negative PMUC with positive RPUC or RSC. RPUC and RSC can help guide prompt and appropriate antibiotic treatment for patients who develop postoperative infectious complications after PCNL.

J ENDOUROL. 2017 AUG 21.

OUTCOMES OF URETERORENOSCOPIC STONE TREATMENT IN 301 PATIENTS WITH A SOLITARY KIDNEY.

Legemate JD, Gonzalez FM, Bouzouita A, Li S, McIlhenny C, Miller NL, Saita A, de la Rosette JJMCH.

OBJECTIVES: To determine the stone-free rates and intra- and postoperative complication rates and grades of ureterorenoscopic stone treatment in patients with a solitary kidney. METHODS: This study is a sub-analysis of the CROES-URS study, which is a prospective international multicenter observational study. Over a one year period consecutive patients treated with ureterorenoscopy for urinary stones were included. Patients entered in this analysis were those with a solitary functioning kidney. Descriptive data on patient characteristics, stone-free rates, complication rates and grades were evaluated for three separate groups: patients treated with ureteroscopy for ureteral stones, for renal stones and a combination of renal and ureteral stones. RESULTS: A total of 301 patients were treated for stones in a solitary kidney; 219 were treated for ureteral stones. In this group the stone free-rate was 88.6%, with an intra-operative complication rate of 7.4% and postoperative complication rate of 4.1%. Totally 57 patients were treated for renal stones. In this group the stone-free rate was 56.4%, with an intra-operative complication rate of 7.0% and postoperative complication rate of 10.5%. There were 25 patients who were treated for renal stones in combination with ureter stones. In this group the stone-free rate was 60.0%, with an intra-operative complication rate of 12.0% and postoperative complication rate of 10.5%. Within the three groups 72% of the postoperative complications were classified as Clavien I and II. CONCLUSION: Ureteroscopy is an effective and safe treatment modality for the removal of ureteral and renal stones in patients with a solitary kidney. Stone location as well as total stone burden seems to be important factors influencing the ability to render patients stone free. More, single session ureteroscopic stone removal was less effective for the treatment of larger renal stones or renal stones in combination with ureteral stones.

LOW URIN TRACT SYMPTOMS. 2017 JUL 13.

CORRELATION OF XIPHOPUBIC DISTANCE, BODY WEIGHT, HEIGHT AND BODY MASS INDEX WITH INTRAVESICAL AND ABDOMINAL INITIAL RESTING PRESSURES IN URODYNAMIC TESTING IN THE SITTING POSITION.

Valdevenito JP, García-Mora A, Rodriguez J, Gammie A.

OBJECTIVES: To compare the initial resting intravesical pressure (p_{ves}) and abdominal pressure (p_{abd}) in the sitting position with the typical range of values, to assess the correlation between such pressures and patient xipho-pubic distance, body weight, height and body mass index (BMI), and to estimate if xipho-pubic distance can be a guide to interpret initial resting pressures in urodynamic testing. METHODS: Women with lower urinary tract symptomatology referred for urodynamic testing were consecutively enrolled in a prospective study. Conventional cystometry was done following "good urodynamic practices". The correlation between initial resting p_{ves} and p_{abd} and xipho-pubic distance, body weight, height and BMI were studied using simple and multiple linear regression analysis. Statistical significance was defined as $P < 0.05$. RESULTS: One hundred women aged (mean ± SD) 59.2 ± 13.3 were studied. There was a significant correlation between both p_{ves} and p_{abd}, and xipho-pubic distance, body weight and BMI and no correlation with height. Over the multiple analysis, xipho-pubic distance and body weight correlated independently with p_{ves} ; body weight correlated independently with p_{abd} . Three patients had p_{ves} and/or p_{abd} out of typical range, with BMIs values of 18.48, 18.72 and 35.81 kg/m^2 . There was a wide range of difference between xipho-pubic distance and initial resting pressures. CONCLUSIONS: Out of range initial resting pressures occur in underweight (or close to) or severely obese patients. Xipho-pubic distance and body weight correlated independently with p_{ves} . Body weight correlated independently with p_{abd} . Xipho-pubic distance cannot be a guide to interpret the initial resting pressures.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

EAT WEIGHT DISORD. 2017 MAR;22(1):13-26.

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.

CURR NEUROPHARMACOL. 2017 APR;15(3):402-408.

ATHANASIOS KOUKOPOULOS' PSYCHIATRY: THE PRIMACY OF MANIA AND THE LIMITS OF ANTIDEPRESSANTS.

Ghaemi SN, Vohringer PA.

BACKGROUND: Athanasios Koukopoulos provided a radical model for understanding depressive and manic conditions. OBJECTIVE: To review, explain, and analyze Koukopoulos' concept of the primacy of mania, with special attention to the role of antidepressants. METHOD: A conceptual review of Koukopoulos' writings and lectures on this topic is given. RESULTS: Koukopoulos held that depressive states are caused by manic states; the former do not occur without the latter. The most common scenario of the inseparability of depressive and manic symptoms occurs in mixed states, which we estimate to represent about one-half of all depressive episodes in all patients (not just bipolar illness). In a review of the empirical evidence for this topic, we conclude that empirical evidence exists to support the primary of mania thesis in almost 80% of depressed patients. Since antidepressants worsen mania, they would be expected to worsen depression as well in this model. We provide evidence that supports this view in most persons with depressive states. CONCLUSION: Koukopoulos' model of affective illness is one where manic states are the primary pathology, and depressive conditions are a secondary consequence. Hence treatment of depression with antidepressants would be less effective than treatment with mood stabilizers, since treating an effect is less successful than treating its cause. This approach would reverse current assumptions in psychiatry.

FRONT PSYCHOL. 2017 DEC 18;8:2131.

CHILEAN ADAPTATION AND VALIDATION OF THE EARLY ADOLESCENT TEMPERAMENT QUESTIONNAIRE-REVISED VERSION.

Hoffmann M, Pérez JC, García C, Rojas G, Martínez V.

The aim of this study was to develop an adapted version of the Early Adolescent Temperament Questionnaire-Revised (EATQ-R) that would be valid and reliable for assessing temperament and its components in Chileans between 12 and 18 years of age. Originally, Ellis and Rothbart (2001) developed this questionnaire (EATQ-R) to be used in North American adolescents. For the study in Chile, a translation protocol was developed, to maintain the original instrument's cultural and linguistic equivalence in the adapted version. Psychometric properties of the EATQ-R, such as factor structure, internal consistency, and convergent validity, were also assessed. The adaption and validation was carried out in two stages, with two different studies. The first study, which included 612 adolescent students from educational establishments in the cities of Santiago and Concepcion, Chile, developed the Chilean version of the 83-item EATQ-R, which has 13 dimensions, belonging to 4 theoretical factors with adequate internal consistency (Cronbach's alpha = 0.79-0.82). The second study assessed the questionnaire's convergent validity, through its application to 973 adolescent students in Santiago. Results show that the effortful control subscale was significantly inversely related to indicators of adolescent maladjustment, such as substance abuse and behavioral problems. In addition, it was directly associated with indicators of self-concept, including self-esteem and self-efficacy. The opposite pattern was observed when considering negative affect. These findings coincide with current knowledge on the relationship between temperament and adjustment in adolescents.

