

El material que se presenta a continuación es el resultado de búsquedas realizadas por nuestra Revista.

Abstracts de publicaciones ISI 2019

DEPARTAMENTO DE ANESTESIOLOGÍA Y MEDICINA OPERATORIA

J NEUROSURG SCI. 2019 SEP 23. DOI: 10.23736/S0390-5616.19.04715-5.

ASSOCIATION BETWEEN PRE-OPERATIVE SERUM LACTATE CONCENTRATE WITH TUMOUR CELL PROLIFERATIVE INDEX IN PRIMARY BRAIN TUMOUR.

Maldonado F, Fábregas N, Aldecoa I, González J, García M, Belda I, Hurtado P, Gracia I, de Riva N, Tercero J, Carrero E, Valero R.

BACKGROUND: Elevated preoperative lactate levels have been reported in patients admitted for resection of brain tumors. As histologic type and tumor grade have also been linked to lactate concentration, we hypothesized that preoperative lactate concentration in patients with brain tumors may be associated with tumor proliferation. We describe the relationship between preoperative plasma lactate levels, and the cell proliferation marker Ki-67 in brain tumor surgery. **METHODS:** In this cross-sectional study, records of patients who underwent craniotomy between June 2017 and February 2018 at our Hospital were reviewed to select glioma and meningioma cases in which lactate concentrations in plasma and degree of cell proliferation were registered. Bivariable and linear regression analyses were used to assess the association between lactate concentrations and the Ki-67 index. **RESULTS:** Lactate concentrations in plasma and Ki-67 index were available in 55 patients. Meningioma cases had a mean concentration of 1.2 (0.1) mmol/L compared to diffuse astrocytic and oligodendroglial tumours cases with 1.7 (0.1) mmol/L ($p < .01$). Both variables had a low positive correlation in meningiomas (Spearman's r , 0.29; 95% CI, -0.10-0.61; $p = .13$) and a high correlation in gliomas (Spearman's r , 0.64; 95% CI, 0.33-0.82; $p < .01$). The pooled analysis showed a high correlation index (Spearman's r , 0.61; 95% CI, 0.40-0.76; $p < .01$). A linear regression model showed that the Ki-67 index explained 43% of the variation in lactate ($p < .01$). **CONCLUSIONS:** Brain tumors with higher rates of cell proliferation have higher plasma lactate levels. In this scenario, lactate concentrations may not only reflect systemic perfusion.

REG ANESTH PAIN MED. 2019 JAN;44(1):46-51. DOI: 10.1136/RAPM-2018-000032.

A MULTICENTER, RANDOMIZED COMPARISON BETWEEN 2, 5, AND 8 MG OF PERINEURAL DEXAMETHASONE FOR ULTRASOUND-GUIDED INFRACLAVICULAR BLOCK.

Bravo D, Aliste J, Layera S, Fernández D, Leurcharusmee P, Samerchua A, Tangjitbampenbun A, Watanitanon A, Arnuntasupakul V, Tunprasit C, Gordon A, Finlayson RJ, Tran DQ.

BACKGROUND AND OBJECTIVES: This multicenter, randomized trial compared 2, 5, and 8 mg of perineural dexamethasone for ultrasound-guided infraclavicular brachial plexus block. Our research hypothesis was that all three doses of dexamethasone would result in equivalent durations of motor block (equivalence margin=3.0 hours). **METHODS:** Three hundred and sixty patients undergoing upper limb surgery with ultrasound-guided infraclavicular block were randomly allocated to receive 2, 5, or 8 mg of preservative-free perineural dexamethasone. The local anesthetic agent (35 mL of lidocaine 1%-bupivacaine 0.25% with epinephrine 5 µg/mL) was identical in all subjects. Patients and operators were blinded to the dose of dexamethasone. During the performance of the block, the performance time, number of needle passes, procedural pain, and complications (vascular puncture, paresthesia) were recorded. Subsequently a blinded observer assessed the success rate (defined as a minimal sensorimotor composite score of 14 out of 16 points at 30 min), onset time as well as the incidence of surgical anesthesia (defined as the ability to complete surgery without local infiltration, supplemental blocks, intravenous opioids, or general anesthesia). Postoperatively, the blinded observer contacted patients with successful blocks to inquire about the duration of motor block, sensory block, and postoperative analgesia. The main outcome variable was the duration of motor block. **RESULTS:** No intergroup differences were observed in terms of technical execution (performance time/number of needle passes/procedural pain complications), onset time, success rate, and surgical anesthesia. Furthermore, all three doses of dexamethasone provided similar durations of motor block (14.9-16.1 hours) and sensory block. Although 5 mg provided a longer analgesic duration than 2 mg, the difference (2.7 hours) fell

within our pre-established equivalence margin (3.0 hours). CONCLUSIONS: 2, 5, and 8 mg of dexamethasone provide clinically equivalent sensorimotor and analgesic durations for ultrasound-guided infraclavicular block. Further trials are required to compare low (ie, 2 mg) and ultra-low (eg, 0.5-1 mg) doses of perineural dexamethasone for brachial plexus blocks.

REG ANESTH PAIN MED. 2019 JAN 11. PII: RAPM-2018-100055. DOI: 10.1136/RAPM-2018-100055.

RANDOMIZED COMPARISON BETWEEN INTERSCALENE AND COSTOCLAVICULAR BLOCKS FOR ARTHROSCOPIC SHOULDER SURGERY.

Aliste J, Bravo D, Layera S, Fernández D, Jara Á, Maccioni C, Infante C, Finlayson RJ, Tran DQ.