BMJ OPEN. 2017 JUL 20;7(7):E011249.

EFFECTIVENESS OF THE MANAGEMENT OF MAJOR DEPRESSIVE EPISODES/DISORDER IN ADULTS WITH COMORBID CHRONIC PHYSICAL DISEASES: A PROTOCOL FOR A SYSTEMATIC REVIEW AND META-ANALYSIS.

Martínez P, Castro A, Alonso D, Vöhringer PA, Rojas G.

INTRODUCTION: Depression is a global-scale public health problem, and a significant association has been established between depression and chronic physical diseases. This growing comorbidity poses a challenge to healthcare systems. We aim to assess the effectiveness of the management of major depressive episodes/disorder in adults with comorbid chronic physical diseases. METHODS AND ANALYSIS: We will conduct a systematic review and meta-analysis of randomised clinical trials. Two databases MEDLINE and Cochrane Library (Cochrane Database for Systematic Reviews and CENTRAL), as well as the reference lists of the included articles, will be searched for studies either in English or Spanish with published results within the 2005-2015 period. Studies must fulfil the following conditions: (1) participants aged 18 years or older, diagnosed as having a major depressive episodes/disorder according to standardised criteria and chronic physical diseases; (2)interventions (be it pharmacological, psychological, psychosocial or a combination) must be compared with control conditions (other 'active' intervention, treatment as usual, waiting list or placebo); (3)and must report reduction in depressive symptoms after treatment, response to treatment, remission of major depressive episodes/disorder and significant improvement in quality of life. Data extraction, risk of bias evaluation, results summarisation and quality of the evidence (GRADE) will be performed as recommended by the Cochrane Collaboration. A qualitative synthesis and a random effects meta-analysis will be carried out. Effect sizes will be calculated (relative risk and Cohen's d), I^2 and Q statistics will be employed to study heterogeneity and publication bias analysis will be performed. Subgroup analyses and meta-regression will be carried out. ETHICS AND DISSEMINATION: Results are expected to be published in specialised peer-reviewed journals (preferred topics: Mental Health, Psychology, Psychiatry and/or Systematic Reviews) and dissemination activities will be targeted to all the healthcare providers.

TRIALS. 2017 MAY 25;18(1):233.

THE EFFECT OF A MINDFULNESS-BASED INTERVENTION IN COGNITIVE FUNCTIONS AND PSYCHOLOGICAL WELL-BEING APPLIED AS AN EARLY INTERVENTION IN SCHIZOPHRENIA AND HIGH-RISK MENTAL STATE IN A CHILEAN SAMPLE: STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL.

Langer ÁI, Schmidt C, Mayol R, Díaz M, Lecaros J, Krogh E, Pardow A, Vergara C, Vergara G, Pérez-Herrera B, Villar MJ, Maturana A, Gaspar PA.

BACKGROUND: According to the projections of the World Health Organization, 15% of all disabilities will be associated with mental illnesses by 2020. One of the mental disorders with the largest social impacts due to high personal and family costs is psychosis. Among the most effective psychological approaches to treat schizophrenia and other psychotic disorders at the world level is cognitive behavioral therapy. Recently, cognitive behavioral therapy has introduced several tools and strategies that promote psychological processes based on acceptance and mindfulness. A large number of studies support the effectiveness of mindfulness in dealing with various mental health problems, including psychosis. This study is aimed at determining the efficiency of a mindfulness-based program in increasing cognitive function and psychological well-being in patients with a first episode of schizophrenia and a high risk mental state (those at risk of developing an episode of psychosis). METHODS AND DESIGN: This is an experimentally designed, multi-center randomized controlled trial, with a 3-month follow-up period. The study participants will be 48 patients diagnosed with schizophrenia (first episode) and 48 with a high-risk mental state, from Santiago, Chile, aged between 15 and 35 years. Participants will be submitted to a mindfulness-based

intervention (MBI), which will involve taking part in eight mindfulness workshops adapted for people with psychosis. Workshops will last approximately 1.5 hours and take place once a week, over 8 weeks. The primary outcome will be the cognitive function through Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) and the secondary outcome will be psychological well-being measured by self-reporting questionnaires. DISCUSSION: The outcomes of this trial will add empirical evidence to the benefits and feasibility of MBIs for the psychotherapeutic treatment of patients with schizophrenia and high-risk mental states in reducing cognitive impairment in attention, working memory, and social cognition, as well as increasing the psychological well-being by empowering the patients' personal resources in the management of their own symptoms and psychotic experiences.

INT J LAW PSYCHIATRY. 2017 MAY - JUN;52:55-61.

BURDEN OF SEPARATION AND SUICIDE RISK OF PRISONERS WITH MINOR CHILDREN.

Krüger S, Priebe S, Fritsch R, Mundt AP.

The present study aimed to explore the burden of separation from children and its relationship with suicide risk in prisoners with minor children at the moment of admission into the penal justice system. Suicide risk was assessed using the Mini International Neuropsychiatric Interview in newly admitted female (n=198) and male (n=229) prisoners in Santiago de Chile. The burden of separation from minor children was rated on a numeric rating scale. Both genders showed high burden of separation from children at imprisonment. Mothers had significantly lower suicide risk than women without children. The relative risk was 0.31 (95% CI [0.16-0.6], p<0.001) to show 'high suicide risk'. There was no difference of suicide risk between imprisoned fathers and male prisoners without children. Within the group of fathers, the suicide risk associated with the burden of separation. Our study indicates that strengthening the parent role and facilitating parent-child contacts during imprisonment could be an important element of suicide prevention interventions.

BRAIN. 2017 MAY 1;140(5):1371-1383.

NEUROIMAGING AND CLINICAL FEATURES IN ADULTS WITH A 22Q11.2 DELETION AT RISK OF PARKINSON'S DISEASE.

Butcher NJ, Marras C, Pondal M, Rusjan P, Boot E, Christopher L, Repetto GM, Fritsch R, Chow EWC, Masellis M, Strafella AP, Lang AE, Bassett AS

The recurrent 22q11.2 deletion is a genetic risk factor for early-onset Parkinson's disease. Adults with the associated 22q11.2 deletion syndrome (22q11.2DS) may exhibit phenotypes that could help identify those at highest risk and reveal disease trajectories. We investigated clinical and neuroimaging features relevant to Parkinson's disease in 26 adults: 13 with 22q11.2DS at genetic risk of Parkinson's disease (mean age = 41.5 years, standard deviation = 9.7), 12 healthy age and sex-matched controls, and a 22q11.2DS patient with l-DOPA-responsive early-onset Parkinson's disease. Neuroimaging included transcranial sonography and positron emission tomography using 11C-dihydrotetrabenazine (11C-DTBZ), a radioligand that binds to the presynaptic vesicular monoamine transporter. The 22q11.2DS group without Parkinson's disease demonstrated significant motor and olfactory deficits relative to controls. Eight (61.5%) were clinically classified with parkinsonism. Transcranial sonography showed a significantly larger mean area of substantia nigra echogenicity in the 22q11.2DS risk group compared with controls (P = 0.03). The 22q11.2DS patient with Parkinson's disease showed the expected pattern of severely reduced striatal 11C-DTBZ binding. The 22q11.2DS group without Parkinson's disease however showed significantly elevated striatal 11C-DTBZ binding relative to controls (~33%; P < 0.01). Results were similar within the 22q11.2DS group for those with (n = 7) and without (n = 6) psychotic illness. These findings suggest that manifestations of parkinsonism and/or evolution to Parkinson's disease in this genetic at-risk population may include a hyperdopaminergic mechanism. Adequately powered longitudinal studies and animal models are needed to evaluate the relevance of the observed clinical and imaging phenotypes to Parkinson's disease and other disorders that are more prevalent in 22q11.2DS, such as schizophrenia.

SCHIZOPHR RES. 2017 APR 18. PII: S0920-9964(17)30197-4.

THE RELATIVE PREVALENCE OF SCHIZOPHRENIA AMONG CANNABIS AND COCAINE USERS ATTENDING ADDICTION SERVICES.

Libuy N, de Angel V, Ibáñez C, Murray RM, Mundt AP.

BACKGROUND: Cannabis and cocaine are the most common illicit drugs for which people are treated in addiction services in Latin America. Much research has suggested that the use of cannabis increases the risk of schizophrenia; there is less evidence concerning cocaine. The aim of the present study was to establish the relative prevalence of schizophrenia in people treated for cannabis use and cocaine use disorders in Chile. METHODS: A sample of 22,615 people treated for illicit drug use disorders was obtained from a national registry of addiction service users in Chile. Clinical diagnoses were established at admission to substance use treatment programs or at any point during the period of treatment. Prevalence rates of schizophrenia and related disorders, and affective disorders were calculated for the groups of people with cocaine use disorders, and cannabis use disorders. Odds ratios (OR) for schizophrenia and for affective disorders were calculated for cannabis users using the group of people treated for cocaine use disorders as reference category. RESULTS: The prevalence of schizophrenia and related disorders was 1.1% in those with cocaine use disorders, but 5.2% in those with cannabis use disorders (OR 4.9; p<0.01). The prevalence of affective disorders was 9.3% in cocaine use disorders, and 13.2% in cannabis use disorders (OR 1.5; p<0.01). CONCLUSIONS: The prevalence of schizophrenia and to a lesser extent affective disorders is higher among people with cannabis use disorder than cocaine use disorder among those attending addiction services.

QUAL LIFE RES. 2017 DEC;26(12):3211-3225.

STANDARDIZATION OF HEALTH OUTCOMES ASSESSMENT FOR DEPRESSION AND ANXIETY: RECOMMENDATIONS FROM THE ICHOM DEPRESSION AND ANXIETY WORKING GROUP.

Obbarius A, van Maasakkers L, Baer L, Clark DM, Crocker AG, de Beurs E, Emmelkamp PMG, Furukawa TA, Hedman-Lagerlöf E, Kangas M, Langford L, Lesage A, Mwesigire DM, Nolte S, Patel V, Pilkonis PA, Pincus HA, Reis RA, Rojas G, Sherbourne C, Smithson D, Stowell C, Woolaway-Bickel K, Rose M.

PURPOSE: National initiatives, such as the UK Improving Access to Psychological Therapies program (IAPT), demonstrate the feasibility of conducting empirical mental health assessments on a large scale, and similar initiatives exist in other countries. However, there is a lack of international consensus on which outcome domains are most salient to monitor treatment progress and how they should be measured. The aim of this project was to propose (1) an essential set of outcome domains relevant across countries and cultures, (2) a set of easily accessible patient-reported instruments, and (3) a psychometric approach to make scores from different instruments comparable. METHODS: Twenty-four experts, including ten health outcomes researchers, ten clinical experts from all continents, two patient advocates, and two ICHOM coordinators worked for seven months in a consensus building exercise to develop recommendations based on existing evidence using a structured consensus-driven modified Delphi technique. RESULTS: The group proposes to combine an assessment of potential outcome predictors at baseline (47 items: demographics, functional, clinical status, etc.), with repeated assessments of disease-specific symptoms during the treatment process (19 items: symptoms, side effects, etc.), and a comprehensive annual assessment of broader treatment outcomes (45 items: remission, absenteeism, etc.). Further, it is suggested reporting disease-specific symptoms for depression and anxiety on a standardized metric to increase comparability with other legacy instruments. All recommended instruments are provided online (www.ichom.org). CONCLUSION: An international standard of health outcomes assessment has the potential to improve clinical decision making, enhance health care for the benefit of patients, and facilitate scientific knowledge.

DEPARTANMENTO DE OTORRINOLARINGOLOGÍA

INT J DEV NEUROSCI. 2017 APR;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.

ACTA OTORRINOLARINGOL ESP. 2017 JAN - FEB;68(1):1-8.

REVISION ENDOSCOPIC SINONASAL SURGERY.

Cantillano P, Rubio F, Naser A, Nazar R.

INTRODUCTION AND OBJECTIVES: Endoscopic sinonasal surgery is the procedure of choice in the treatment of chronic rhinosinusitis and sinonasal polyposis refractory to medical treatment, with high rates of success (76% to 97.5%). However, 2.5%-24% of those patients will require revision surgery (RESS). In this study, we present the clinical, anatomical, radiological and histological features of patients receiving RESS in our centre during a 3-year period. METHODS: A retrospective review of clinical, anatomical, radiological and histopathological data of patients receiving revision endoscopic sinonasal surgery between 2012 and 2014 was carried out. RESULTS: From 299 surgery procedures performed, 27 (9%) were revision surgeries. The mean patient age was 46 years, with a male/female ratio of 1.4/1. The most frequent preoperative and postoperative diagnosis was chronic polypoid rhinosinusitis. The mean time since the previous surgery was 6.1 years, with 11.9 months of mean follow-up since that surgery. Stenotic antrostomy was found during revision in 81.5% of the patients and incomplete anterior ethmoidectomy and persistent uncinate process, in 59.3%. In radiology, 70.4% of patients had persistent anterior ethmoidal cells. Antrostomy or widening of antrostomy was performed in 96.3% of cases and anterior ethmoidectomy or completion of it was performed in 66.7%. CONCLUSIONS: Polyps, stenotic antrostomy and incomplete ethmoidectomy were the most frequent causes of revision surgery, in concordance with the procedures performed. The patients had long periods of time without follow-up between surgeries. Further investigation is necessary to generate measures to reduce the number of revision surgeries.

FRONT CELL NEUROSCI. 2017 NOV 8;11:357.