BACKGROUND: This randomized trial compared ultrasound-guided interscalene block (ISB) and costoclavicular brachial plexus block (CCB) for arthroscopic shoulder surgery. We hypothesized that CCB would provide equivalent analgesia to ISB 30 min after surgery without the risk of hemidiaphragmatic paralysis. METHODS: All 44 patients received an ultrasound-guided block of the intermediate cervical plexus. Subsequently, they were randomized to ISB or CCB. The local anesthetic agent (20 mL of levobupivacaine 0.5% and epinephrine 5 µg/mL) and pharmacological block adjunct (4 mg of intravenous dexamethasone) were identical for all study participants. After the block performance, a blinded investigator assessed ISBs and CCBs every 5 min until 30 min using a composite scale that encompassed the sensory function of the supraclavicular nerves, the sensorimotor function of the axillary nerve and the motor function of the suprascapular nerve. A complete block was defined as one displaying a minimal score of six points (out of a maximum of eight points) at 30 min. Onset time was defined as the time required to reach the six-point minimal composite score. The blinded investigator also assessed the presence of hemidiaphragmatic paralysis at 30 min with ultrasonography. Subsequently, all patients underwent general anesthesia. Postoperatively, a blinded investigator recorded pain scores at rest at 0.5, 1, 2, 3, 6, 12, and 24 hours. Patient satisfaction at 24 hours, consumption of intraoperative and postoperative narcotics, and opioid-related side effects (eg, nausea/vomiting, pruritus) were also tabulated. RESULTS: Both groups displayed equivalent postoperative pain scores at 0.5, 1, 2, 3, 6, 12, and 24 hours. ISB resulted in a higher incidence of hemidiaphragmatic paralysis (100% vs 0%; $P < 0.001$) as well as a shorter onset time (14.0 (5.0) vs 21.6 (6.4) minutes; $p < 0.001$). However, no intergroup differences were found in terms of proportion of patients with minimal composite scores of 6 points at 30 min, intraoperative/postoperative opioid consumption, side effects, and patient satisfaction at 24 hours. CONCLUSION: Compared to ISB, CCB results in equivalent postoperative analgesia while circumventing the risk of hemidiaphragmatic paralysis. Further confirmatory trials are required. Future studies should also investigate if CCB can provide surgical anesthesia for arthroscopic shoulder surgery.

J CLIN ANESTH. 2019 MAR;53:5-10. DOI: 10.1016/J.JCLINANE.2018.09.030.

A SYSTEMATIC REVIEW OF DURAL PUNCTURE EPIDURAL ANALGESIA FOR LABOR.

Layera S, Bravo D, Aliste J, Tran DQ.

STUDY OBJECTIVE: This systematic review aimed to summarize the evidence derived from randomized controlled trials (RCTs) comparing dural puncture epidural analgesia (DPEA) and conventional lumbar epidural analgesia (LEA) for women undergoing labor. INTERVENTIONS: The MEDLINE and EMBASE databases were searched from inception to July 2018 in order to find RCTs published in the English language, which investigated DPEA in laboring women. MAIN RESULTS: Six RCTs were included in the final analysis. Their collective results remain ambiguous. Dural puncture with small (i.e., 26- or 27-gauge) spinal needles seems to confer either minimal benefits or improved analgesic quality and lower pain scores in the first 10 min. Dural puncture with 25-gauge spinal needles has been reported to provide higher success rate than conventional LEA in one trial; however two other studies could only agree on the fact that DPEA results in improved sacral blockade and fewer unilateral blocks compared to LEA. CONCLUSIONS: The current evidence regarding DPEA for labor analgesia remains ambiguous. Future research should investigate the optimal (spinal) needle size for dural puncture as well as factors governing transmeningeal flux of local anesthetics and opioids in the presence of a dural hole.

FRONT SYST NEUROSCI. 2019 OCT 18;13:56. DOI: 10.3389/FNSYS.2019.00056.

INTRAOPERATIVE LOW ALPHA POWER IN THE ELECTROENCEPHALOGRAM IS ASSOCIATED WITH POSTOPERATIVE SUBSYNDROMAL DELIRIUM.

Gutierrez R, Egaña JI, Saez I, Reyes F, Briceño C, Venegas M, Lavado I, Penna A.

BACKGROUND: Postoperative delirium (PD) and subsyndromal delirium (PSSD) are frequent complications in older patients associated with poor long-term outcome. It has been suggested that certain electroencephalogram features may be capable of identifying patients at risk during surgery. Thus, the goal of this study was to characterize intraoperative electroencephalographic markers to identify patients prone to develop PD or PSSD. METHODS: We conducted an exploratory observational study in older patients scheduled for elective major abdominal surgery. Intraoperative 16 channels electroencephalogram was recorded, and PD/PSSD were diagnosed after surgery with the confusion assessment method (CAM). The total power spectra and relative power of alpha band were calculated. RESULTS: PD was diagnosed in 2 patients (6.7%), and 11 patients (36.7%) developed PSSD. All of them (13 patients, PD/PSSD group) were compared with patients without any alterations in CAM (17 patients, control group). There were no detectable power spectrum differences before anesthesia between both groups of patients. However, PD/PSSD group in comparison with control group had a lower intraoperative absolute alpha power during anesthesia (4.4 ± 3.8 dB vs. 9.6 ± 3.2 dB, $p = 0.0004$) and a lower relative alpha power (0.09 ± 0.06 vs. 0.21 ± 0.08 , $p < 0.0001$). These

differences were independent of the anesthetic dose. Finally, relative alpha power had a good ability to identify patients with CAM alterations in the ROC analysis (area under the curve 0.90 (CI 0.78-1), $p < 0.001$). **DISCUSSION:** In conclusion, a low intraoperative alpha power is a novel electroencephalogram marker to identify patients who will develop alterations in CAM - i.e., with PD or PSSD - after surgery.

REG ANESTH PAIN MED. 2019 SEP 20. PII: RAPM-2019-100908. DOI: 10.1136/RAPM-2019-100908.

DIAPHRAGM-SPARING NERVE BLOCKS FOR SHOULDER SURGERY, REVISITED.