DIFFERENCE IN PERSEVERATIVE ERRORS DURING A VISUAL ATTENTION TASK WITH AUDITORY DISTRACTORS IN ALPHA-9 NICOTINIC RECEPTOR SUBUNIT WILD TYPE AND KNOCK-OUT MICE.

Jorratt P, Delano PH, Delgado C, Dagnino-Subiabre A, Terreros G.

The auditory efferent system is a neural network that originates in the auditory cortex and projects to the cochlear receptor through olivocochlear (OC) neurons. Medial OC neurons make cholinergic synapses with outer hair cells (OHCs) through nicotinic receptors constituted by α9 and α10 subunits. One of the physiological functions of the α9 nicotinic receptor subunit (α9-nAChR) is the suppression of auditory distractors during selective attention to visual stimuli. In a recent study we demonstrated that the behavioral performance of alpha-9 nicotinic receptor knock-out (KO) mice is altered during selective attention to visual stimuli with auditory distractors since they made less correct responses and more omissions than wild type (WT) mice. As the inhibition of the behavioral responses to irrelevant stimuli is an important mechanism of the selective attention processes, behavioral errors are relevant measures that can reflect altered inhibitory control. Errors produced during a cued attention task can be classified as premature, target and perseverative errors. Perseverative responses can be considered as an inability to inhibit the repetition of an action already planned, while premature responses can be considered as an index of the ability to wait or retain an action. Here, we studied premature, target and perseverative errors during a visual attention task with auditory distractors in WT and KO mice. We found that α9-KO mice make fewer perseverative errors with longer latencies than WT mice in the presence of auditory distractors. In addition, although we found no significant difference in the number of target error between genotypes, KO mice made more short-latency target errors than WT mice during the presentation of auditory distractors. The fewer perseverative error made by α9-KO mice could be explained by a reduced motivation for reward and an increased impulsivity during decision making with auditory distraction in KO mice.

FRONT CELL NEUROSCI. 2017 OCT 10;11:302.

THE SLEEP-WAKE CYCLE IN THE NICOTINIC ALPHA-9 ACETYLCHOLINE RECEPTOR SUBUNIT KNOCK-OUT MICE.

Madrid-López N, Estrada J, Díaz J, Bassi A, Délano PH, Ocampo-Garcés A.

There is a neural matrix controlling the sleep-wake cycle (SWC) embedded within high ranking integrative mechanisms in the central nervous system. Nicotinic alpha-9 acetylcholine receptor subunit (alpha-9 nAChR) participate in physiological processes occurring in sensory, endocrine and immune systems. There is a relationship between the SWC architecture, body homeostasis and sensory afferents so that disruption of afferent signaling is expected to affect the temporal organization of sleep and wake states. The analysis of the SWC of 9 nAChR knock-out animals may help to reveal the contribution of alpha-9 nAChR to sleep chronobiological determinants. Here we explore the polysomnogram in chronically implanted alpha-9 nAChR knock-out (KO) and wild-type (WT) individuals of the hybrid CBA/Sv129 mouse strain. Records were obtained in isolation chambers under a stable 12:12 light:dark cycle (LD). To unmask the 24-h modulation of the SWC a skeleton photoperiod (SP) protocol was performed. Under LD the daily quota (in %) of wakefulness (W), NREM sleep and REM sleep obtained in KO and WT animals were 45, 48 and 7, and 46, 46 and 8 respectively. Both groups exhibit nocturnal phase preference of W as well as diurnal and unimodal phase preference of NREM and REM sleep. The acrophase mean angles of KO vs. WT genotypes were not different (Zeitgeber Time: 6.5 vs. 14.9 for W, 4.3 vs. 2.8 for NREM sleep and 5.3 vs. 3.4 for REM sleep, respectively). Transference to SP do not affect daily state quotas, phase preferences and acrophases among genotypes. Unmasking phenomena of the SWC such as wake increment during the rest phase under SP was evident only among WT mice suggesting the involvement of retinal structures containing alpha-9 nAChR in masking processes. Furthermore, KO animals exhibit longer NREM and REM sleep episodes that is independent of illumination conditions. Consolidated diurnal NREM sleep contributed to obtain higher values of NREM sleep delta-EEG activity among KO mice during rest phase. In conclusion, circadian and sleep homeostatic aspects of the SWC are operative among alpha-9 nAChR KO animals. We propose that alpha-9 nAChR participate in retinal signaling processes responsible of the positive masking of sleep by light.

FRONT NEUROL. 2017 MAR 13;8:90.

ALTERED CERVICAL VESTIBULAR-EVOKED MYOGENIC POTENTIAL IN CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Isaac V, Olmedo D, Aboitiz F, Delano PH.

OBJECTIVE: Emerging evidence suggests that children with attention deficit and hyperactivity disorder (ADHD) present more difficulties in standing and walking balance than typically developing children. Most of previous studies have assessed these functions using postural and sensory organization tests showing differences in balance performance between control and ADHD children. However, to date, it is unknown whether these balance alterations are accompanied with vestibular dysfunction. The principal aim of this study is to evaluate vestibular otolith function in ADHD and matched control children. METHODS: We assessed vestibular otolith function in children with ADHD and controls using the subjective visual vertical (SVV) bucket test and cervical vestibular-evoked myogenic potentials (cVEMPs). In addition, gait and balance were evaluated using the dynamic gait index (DGI) and computerized posturography. RESULTS: Non-significant differences between groups were obtained in SVV evaluation. DGI results show lower scores for overall test performance in children with ADHD ($p < 0.001$), while computerized postural recordings showed significant differences for the limit of stability between groups ($p = 0.02$). cVEMPs in response to 500 Hz tone bursts presented at 100 dB were absent or reduced in children with ADHD, as revealed by differences in P1 and N1 peak-to-peak amplitudes between groups ($p < 0.01$). CONCLUSION: These findings suggest that vestibular brainstem reflexes are altered in a subset of children with ADHD. We propose to include cVEMP reflexes in the clinical evaluation of ADHD patients.

SERVICIO BANCO DE SANGRE

FRONT IMMUNOL. 2017 OCT 23;8:1350.

DEXAMETHASONE AND MONOPHOSPHORYL LIPID A INDUCE A DISTINCTIVE PROFILE ON MONOCYTE-DERIVED DENDRITIC CELLS THROUGH TRANSCRIPTIONAL MODULATION OF GENES ASSOCIATED WITH ESSENTIAL PROCESSES OF THE IMMUNE RESPONSE.

García-González PA, Schinnerling K, Sepúlveda-Gutiérrez A, Maggi J, Mehdi AM, Nel HJ, Pesce B, Larrondo ML, Aravena O, Molina MC, Catalán D[1,2], Thomas R, Verdugo RA, Aguillón JC.