Tran DQ, Layera S, Bravo D, Cristi-Sánchez I, Bermudéz L, Aliste J.

Although interscalene brachial plexus block (ISB) remains the gold standard for analgesia after shoulder surgery, the inherent risks of ipsilateral phrenic nerve block and hemidiaphragmatic paralysis (HDP) limit its use in patients with preexisting pulmonary compromise. In a previous Daring Discourse (2017), our research team has identified potential diaphragm-sparing alternatives to ISB for patients undergoing shoulder surgery. In recent years, the field has been fertile with research, with the publication of multiple randomized controlled trials investigating supraclavicular blocks, upper trunk blocks, anterior suprascapular nerve blocks, costoclavicular blocks, and combined infraclavicular-suprascapular blocks. To date, the cumulative evidence (pre-2017 and post-2017) suggests that costoclavicular blocks may provide similar postoperative analgesia to ISB coupled with a 0%-incidence of HDP. However, in light of the small number of patients recruited by the single study investigating costoclavicular blocks, further confirmatory trials are required. Moreover, future investigation should also be undertaken to determine if costoclavicular blocks could achieve surgical anesthesia for shoulder surgery. Anterior suprascapular nerve blocks have been demonstrated to provide surgical anesthesia and similar analgesia to ISB. However, their risk of HDP has not been formally quantified. Of the remaining diaphragm-sparing nerve blocks, supraclavicular blocks (with local anesthetic injection posterolateral to the brachial plexus), upper trunk blocks, and combined infraclavicular-anterior suprascapular blocks merit further investigation, as they have been shown to achieve similar analgesia to ISB, coupled with an HDP incidence $<10\%$.

REG ANESTH PAIN MED. 2019 MAY 14. PII: RAPM-2019-100478. DOI: 10.1136/RAPM-2019-100478.

RANDOMIZED COMPARISON BETWEEN EPIDURAL WAVEFORM ANALYSIS THROUGH THE NEEDLE VERSUS THE CATHETER FOR THORACIC EPIDURAL BLOCKS.

Tangjitbampenbun A, Layera S, Arnuntasupakul V, Apinyachon W, Venegas K, Godoy J, Aliste J, Bravo D, Blanch A, Webar J, Saadawi M, Owen A, Finlayson RJ, Tran DQ.

BACKGROUND: Epidural waveform analysis (EWA) provides a simple confirmatory adjunct for loss of resistance (LOR): when the needle/catheter tip is correctly positioned inside the epidural space, pressure measurement results in a pulsatile waveform. Epidural waveform analysis can be carried out through the tip of the needle (EWA-N) or the catheter (EWA-C). In this randomized trial, we compared the two methods. We hypothesized that, compared with EWA-C, EWA-N would result in a shorter performance time. **METHODS:** One hundred and twenty patients undergoing thoracic epidural blocks for thoracic or abdominal surgery were randomized to EWA-N or EWA-C. In the EWA-N group, LOR was confirmed by connecting the epidural needle to a pressure transducer. After obtaining a satisfactory waveform, the epidural catheter was advanced 5 cm beyond the needle tip. In the EWA-C group, the epidural catheter was first advanced 5 cm beyond the needle tip after the occurrence of LOR. Subsequently, the catheter was connected to the pressure transducer to detect the presence of waveforms. In both study groups, the block procedure was repeated at different intervertebral levels until positive waveforms could be obtained (through the needle or catheter as per the allocation) or until a predefined maximum of three intervertebral levels had been reached. Subsequently, the operator administered a 4 mL test dose of lidocaine 2% with epinephrine 5 µg/mL through the catheter. An investigator present during the performance of the block recorded the performance time (defined as the temporal interval between skin infiltration and local anesthetic administration through the epidural catheter). Fifteen minutes after the test dose, a blinded investigator assessed the patient for sensory block to ice. Success was defined as a bilateral block in at least two dermatomes. Furthermore, postoperative pain scores, local anesthetic consumption, and breakthrough analgesic consumption were recorded. **RESULTS:** No intergroup differences were found in terms of performance time, success rate, postoperative pain, local anesthetic requirement, and breakthrough analgesic consumption. **CONCLUSION:** EWA can be carried out through the needle or through the catheter with similar efficiency (performance time) and efficacy (success rate, postoperative analgesia).

REG ANESTH PAIN MED. 2019 MAY 22. PII: RAPM-2019-100608. DOI: 10.1136/RAPM-2019-100608.

DURAL PUNCTURE EPIDURAL ANALGESIA FOR LABOR: A RANDOMIZED COMPARISON BETWEEN 25-GAUGE AND 27-GAUGE PENCIL POINT SPINAL NEEDLES.

Contreras F, Morales J, Bravo D, Layera S, Jara Á, Riaño C, Pizarro R, De La Fuente N, Aliste J, Finlayson RJ, Tran DQ.

BACKGROUND: This double-blind, randomized trial compared dural puncture epidural analgesia (DPEA) for labor using 25-gauge and 27-gauge pencil point spinal needles. We hypothesized that both needle sizes would result in similar onset time (equivalence margin=2.5min) and therefore designed the study as an equivalence trial. **METHODS:** One hundred and forty patients undergoing labor were randomized to DPEA with 25-gauge (n=70) or 27-gauge (n=70) pencil point spinal needles. After the placement of the epidural catheter, a bolus of 20 mL of

bupivacaine 0.125% and fentanyl 2 µg/mL was administered to all subjects. Thereafter, patients received boluses of 12 mL of bupivacaine 0.125% every 2 hours as needed. A blinded investigator recorded the onset time (defined as the temporal interval required to achieve a pain score ≤ 1 on a 0-10 scale), S2 block, sensory block height (30 min after the initial bolus of local anesthetic), presence of motor block (30 min after the initial bolus of local anesthetic), number of top-up doses required during labor and incidence of postural headache. RESULTS: Out of the 140 recruited patients, 135 were retained for analysis. Compared with their 27-gauge counterparts, 25-gauge pencil point spinal needles provided a 1.6 min shorter DPEA onset (95% CI of the difference of the means: -3.2 to -0.1 min). However, there were no intergroup differences in terms of S2 block, sensory block height, motor block, number of top-up doses and incidence of postural headache. CONCLUSION: Dural puncture epidural analgesia with 25-gauge pencil point spinal needles provides a 1.6 min shorter onset time than DPEA with 27-gauge spinal needles. Although statistically significant, such a difference may not be clinically relevant. Further investigation is required to compare 25-gauge and 27-gauge spinal needles for DPEA in the setting of different local anesthetic infusion strategies.

REG ANESTH PAIN MED. 2019 JUL 11. PII: RAPM-2019-100680. DOI: 10.1136/RAPM-2019-100680.

RANDOMIZED COMPARISON BETWEEN PERINEURAL DEXAMETHASONE AND DEXMEDETOMIDINE FOR ULTRASOUND-GUIDED INFRACLAVICULAR BLOCK.

Aliste J, Layera S, Bravo D, Fernández D, Jara Á, García A, Finlayson RJ, Tran DQ.

BACKGROUND: This randomized trial compared perineural dexamethasone (5 mg) and dexmedetomidine (100 µg) for ultrasound-guided infraclavicular brachial plexus block. We hypothesized that both adjuvants would result in similar durations of motor block and therefore designed the study as an equivalence trial (equivalence margin=3.0 hours). METHODS: One hundred and twenty patients undergoing upper limb surgery with ultrasound-guided infraclavicular block (using 35 mL of lidocaine 1%-bupivacaine 0.25% with epinephrine 5 µg/mL) were randomly allocated to receive perineural dexamethasone (5 mg) or dexmedetomidine (100 µg). Patients and operators were blinded to the nature of the perineural adjuvant. After the performance of the block, a blinded observer assessed the success rate (defined as a minimal sensorimotor composite score of 14 out of 16 points at 30 min) as well as the incidence of surgical anesthesia (defined as the ability to complete surgery without local infiltration, supplemental blocks, intravenous opioids, or general anesthesia). Heart rate and blood pressure were recorded before the block as well as during the first 2 hours after its performance. Furthermore, the level of sedation (using the Ramsay Sedation Scale) was recorded in the postanesthesia care unit. Postoperatively, the blinded observer contacted patients with successful blocks to inquire about the duration of motor block, sensory block, and postoperative analgesia. RESULTS: No intergroup differences were observed in terms of success rate and surgical anesthesia. Compared with dexmedetomidine, dexamethasone provided longer durations of motor block (17.4 (4.0) vs 14.3 (3.0) hours; $p < 0.001$; 95% CI 1.7 to 4.5), sensory block (19.0 (4.0) vs 15.0 (3.2) hours; $p < 0.001$; 95% CI 2.6 to 5.4), and analgesia (22.2 (3.6) vs 16.9 (3.9) hours; $p < 0.001$; 95% CI 3.7 to 6.9). Dexmedetomidine resulted in lower heart rate and blood pressure after the performance of the block, as well as an increased level of sedation postoperatively. CONCLUSION: Compared with dexmedetomidine (100 µg), dexamethasone (5 mg) results in longer sensorimotor block and analgesic durations, as well as a decreased level of patient sedation. Further studies are required to compare dexamethasone and dexmedetomidine using different doses, local anesthetic agents, and approaches to the brachial plexus.

DEPARTAMENTO CARDIOVASCULAR

DRUG RES (STUTTIG). 2019 DEC;69(12):688-694. DOI: 10.1055/A-0983-1402.

NITRIC OXIDE AND OPIOIDS INVOLVEMENT IN ISOBLOGRAPHIC NSAIDS ANTINOCICEPTION.

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

Different NSAIDs are used as antinociceptive in various analgesic assays, among which should be mentioned: ibuprofen, ketorolac, ketoprofen, meloxicam, paracetamol and others. It has been shown that NSAIDs possess antinociceptive activity by blocking cyclooxygenase enzymes (COXs). The present study was designed to evaluate the possible involvement of the nitridergic pathway due to L-NAME and the opioidergic route by NTX in the antinociception induced by NSAIDs using a murine pain model the tail flick test in an automatic tail flick algometer. The antinociception was evaluated by means of isobolographic analysis. The interaction between the combination of NSAIDs, via i.p., on basis of their ED₂₅, demonstrated that the coadministration of the drugs was synergistic with the exception of the lack of effect in combination of meloxicam with ibuprofen and with ketorolac, since the result was additive. These data validate that the NSAIDs administered alone or in combinations produce antinociception in which other mechanisms of action must be added to the simple inhibition of COXs. In addition, the pretreatment of the mice with L-NAME and NTX does not change previous isobolographic parameters of the mixture of NSAIDs.

DRUG RES (STUTTIG). 2019 OCT;69(10):572-578. DOI: 10.1055/A-0956-673.

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN TONIC, PHASIC AND INFLAMMATORY MOUSE MODELS.

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

The principal mechanism of action of non-steroidal anti-inflammatory drugs (NSAIDs) is the inhibition of cyclooxygenases. In this study was evaluated if NSAIDs could induce antinociceptive differences according to the type of murine pain model. Male mice were injected

intraperitoneally with meloxicam, diclofenac, piroxicam, metamizol, ibuprofen, naproxen and paracetamol in the writhing, tail flick and formalin orofacial tests and dose-response were analyzed to obtain the ED50 of each drugs. Administration of NSAIDs produced in a dose-dependent antinociception with different potency in the tests. The relative potency of NSAIDs among the tests shows a value of 5.53 in the orofacial formalin test in phase I and 6.34 in phase II between meloxicam and paracetamol; of 7.60 in the writhing test between meloxicam and paracetamol and of 8.46 in the tail flick test between ibuprofen and paracetamol. If the comparison is made for each NSAID in the different tests, the minimum value was 0.01 for between writhing and phase II of the orofacial formalin. Meanwhile, the highest power ratio was 11.71 for diclofenac between writhing and tail flick tests. In conclusion, the results suggests that intraperitoneal NSAIDs administration induce antinociceptive activity depending on the type of pain. The results support that NSAIDs administration, induce a wide variety of antinociceptive effect, depending on the type of pain. This suggest the participation of different mechanisms of action that can be added to the simple inhibition of COXs controlled by NSAIDs.