There is growing interest in the use of tolerogenic dendritic cells (tolDCs) as a potential target for immunotherapy. However, the molecular bases that drive the differentiation of monocyte-derived DCs (moDCs) toward a tolerogenic state are still poorly understood. Here, we studied the transcriptional profile of moDCs from healthy subjects, modulated with dexamethasone (Dex) and activated with monophosphoryl lipid A (MPLA), referred to as Dex-modulated and MPLA-activated DCs (DM-DCs), as an approach to identify molecular regulators and pathways associated with the induction of tolerogenic properties in tolDCs. We found that DM-DCs exhibit a distinctive transcriptional profile compared to untreated (DCs) and MPLA-matured DCs. Differentially expressed genes downregulated by DM included MMP12, CD1c, IL-1B, and FCER1A involved in DC maturation/inflammation and genes upregulated by DM included JAG1, MERTK, IL-10, and IDO1 involved in tolerance. Genes related to chemotactic responses, cell-to-cell signaling and interaction, fatty acid oxidation, metal homeostasis, and free radical scavenging were strongly enriched, predicting the activation of alternative metabolic processes than those driven by counterpart DCs. Furthermore, we identified a set of genes that were regulated exclusively by the combined action of Dex and MPLA, which are mainly involved in the control of zinc homeostasis and reactive oxygen species production. These data further support the important role of metabolic processes on the control of the DC-driven regulatory immune response. Thus, Dex and MPLA treatments modify gene expression in moDCs by inducing a particular transcriptional profile characterized by the activation of tolerance-associated genes and suppression of the expression of inflammatory genes, conferring the potential to exert regulatory functions and immune response modulation.

FRONT NEUROSCI. 2017 JUL 11;11:395.

ON THE ORIGIN OF THE 1,000 HZ PEAK IN THE SPECTRUM OF THE HUMAN TYMPANIC ELECTRICAL NOISE.

Pardo-Jadue J, Dragicevic CD, Bowen M, Delano PH.

The spectral analysis of the spontaneous activity recorded with an electrode positioned near the round window of the guinea pig cochlea shows a broad energy peak between 800 and 1,000 Hz. This spontaneous electric activity is called round window noise or ensemble background activity. In guinea pigs, the proposed origin of this peak is the random sum of the extracellular field potentials generated by action potentials of auditory nerve neurons. In this study, we used a non-invasive method to record the tympanic electric noise (TEN) in humans by means of a tympanic wick electrode. We recorded a total of 24 volunteers, under silent conditions or in response to stimuli of different modalities, including auditory, vestibular, and motor activity. Our results show a reliable peak of spontaneous activity at ~1,000 Hz in all studied subjects. In addition, we found stimulus-driven responses with broad-band noise that in most subjects produced an increase in the magnitude of the energy band around 1,000 Hz (between 650 and 1,200 Hz). Our results with the vestibular stimulation were not conclusive, as we found responses with all caloric stimuli, including 37°C. No responses were observed with motor tasks, like eye movements or blinking. We demonstrate the feasibility of recording neural activity from the electric noise of the tympanic membrane with a non-invasive method. From our results, we suggest that the 1,000 Hz component of the TEN has a mixed origin including peripheral and central auditory pathways. This research opens up the possibility of future clinical non-invasive techniques for the functional study of auditory and vestibular nerves in humans.

DEPARTAMENTO DE OFTAMOLOGÍA

OCUL IMMUNOL INFLAMM. 2017 AUG;25(4):455-459.

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: o 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.

CURR EYE RES. 2017 JUL;42(7):1029-1034.
CLINICAL FEATURES AND PROGNOSTIC FACTORS IN PRESUMED OCULAR TUBERCULOSIS.
Urzua CA, Lantigua Y, Abuauad S, Liberman P, Berger O, Sabat P, Velasquez V, Castiglione E, Calonge M.

PURPOSE: To characterize the clinical features in patients with presumed ocular tuberculosis (TB) and determine prognostic factors of visual outcomes and complications in this disease. MATERIAL AND METHODS: Retrospective case series of 35 patients (29 females, 6 males) with presumed ocular TB from referral centers in Chile and Spain between 2002 and 2012. Medical records were reviewed, and data regarding clinical features, complications, best-corrected visual acuity (BCVA), duration of disease, extraocular manifestations, and therapy were retrieved. Prognostic factors for low vision (BCVA 20/50 or less), legal blindness (BCVA 20/200 or less), and complications (cataract, glaucoma, and macular lesion) were evaluated. To calculate correlations, we used Spearman's rank correlation test. To determine clinical predictors, we used the binary logistic regression test. RESULTS: Anterior and non-granulomatous uveitis was the most common types of inflammation. Only 2 (5.7%) patients had respiratory symptoms, and 6 (17.1%) patients had an abnormal chest X-ray at diagnosis. All patients received combined antitubercular therapy with a mean duration of 6.9 ± 2.3 months. A longer duration of symptoms at diagnosis was associated with both low vision and legal blindness. Older patients had a higher risk of legal blindness. A longer duration of symptoms as well as anterior inflammation demonstrated an increased risk for cataract formation. The duration of the symptoms and baseline BCVA had a positive correlation with the final BCVA. Prognostic factors of macular lesions were not found. CONCLUSIONS: The diagnosis of ocular TB can be difficult due to the lack of extraocular manifestations and the broad spectrum of ocular features. A longer duration of symptoms at diagnosis was associated with poorer visual outcomes and cataracts. Therefore, efforts should be made to avoid a delay in the diagnosis of ocular TB and to identify prognostic factors for visual outcomes and complications.

SERVICIO ANESTESIOLOGÍA Y REANIMACIÓN

REG ANESTH PAIN MED. 2017 JAN/FEB;42(1):32-38.
DIAPHRAGM-SPARING NERVE BLOCKS FOR SHOULDER SURGERY.
Tran DQ, Elgueta MF, Aliste J, Finlayson RJ.

Shoulder surgery can result in significant postoperative pain. Interscalene brachial plexus blocks (ISBs) constitute the current criterion standard for analgesia but may be contraindicated in patients with pulmonary pathology due to the inherent risk of phrenic nerve block and symptomatic hemidiaphragmatic paralysis. Although ultrasound-guided ISB with small volumes (5 mL), dilute local anesthetic (LA) concentrations, and LA injection 4 mm lateral to the brachial plexus have been shown to reduce the risk of phrenic nerve block, no single intervention can decrease its incidence below 20%. Ultrasound-guided supraclavicular blocks with LA injection posterolateral to the brachial plexus may anesthetize the shoulder without incidental diaphragmatic dysfunction, but further confirmatory trials are required. Ultrasound-guided C7 root blocks also seem to offer an attractive, diaphragm-sparing alternative to ISB. However, additional large-scale studies are needed to confirm their efficacy and to quantify the risk of periforaminal vascular breach. Combined axillary-suprascapular nerve blocks may provide adequate postoperative analgesia for minor shoulder surgery but do not compare favorably to ISB for major surgical procedures. One intriguing solution lies in the combined use of infraclavicular brachial plexus blocks and suprascapular nerve blocks. Theoretically, the infraclavicular approach targets the posterior and lateral cords, thus anesthetizing the axillary nerve (which supplies the anterior and posterior shoulder joint), as well as the subscapular and lateral pectoral nerves (both of which supply the anterior shoulder joint), whereas the suprascapular nerve block anesthetizes the posterior shoulder. Future randomized trials are required to validate the efficacy of combined infraclavicular-suprascapular blocks for shoulder surgery.