STROKE. 2019 JUN;50(6):1356-1363. DOI: 10.1161/STROKEAHA.118.023534.

STROKE IN PATIENTS WITH PERIPHERAL ARTERY DISEASE.

Kolls BJ, Sapp S, Rockhold FW, Jordan JD, Dombrowski KE, Fowkes FGR, Mahaffey KW, Berger JS, Katona BG, Blomster JL, Norgren L, Abramson BL, Leiva-Pons JL, Prieto JC, Sokurenko G, Hiatt WR, Jones WS, Patel MR.

Background and Purpose- Predictors of stroke and transient ischemic attack (TIA) in patients with peripheral artery disease (PAD) are poorly understood. The primary aims of this analysis were to (1) determine the incidence of ischemic/hemorrhagic stroke and TIA in patients with symptomatic PAD, (2) identify predictors of stroke in patients with PAD, and (3) compare the rate of stroke in ticagrelor- and clopidogrel-treated patients. **Methods-** EUCLID (Examining Use of Ticagrelor in Peripheral Artery Disease) randomized 13885 patients with symptomatic PAD to receive monotherapy with ticagrelor or clopidogrel for the prevention of major adverse cardiovascular events (cardiovascular death, myocardial infarction, or ischemic stroke). Ischemic/hemorrhagic stroke and TIA were adjudicated and measured as incidence rates postrandomization and cumulative incidence (per patient-years). Post hoc multivariable competing risk hazards analyses were performed using baseline characteristics to determine factors associated with all-cause stroke in patients with PAD. **Results-** A total of 458 cerebrovascular events in 424 patients (317 ischemic strokes, 39 hemorrhagic strokes, and 102 TIAs) occurred over a median follow-up of 30 months, for a cumulative incidence of 0.87, 0.11, and 0.27 per 100 patient-years, respectively. Age, prior stroke, prior atrial fibrillation/flutter, diabetes mellitus, geographic region, ankle-brachial index <0.60, prior amputation, and systolic blood pressure were independent baseline factors associated with the occurrence of all-cause stroke. After adjustment for baseline factors, the rates of ischemic stroke and all-cause stroke remained lower in patients treated with ticagrelor as compared with those receiving clopidogrel. There was no significant difference in the incidence of hemorrhagic stroke or TIA between the 2 treatment groups. **Conclusions-** In patients with symptomatic PAD, ischemic stroke and TIA occur frequently over time. Comorbidities such as age, prior stroke, prior atrial fibrillation/flutter, diabetes mellitus, higher blood pressure, prior amputation, lower ankle-brachial index, and geographic region were each independently associated with the occurrence of all-cause stroke. Use of ticagrelor, as compared with clopidogrel, was associated with a lower adjusted rate of ischemic and all-cause stroke. Further study is needed to optimize medical management and risk reduction of all-cause stroke in patients with PAD.

J AM COLL CARDIOL. 2019 SEP 3;74(9):1167-1176. DOI: 10.1016/J.JACC.2019.03.013.

ALIROCUMAB IN PATIENTS WITH POLYVASCULAR DISEASE AND RECENT ACUTE CORONARY SYNDROME: ODYSSEY OUTCOMES TRIAL.

Jukema JW Szarek M, Zijlstra LE, de Silva HA, Bhatt DL, Bittner VA, Diaz R, Edelberg JM, Goodman SG, Hanotin C, Harrington RA, Karpov Y, Moryusef A, Pordy R, Prieto JC *et al*

BACKGROUND: Patients with acute coronary syndrome (ACS) and concomitant noncoronary atherosclerosis have a high risk of major adverse cardiovascular events (MACEs) and death. The impact of lipid lowering by proprotein convertase subtilisin-kexin type 9 inhibition in such patients is undetermined. **OBJECTIVES:** This pre-specified analysis from ODYSSEY OUTCOMES (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab) determined whether polyvascular disease influenced risks of MACEs and death and their modification by alirocumab in patients with recent ACS and dyslipidemia despite intensive statin therapy. **METHODS:** Patients were randomized to alirocumab or placebo 1 to 12 months after ACS. The primary MACEs endpoint was the composite of coronary heart disease death, nonfatal myocardial infarction, fatal or nonfatal ischemic stroke, or unstable angina requiring hospitalization. All-cause death was a secondary endpoint. **RESULTS:** Median follow-up was 2.8 years. Of 18,924 patients, 17,370 had monovascular (coronary) disease, 1,405 had polyvascular disease in 2 beds (coronary and peripheral artery or cerebrovascular), and 149 had polyvascular disease in 3 beds (coronary, peripheral artery, cerebrovascular). With placebo, the incidence of MACEs by respective vascular categories was 10.0%, 22.2%, and 39.7%. With alirocumab, the corresponding absolute risk reduction was 1.4% (95% confidence interval [CI]: 0.6% to 2.3%), 1.9% (95% CI: -2.4% to 6.2%), and 13.0% (95% CI: -2.0% to 28.0%). With placebo, the incidence of death by respective vascular categories was 3.5%, 10.0%, and 21.8%; the absolute risk reduction with alirocumab was 0.4% (95% CI: -0.1% to 1.0%), 1.3% (95% CI: -1.8% to 4.3%), and 16.2% (95% CI: 5.5% to 26.8%). **CONCLUSIONS:** In patients with recent ACS and dyslipidemia despite intensive statin therapy, polyvascular

disease is associated with high risks of MACEs and death. The large absolute reductions in those risks with alirocumab are a potential benefit for these patients. (Evaluation of Cardiovascular Outcomes After an Acute Coronary Syndrome During Treatment With Alirocumab [ODYSSEY OUTCOMES]: NCT01663402).

DEPARTAMENTO CIRUGÍA

SURGERY. 2019 NOV;166(5):886-894. DOI: 10.1016/J.SURG.2019.04.024.

LONG-TERM (15-YEAR) OBJECTIVE EVALUATION OF 150 PATIENTS AFTER LAPAROSCOPIC NISSEN FUNDOPLICATION.

Csendes A, Orellana O, Cuneo N, Martínez G, Figueroa M.

INTRODUCTION: Laparoscopic Nissen fundoplication is the preferred operative treatment for patients with gastroesophageal reflux disease. The most recent published results only refer to clinical evaluations and few discuss objective measurements. Our purpose was to determine the late results of laparoscopic Nissen fundoplication, performing clinical, endoscopic, histologic, and functional studies. **MATERIAL AND METHODS:** A total of 179 patients were included in a prospective study. All had gastroesophageal reflux disease symptoms of at least 5-year duration, daily dependence on proton pump inhibitors, and a type I hiatal hernia less than 5 cm. Exclusion criteria included Barrett's esophagus, hiatal hernia >5 cm, failed antireflux surgery, and obesity (body mass index >30). We performed a radiologic study, 3 or more endoscopic procedures with biopsy samples of the antrum and esophagogastric junction, esophageal manometry, and 24-hour pH monitoring. **RESULTS:** We found that 4 patients (2.2%) died 3-4 years after operation from nonoperative reasons. A total of 25 patients (14%) were lost to follow-up, and 150 patients (83.8%) submitted to late objective evaluations (15 years). Visick I-II symptoms were observed in 79.3% and III-IV (failures) in 20.7%. Endoscopy showed a normal positioning of the esophagogastric junction in the Visick I-II patients and a type III cardia or hiatal hernia with erosive esophagitis in Visick III-IV patients. Short-segment Barrett's esophagus developed in 5.3% of patients. Lower esophageal sphincter pressure remained increased over the preoperative value in all groups. The 24-hour pH monitoring also was decreased over the preoperative value in Visick I-II patients but showed no significant change in Visick III-IV patients. Carditis at the esophagogastric junction regressed to fundic mucosa in 50% of Visick I-II patients. **CONCLUSION:** Laparoscopic Nissen fundoplication produces control of symptoms in 80% of patients late (up to 15 years) after surgeries corroborated by endoscopic, histologic examinations, and functional studies. It is essential to perform these objective evaluations to demonstrate the "antireflux effect" after laparoscopic Nissen fundoplication.

SURG LAPAROSC ENDOSC PERCUTAN TECH. 2019 DEC;29(6):451-455

PATIENTS REMAIN AT HIGH RISK OF GALLSTONES DEVELOPMENT LATE (10Y) AFTER SLEEVE GASTRECTOMY?

Csendes A, Csendes P, Orellana O, Cuneo N, Figueroa M, Martinez G.

BACKGROUND: Sleeve gastrectomy (SG) is an established bariatric procedure which produces substantial and rapid weight loss and hence can lead to an increase in gallstones development. **OBJECTIVES:** To demonstrate the early and late appearance of gallstones after SG. **MATERIALS AND METHODS:** A prospective protocol was established in consecutive patients submitted to SG. Clinical and ultrasound evaluations were performed early (1 to 2y) and late after surgery (over 6y). **RESULTS:** From 109 patients included, 13 (13.1%) had a previous and 10 (10.1%) had simultaneous cholecystectomy at the time of SG. Therefore, 86 patients were submitted to surveillance. Seven patients were unreachable, leaving 79 patients for late follow-up. Forty-five patients (57%) had alithiasic gallbladder late after surgery, whereas 34 patients (43%) showed appearance of gallstone. From them, 53% developed gallstones late after surgery (mean, 7.5y). Among the group with early development of stones, 69% were symptomatic and in the latter group only 17%. **CONCLUSIONS:** Study with 92% of follow-up late after SG demonstrated a 43% development of gallstones: half earlier and half late after surgery. We emphasize the need for late control to detect the real appearance of gallstones after SG.

ARQ BRAS CIR DIG. 2019 AUG 26;32(2):E1440. DOI: 10.1590/0102-672020190001E1440.

FAILURE AFTER FUNDOPLICATION: RE-FUNDOPLICATION? IS THERE A ROOM FOR GASTRECTOMY? IN WHICH CLINICAL SCENARIOS?

Braghetto I, Csendes A.

BACKGROUND: Re-fundoplication is the most often procedure performed after failed fundoplication, but re-failure is even higher. **AIM:** The objectives are: a) to discuss the results of fundoplication and re-fundoplication in these cases, and b) to analyze in which clinical situation there is a room for gastrectomy after failed fundoplication. **METHOD:** This experience includes 104 patients submitted to re-fundoplication after failure of the initial operation, 50 cases of long segment Barrett's esophagus and 60 patients with morbid obesity, comparing the postoperative outcome in terms of clinical, endoscopic, manometric and 24h pH monitoring results. **RESULTS:** In patients with failure after initial fundoplication, redo-fundoplication shows the worst clinical results (symptoms, endoscopic esophagitis, manometry and 24 h pH monitoring). In patients with long segment Barrett's esophagus, better results were observed after fundoplication plus Roux-en-Y distal

gastrectomy and in obese patients similar results regarding symptoms, endoscopic esophagitis and 24h pH monitoring were observed after both fundoplication plus distal gastrectomy or laparoscopic resectional gastric bypass, while regarding manometry, normal LES pressure was observed only after fundoplication plus distal gastrectomy. CONCLUSION: Distal gastrectomy is recommended for patients with failure after initial fundoplication, patients with long segment Barrett's esophagus and obese patients with gastroesophageal reflux disease and Barrett's esophagus. Despite its higher morbidity, this procedure represents an important addition to the surgical armamentarium.