PLOS ONE. 2017 SEP 12;12(9):E0184189.
AGED BLOOD FACTORS DECREASE CELLULAR RESPONSES ASSOCIATED WITH DELAYED GINGIVAL WOUND REPAIR.
Saldías MP, Fernández C, Morgan A, Díaz C, Morales D, Jaña F, Gómez A, Silva A, Briceño F, Oyarzún A, Maldonado F, Cerda O, Smith PC, Cáceres M.

Aging is a gradual biological process characterized by a decrease in cell and organism functions. Gingival wound healing is one of the impaired processes found in old rats. Here, we studied the in vivo wound healing process using a gingival repair rat model and an in vitro model using human gingival fibroblast for cellular responses associated to wound healing. To do that, we evaluated cell proliferation of both epithelial and connective tissue cells in gingival wounds and found decreased of Ki67 nuclear staining in old rats when compared to their young counterparts. We next evaluated cellular responses of primary gingival fibroblast obtained from young subjects in the presence human blood serum of individuals of different ages. Eighteen to sixty five years old masculine donors were classified into 3 groups: "young" from 18 to 22 years old, "middle-aged" from 30 to 48 years old and "aged" over 50 years old. Cell proliferation, measured through immunofluorescence for Ki67 and flow cytometry for DNA content, was decreased when middle-aged and aged serum was added to gingival fibroblast compared to young serum. Myofibroblastic differentiation, measured through alpha-smooth muscle actin (α-SMA), was stimulated with young but not middle-aged or aged serum both the protein levels and incorporation of α-SMA into actin stress fibers. High levels of PDGF, VEGF, IL-6R were detected in blood serum from young subjects when compared to middle-aged and aged donors.

In addition, the pro-inflammatory cytokines MCP-1 and TNF were increased in the serum of aged donors. In old rat wound there is an increased of staining for TNF compared to young wound. Moreover, healthy gingiva (non injury) shows less staining compared to a wound site, suggesting a role in wound healing. Moreover, serum from middle-aged and aged donors was able to stimulate cellular senescence in young cells as determined by the expression of senescence associated beta-galactosidase and histone H2A.X phosphorylated at Ser139. Moreover, we detected an increased frequency of γ-H2A.X-positive cells in aged rat gingival tissues. The present study suggests that serum factors present in middle-aged and aged individuals may be responsible, at least in part, for the altered responses observed during wound healing in aging.

ANESTHESIOLOGY. 2017 APR;126(4):666-677.
KETAMINE INCREASES THE FUNCTION OF γ-AMINOBUTYRIC ACID TYPE A RECEPTORS IN HIPPOCAMPAL AND CORTICAL NEURONS.
Wang DS, Penna A, Orser BA.

BACKGROUND: The "dissociative" general anesthetic ketamine is a well-known N-methyl-D-aspartate receptor antagonist. However, whether ketamine, at clinically relevant concentrations, increases the activity of inhibitory γ-aminobutyric acid (GABA) receptor type A (GABAA) receptors in different brain regions remains controversial. Here, the authors studied the effects of ketamine on synaptic and extrasynaptic GABAA receptors in hippocampal neurons. Ketamine modulation of extrasynaptic GABAA receptors in cortical neurons was also examined. METHODS: Whole cell currents were recorded from cultured murine neurons. Current evoked by exogenous GABA, miniature inhibitory postsynaptic currents, and currents directly activated by ketamine were studied. RESULTS: Ketamine did not alter the amplitude, frequency, or kinetics of postsynaptic currents but increased a tonic inhibitory current generated by extrasynaptic GABAA receptors in hippocampal neurons. For example, ketamine (100 μM) increased the tonic current by 33.6 ± 6.5% (mean ± SEM; 95% CI, 18.2 to 48.9; n = 8, P < 0.001). Ketamine shifted the GABA concentration-response curve to the left, but only when GABAA receptors were activated by low concentrations of GABA (n = 6). The selective increase in tonic current was attributed to ketamine increasing the apparent potency of GABA at high-affinity extrasynaptic GABAA receptors. Ketamine also increased a tonic current in cortical neurons (n = 11). Ketamine directly gated the opening of GABAA receptors, but only at high concentrations that are unlikely to occur during linical use. CONCLUSIONS: Clinically relevant concentrations of ketamine increased the activity of high-affinity extrasynaptic GABAA receptors in the hippocampus and cortex, an effect that likely contributes to ketamine's neurodepressive properties.

UNIDAD PACIENTES CRÍTICOS

CURR PSYCHIATRY REP. 2017 JAN;19(1):2.
SCHIZOPHRENIA: IMPACT ON FAMILY DYNAMICS.
Caqueo-Urízar A, Rus-Calafell M, Craig TK, Irarrazaval M, Urzúa A, Boyer L, Williams DR.

In many societies, family members are now the primary caregivers of mental health patients, taking on responsibilities traditionally under the purview of hospitals and medical professionals. The impact of this shift on the family is high, having both an emotional and economic toll. The aim of this paper is to review the main changes that occur in family dynamics for patients with schizophrenia. The article addresses three central themes: (i) changes in the family at the onset of the disorder, (ii) consequences for family members because of their caregiver role, and (iii) family interventions aimed at improving the complex dynamics within the family. After analyzing and discussing these themes, it is observed that despite advances in the field, the viability of taking care of a patient with schizophrenia by the family remains a challenge. Improving care will require commitments from the family, the mental health service system, and local and national governments for greater investments to improve the quality of life of society in general and individuals with schizophrenia in particular.

RESPIR CARE. 2017 FEB;62(2):144-149.
ABILITY OF ICU HEALTH-CARE PROFESSIONALS TO IDENTIFY PATIENT-VENTILATOR ASYNCHRONY USING WAVEFORM ANALYSIS.
Ramirez II, Arellano DH, Adasme RS, Landeros JM, Salinas FA, Vargas AG, Vasquez FJ, Lobos IA, Oyarzun ML, Restrepo RD.

BACKGROUND: Waveform analysis by visual inspection can be a reliable, noninvasive, and useful tool for detecting patient-ventilator asynchrony. However, it is a skill that requires a properly trained professional. METHODS: This observational study was conducted in 17 urban ICUs. Health-care professionals (HCPs) working in these ICUs were asked to recognize different types of asynchrony shown in 3 evaluation videos. The health-care professionals were categorized according to years of experience, prior training in mechanical ventilation, profession, and number of asynchronies identified correctly. RESULTS: A total of 366 HCPs were evaluated. Statistically significant differences were found when HCPs with and without prior training in mechanical ventilation (trained vs non-trained HCPs) were compared according to the number of asynchronies detected correctly (of the HCPs who identified 3 asynchronies, 63 [81%] trained vs 15 [19%] non-trained, P < .001; 2 asynchronies, 72 [65%] trained vs 39 [35%] non-trained, P = .034; 1 asynchrony, 55 [47%] trained vs 61 [53%] non-trained, P = .02; 0 asynchronies, 17 [28%] trained vs 44 [72%] non-trained, P < .001). HCPs who had prior training in mechanical

ventilation also increased, nearly 4-fold, their odds of identifying ≥2 asynchronies correctly (odds ratio 3.67, 95% CI 1.93-6.96, P < .001). However, neither years of experience nor profession were associated with the ability of HCPs to identify asynchrony. CONCLUSIONS: HCPs who have specific training in mechanical ventilation increase their ability to identify asynchrony using waveform analysis. Neither experience nor profession proved to be a relevant factor to identify asynchrony correctly using waveform analysis.

CRIT CARE MED. 2017 AUG;45(8):1325-1336.

ORGANIZATIONAL ISSUES, STRUCTURE, AND PROCESSES OF CARE IN 257 ICUS IN LATIN AMERICA: A STUDY FROM THE LATIN AMERICA INTENSIVE CARE NETWORK.

Estenssoro E, Alegría L, Murias G, Friedman G, Castro R, Nin Vaeza N, Loudet C, Bruhn A, Jibaja M, Ospina-Tascon G, Ríos F, Machado FR, Biasi Cavalcanti A, Dubin A, Hurtado FJ, Briva A, Romero C, Bugedo G, Bakker J, Cecconi M, Azevedo L, Hernandez G; Latin-American Intensive Care Network (LIVEN). OBJECTIVE: Latin America bears an important burden of critical care disease, yet the information about it is scarce. Our objective was to describe structure, organization, processes of care, and research activities in Latin-American ICUs. DESIGN: Web-based survey submitted to ICU directors. SETTINGS: ICUs located in nine Latin-American countries. SUBJECTS: Individual ICUs. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Two hundred fifty-seven of 498 (52%) of submitted surveys responded: 51% from Brazil, 17% Chile, 13% Argentina, 6% Ecuador, 5% Uruguay, 3% Colombia, and 5% between Mexico, Peru, and Paraguay. Seventy-nine percent of participating hospitals had less than 500 beds; most were public (59%) and academic (66%). ICUs were mainly medical-surgical (75%); number of beds was evenly distributed in the entire cohort; 77% had 24/7 intensivists; 46% had a physician-to-patient ratio between 1:4 and 7; and 69% had a nurse-to-patient ratio of 1 ≥ 2.1. The 24/7 presence of other specialists was deficient. Protocols in use averaged 9 ± 3. Brazil (vs the rest) had larger hospitals and ICUs and more quality, surveillance, and prevention committees, but fewer 24/7 intensivists and poorer nurse-to-patient ratio. Although standard monitoring, laboratory, and imaging practices were almost universal, more complex measurements and treatments and portable equipment were scarce after standard working hours, and in public hospitals. Mortality was 17.8%, without differences between countries. CONCLUSIONS: This multinational study shows major concerns in the delivery of critical care across Latin America, particularly in human resources. Technology was suboptimal, especially in public hospitals. A 24/7 availability of supporting specialists and of key procedures was inadequate. Mortality was high in comparison to high-income countries.

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CURRENT CLINICAL NUTRITION PRACTICES IN CRITICALLY ILL PATIENTS IN LATIN AMERICA: A MULTINATIONAL OBSERVATIONAL STUDY.

Vallejo KP, Martínez CM, Matos Adames AA, Fuchs-Tarlovsky V, Nogales GCC, Paz RER, Perman MI, Correia MITD, Waitzberg DL.

BACKGROUND: Malnutrition in critically ill adults in the intensive care unit (ICU) is associated with a significantly elevated risk of mortality. Adequate nutrition therapy is crucial to optimise outcomes. Currently, there is a paucity of such data in Latin America. Our aims were to characterise current clinical nutrition practices in the ICU setting in Latin America and evaluate whether current practices meet caloric and protein requirements in critically ill patients receiving nutrition therapy. METHODS: We conducted a cross-sectional, retrospective, observational study in eight Latin American countries (Argentina, Brazil, Chile, Colombia, Ecuador, Mexico, Panama, and Peru). Eligible patients were critically ill adults hospitalised in the ICU and receiving enteral nutrition (EN) and/or parenteral nutrition (PN) on the Screening Day and the previous day (day -1). Caloric and protein balance on day -1, nutritional status, and prescribed nutrition therapy were recorded. Multivariable logistic regression analysis was performed to identify independent predictors of reaching daily caloric and protein targets. RESULTS: The analysis included 1053 patients from 116 hospitals. Evaluation of nutritional status showed that 74.1% of patients had suspected/moderate or severe malnutrition according to the Subjective Global Assessment. Prescribed nutrition therapy included EN alone (79.9%), PN alone (9.4%), and EN + PN (10.7%). Caloric intake met >90% of the daily target in 59.7% of patients on day -1; a caloric deficit was present in 40.3%, with a mean (±SD) daily caloric deficit of -688.8 ± 455.2 kcal. Multivariable logistic regression analysis showed that combined administration of EN + PN was associated with a statistically significant increase in the probability of meeting >90% of daily caloric and protein targets compared with EN alone (odds ratio, 1.56; 95% confidence interval, 1.02-2.39; p = 0.038). CONCLUSIONS: In the ICU setting in Latin America, malnutrition was highly prevalent and caloric intake failed to meet targeted energy delivery in 40% of critically ill adults receiving nutrition therapy. Supplemental administration of PN was associated with improved energy and protein delivery; however, PN use was low. Collectively, these findings suggest an opportunity for more effective utilisation of supplemental PN in critically ill adults who fail to receive adequate nutrition from EN alone.

REV BRAS TER INTENSIVA. 2017 APR-JUN;29(2):248-252.

COGNITIVE STIMULATION AND OCCUPATIONAL THERAPY FOR DELIRIUM PREVENTION.

Tobar E, Alvarez E, Garrido M.

Delirium is a relevant condition in critically ill patients with long-term impacts on mortality, cognitive and functional status and quality of life. Despite the progress in its diagnosis, prevention and management during the last years, its impact persists being relevant, so new preventive and therapeutic strategies need to be explored. Among non-pharmacologic preventive strategies, recent reports suggest a role for occupational therapy through a series of interventions that may impact the development of delirium. The aim of this review is

to evaluate the studies evaluating the role of occupational therapy in the prevention of delirium in critically ill patient populations, and suggests perspectives to future research in this area.

SERVICIO EMERGENCIA

SCI REP. 2017 AUG 1;7(1):7011.

LOCUS OF ADHESION AND AUTOAGGREGATION (LAA), A PATHOGENICITY ISLAND PRESENT IN EMERGING SHIGA TOXIN-PRODUCING ESCHERICHIA COLI STRAINS.