SURG OBES RELAT DIS. 2019 JUN;15(6):822-826. DOI: 10.1016/J.SOARD.2019.03.034.

DUODENOGASTRIC BILIARY REFLUX ASSESSED BY SCINTIGRAPHIC SCAN IN PATIENTS WITH REFLUX SYMPTOMS AFTER SLEEVE GASTRECTOMY: PRELIMINARY RESULTS.

Braghetto I, Gonzalez P, Lovera C, Figueroa-Giralt M, Piñeres A.

BACKGROUND: Bile reflux is a factor in the appearance of severe esophagitis and Barrett's esophagus, which have been reported after sleeve gastrectomy (SG). Incompetent lower esophageal sphincter and increased gastroesophageal acid reflux have been demonstrated after this operation. Some reports have shown bile content in the antrum during endoscopic control, but no investigations objectively confirm the presence of duodenogastric bile reflux in these patients. OBJECTIVES: To evaluate the presence of duodenogastric bile reflux (DGR) after SG in patients presenting reflux symptoms. SETTING: University hospital. METHODS: Prospective study of 22 patients presenting reflux symptoms who underwent SG for morbid obesity and who received endoscopic evaluation and scintigraphic study to confirm esophagitis and duodenogastric bile reflux. RESULTS: Erosive esophagitis was observed in 11 patients and Barrett's esophagus in 2 patients. Seven patients (31.8%) presented positive DGR. Among them, 3 had type B and C esophagitis. The other 4 patients did not present esophagitis in spite of reflux symptoms. CONCLUSION: DGR may be present in patients with gastroesophageal reflux after SG. This line of investigation requires further studies to confirm this hypothesis.

ARQ BRAS CIR DIG. 2019 AUG 26;32(2):E1441. DOI: 10.1590/0102-672020190001E1441.

INTRODUCTION OF THE NEW LYMPHOPARIETAL INDEX FOR GASTRIC CANCER PATIENTS.

Figueroa-Giralt M, Csendes A, Carrillo K, Danilla S, Lanzarini E, Braghetto I, Musleh M, Cortés S.

BACKGROUND: The identification of prognostic factors of gastric cancer (GC) has allowed to predict the evolution of patients. AIM: Assess the reliability of the lymphoparietal index in the prediction of long-term survival in GC treated with curative intent. METHOD: Prospective study of the Universidad de Chile Clinical Hospital, between May 2004 and May 2012. Included all gastric cancer surgeries with curative intent. Exclusion criteria were: gastrectomies due to benign lesions, stage 4 cancers, R1 resections, palliative procedures, complete esophagogastrectomies and emergency surgeries. RESULTS: A total of 284 patients were included; of the sample 65.4% were male, mean age of 64.5 years, 75% were advanced cancers, 72.5% required a total gastrectomy, 30 lymph nodes harvest. Surgical morbidity and mortality were 17.2% and 1.7%. 5-year survival was 56.9%. The N+/T index could predict long-term survival in all de subgroups ($p < 0.0001$), although had a reliable prediction in early GC ($p = 0.005$), advanced GC ($p < 0.0001$), signet ring cell GC ($p < 0.0001$), proximal GC ($p < 0.0001$) and distal GC ($p < 0.0001$). The ROC curves N+/T index, LNR and T classification presented areas below the curve of 0.789, 0.786 and 0,790 respectively, without a significant statistical difference ($p = 0.96$). CONCLUSION: The N+/T index is a reliable quotient in the prognostic evaluation of gastric adenocarcinoma patients who have been resected with curative intent.

DIS ESOPHAGUS. 2019 JUN 1;32(6). PII: DOZ020. DOI: 10.1093/DOTE/DOZ020.

LATE ESOPHAGOGASTRIC ANATOMIC AND FUNCTIONAL CHANGES AFTER SLEEVE GASTRECTOMY AND ITS CLINICAL CONSEQUENCES WITH REGARDS TO GASTROESOPHAGEAL REFLUX DISEASE.

Braghetto I, Korn O.

Gastroesophageal reflux disease (GERD) is described as a complication after sleeve gastrectomy. Most studies have used only clinical symptoms or upper gastrointestinal endoscopy for evaluation of reflux after surgery. Manometry, acid reflux tests, and esophageal barium swallow have not been commonly used. The objective of this study is to evaluate the short- and long-term incidence of clinical gastroesophageal reflux, the lower esophageal sphincter (LES) pressure, acid reflux, and endoscopic and radiological changes after sleeve gastrectomy (SG). A total of 315 patients were studied after SG; 248 (78.3%) completed more than 5 years of follow-up and 67 (21.4%) have more than 8 years (range 8-10 years) of follow-up. The preoperative weight was $106 + 14.1$ kg with a mean body mass index $38.4 + 3.4$ kg/m². Patients with prior GERD were excluded for SG. During the follow-up patients were subjected to clinical, endoscopic, radiological, manometric, and 24-hour pH monitoring and duodenogastric reflux evaluations. Reflux symptoms were observed in 65.1% of patients at late follow-up. Patients without reflux symptoms presented an LES resting pressure of 13.3 ± 4.2 mmHg while patients with reflux symptoms presented an LES resting pressure of $9.8 + 2.1$ mmHg. In patients with reflux symptoms, a positive acid reflux test was observed in 77.5% of patients with a mean DeMeester score of 41.7 ± 2.9 (range 14.1-131.7). During endoscopy, esophagitis was found in 29.4%, hiatal hernia in 5.7%, and Barrett's esophagus was diagnosed in 4.8%. Positive duodenogastric reflux was found in 31.8% of patients and 57.7% of our patients received proton pump inhibitor treatment after SG. Sleeve gastrectomy presents anatomic and functional changes that are associated with increased GERD.