Montero DA, Velasco J, Del Canto F, Puente JL, Padola NL, Rasko DA, Farfán M, Salazar JC, Vidal R.

Shiga Toxin-producing Escherichia coli (STEC) are a group of foodborne pathogens associated with diarrhea, dysentery, hemorrhagic colitis (HC) and hemolytic uremic syndrome (HUS). Shiga toxins are the major virulence factor of these pathogens, however adhesion and colonization to the human intestine is required for STEC pathogenesis. A subset of STEC strains carry the Locus of Enterocyte Effacement (LEE) pathogenicity island (PAI), which encodes genes that mediate the colonization of the human intestine. While LEE-positive STEC strains have traditionally been associated with human disease, the burden of disease caused by STEC strains that lacks LEE (LEE-negative) has increased recently in several countries; however, in the absence of LEE, the molecular pathogenic mechanisms by STEC strains are unknown. Here we report a 86-kb mosaic PAI composed of four modules that encode 80 genes, including novel and known virulence factors associated with adherence and autoaggregation. Therefore, we named this PAI as Locus of Adhesion and Autoaggregation (LAA). Phylogenomic analysis using whole-genome sequences of STEC strains available in the NCBI database indicates that LAA PAI is exclusively present in a subset of emerging LEE-negative STEC strains, including strains isolated from HC and HUS cases. We suggest that the acquisition of this PAI is a recent evolutionary event, which may contribute to the emergence of these STEC.

DEPARTAMENTO CARDIOVASCULAR

ARCH MED SCI. 2017 APR 1;13(3):558-567.

EFFECTS OF A NOVEL ASCORBATE-BASED PROTOCOL ON INFARCT SIZE AND VENTRICLE FUNCTION IN ACUTE MYOCARDIAL INFARCTION PATIENTS UNDERGOING PERCUTANEOUS CORONARY ANGIOPLASTY.

Ramos C, Brito R, González-Montero J, Valls N, Gormaz JG, Prieto JC, Aguayo R, Puentes Á, Noriega V, Pereira G, Palavecino T, Rodrigo R.

INTRODUCTION: This study was designed to test the hypothesis that high-dose ascorbate prior to reperfusion followed by low chronic oral doses ameliorate myocardial reperfusion injury (MRI) in acute myocardial infarction patients subjected to primary percutaneous coronary angioplasty (PCA). MATERIAL AND METHODS: A randomized double-blind placebo-controlled and multicenter clinical trial was performed on acute myocardial infarction (AMI) patients who underwent PCA. Sodium ascorbate (320 mmol/l, n = 53) or placebo (n = 46) was infused 30 min prior to PCA. Blood samples were drawn at enrolment (M1), after balloon deflation (M2), 6-8 h after M2 (M3) and at discharge (M4). Total antioxidant capacity of plasma (ferric reducing ability of plasma - FRAP), erythrocyte reduced glutathione (GSH) and plasma ascorbate levels were determined in blood samples. Cardiac magnetic resonance (CMR) was performed at 7-15 days and 2-3 months following PCA. Ninety-nine patients were enrolled. In 67 patients, the first CMR was performed, and 40 patients completed follow-up. RESULTS: The ascorbate group showed significantly higher ascorbate and FRAP levels and a decrease in the GSH levels at M2 and M3 ($p < 0.05$). There were no significant differences in the infarct size, indexed end-systolic volume and ejection fraction at both CMRs. There was a significant amelioration in the decreased ejection fraction between the first and second CMR in the ascorbate group ($p < 0.05$). CONCLUSIONS: Ascorbate given prior to reperfusion did not show a significant difference in infarct size or ejection fraction. However, it improved the change in ejection fraction determined between 7-15 days and 2-3 months. This result hints at a possible functional effect of ascorbate to ameliorate MRI.

INFLAMMOPHARMACOLOGY. 2017 FEB;25(1):91-97.

ANTINOCICEPTIVE INTERACTION OF GABAPENTIN WITH MINOCYCLINE IN MURINE DIABETIC NEUROPATHY.

Miranda HF, Sierralta F, Jorquera V, Poblete P, Prieto JC, Noriega V.

OBJECTIVE: Diabetic neuropathy (DN) is the most common complication of diabetes and pain is one of the main symptoms of diabetic neuropathy, however, currently available drugs are often ineffective and complicated by adverse events. The purpose of this research was to evaluate the antinociceptive interaction between gabapentin and minocycline in a mice experimental model of DN by streptozocin (STZ). METHODS: The interaction of gabapentin with minocycline was evaluated by the writhing and hot plate tests at 3 and 7 days after STZ injection or vehicle in male CF1 mice. RESULTS: STZ (150 mg/kg, i.p.) produced a marked increase in plasma glucose levels on day 7 (397.46 ± 29.65 mg/dL) than on day 3 (341.12 ± 35.50 mg/dL) and also developed neuropathic pain measured by algesiometric assays.

Gabapentin produced similar antinociceptive activity in both writhing and hot plate tests in mice pretreated with STZ. However, minocycline was more potent in the writhing than in the hot plate test in the same type of mice. The combination of gabapentin with minocycline produced synergistic interaction in both test. CONCLUSION: The combination of gabapentin with minocycline in a 1:1 proportion fulfills all the criteria of multimodal analgesia and this finding suggests that the combination provide a therapeutic alternative that could be used for human neuropathic pain management.

MEDICINA FÍSICA Y REHABLITACIÓN

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DIZZINESS AND FALLS IN OBESE INPATIENTS UNDERGOING METABOLIC REHABILITATION

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Aim. The relationship between dizziness and falls in the obese population is a relatively unexplored issue. The aims of the present study were to define the 1-year prevalence of dizziness in an obese inpatient population undergoing metabolic rehabilitation and to investigate possible correlations with fall events. Materials and Methods. We recruited 329 obese subjects: 203 female (BMI 43,74 kg/m2 ± 0.5 SE; age 17–83 years, 58.33 ± 0.9 SE) and 126 male (BMI 44,27kg/m2 ± 0.7 DE age 27–79 years, 58.84 ± 1 SE). To assess dizziness we used the validated Italian version (38) of the Dizziness Handicap Inventory (DHI). Results. Out of the experimental sample, 100 subjects did not complain of dizziness and felt confident about their balance control, while 69.6% reported some degree of dizziness. Their mean DHI score was 22.3, which corresponds to mild dizziness. Twenty-one percent reported more severe dizziness (DHI score > 40). The majority of our sample reported minor dizziness and its perception appears to be independent from BMI: DHI scores were consistent across classes of obesity. Discussion. The rate of dizziness and falls (30.1%) in an this obese population was higher than that previously reported in a general matched population. However, obese subjects, in our sample, seem to underestimate their risk of fall and DHI score does not appear a reliable predictor of falls. Since complications associated with falls in obese persons generally require longer treatments than in lean individuals, our findings should be taken into account in order to identify other predictors, including cognitive and perceptual, of risk of fall and to implement fall prevention programs.

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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.