OBES SURG. 2019 DEC;29(12):3809-3817. DOI: 10.1007/S11695-019-04054-5.

CLINICAL, ENDOSCOPIC, AND HISTOLOGIC FINDINGS AT THE DISTAL ESOPHAGUS AND STOMACH BEFORE AND LATE (10.5 YEARS) AFTER LAPAROSCOPIC SLEEVE GASTRECTOMY: RESULTS OF A PROSPECTIVE STUDY WITH 93% FOLLOW-UP.

Csendes A, Orellana O, Martínez G, Burgos AM, Figueroa M, Lanzarini E.

OBJECTIVE: Perform a prospective study based on sequential clinical, endoscopic, and histologic evaluations of the foregut late after laparoscopic sleeve gastrectomy (LSG) in obese patients. After LSG, several studies have suggested an increase in the incidence of clinical gastroesophageal reflux (GERD) while others have reported an improvement but based mainly on clinical questionnaires. **METHODS:** Prospective study of 104 consecutive patients submitted to LSG. Several postoperative endoscopic and histologic evaluations of the esophagogastric junction (EGJ) and the gastric tube (GT) were performed and correlated with symptomatic findings. **RESULTS:** According to clinical preoperative findings, patients were divided into non-refluxers (Group I) and refluxers (Group II). Seven patients were unreachable, leaving 97 (93%) for late evaluation. Among Group I, 58.5% developed de novo GERD, while in Group II just 13.6% showed the disappearance of them. Endoscopic evaluations showed progressive deterioration of the EGJ in Group I, with the development of erosive esophagitis (EE), hiatal hernia (HH), and dilated cardia in a large proportion of them. In the GT, the presence of bile was seen in 40%, and an open immobile pylorus was detected in 82%. Short-segment Barrett's esophagus (BE) appeared in 4%. **CONCLUSIONS:** Patients submitted to LSG showed a significant and progressive increase in the presence of "de novo" GERD. Also, an increased duodenogastric reflux was seen through an open and immobile pylorus. Therefore, based on these results, it seems like LSG is a "pro-reflux" surgical procedure, which should be continuously evaluated late after surgery.

CRANIOMAXILLOFAC TRAUMA RECONSTR. 2019 SEP;12(3):175-182. DOI: 10.1055/S-0038-1641713.

A FIVE-YEAR RETROSPECTIVE COHORT STUDY ANALYZING FACTORS INFLUENCING COMPLICATIONS AFTER NASAL TRAUMA.

Andrades P, Pereira N, Rodríguez D, Borel C, Hernández R, Villalobos R.

The purpose of this study was to assess the outcomes of patients with nasal trauma during a long period of time and determine factors predisposing to complications after nasal trauma treatment. A retrospective cohort study was conducted that included all patients who were attended for a nasal trauma between January and December 2010. In 2015, the charts were retrospectively reviewed and the patients were prospectively followed up looking for outcomes after treatment of nasal trauma. A univariate analysis between complications and risk factors was performed and a logistic regression model was used to explore the prognostic role of the variables considered to have clinical relevance and to estimate the odds ratio for the occurrence of postoperative complications. A total of 220 consecutive patients with nasal trauma were included in the study. The mean follow-up was 44.3 ± 10.3 months (3-67) with 10% of lost patients. The most important factors determining complications after nasal trauma treatment were male gender, acute septal injury, chronic septal deviation, displaced or comminuted fractures in the radiologic study, and late nasal reduction surgery. A decision-making algorithm is proposed based on the fact that nasal bone fracture is not a minor problem and that closed nasal bone reduction is not the treatment of choice for all patients with nasal trauma.

AESTHETIC PLAST SURG. 2019 AUG;43(4):899-904. DOI: 10.1007/S00266-019-01385-7.

WINGED RIBS: AN UNDERESTIMATED PROBLEM THAT MAY COMPROMISE BREAST AUGMENTATION OUTCOMES.

Andrades P, Quispe D, Dominguez C, Jara R, Cisternas JP, Lobos G, Albornoz C, Danilla S, Erazo C, Sepulveda S.

Chest wall shape is an important aspect to consider when planning a breast augmentation. Minor chest wall deformities are usually underestimated by the patient and surgeon and may compromise postoperative outcomes. Lower costal cartilage dysmorphia or winged rib is one of these minor underestimated chest wall deformities characterized by a visible and palpable cartilaginous prominence under the inframammary fold and causes discomfort in patients decreasing the satisfaction with the breast augmentation surgery. For these patients, the author utilized an innovative surgical technique that allows resection of the protruding cartilages and placement of breast implants through the same surgical incision. Six patients with winged ribs underwent breast augmentation and costal cartilage resection via this method and there were no intraoperative or early postoperative complications, and all patients were satisfied with the aesthetic result after 6 months of follow-up. The presented surgical technique has a short learning curve with excellent postoperative results. Cases are presented to demonstrate the improved postoperative chest wall contour combined with breast augmentation outcome. Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

FRONT IMMUNOL. 2019 JUN 21;10:1394. DOI: 10.3389/FIMMU.2019.01394.

INTERLEUKIN 33/ST2 AXIS COMPONENTS ARE ASSOCIATED TO DESMOPLASIA, A METASTASIS-RELATED FACTOR IN COLORECTAL CANCER. Landskron G, De la Fuente López M, Dubois-Camacho K, Díaz-Jiménez D, Orellana-Serradell O, Romero D, Sepúlveda SA, Salazar C, Parada-Venegas D, Quera R, Simian D, González MJ, López-Köstner F, Kronberg U, Abedrapo M, Gallegos I, Contreras HR, Peña C, Díaz-Araya G, Roa JC, Hermoso MA.

Erratum in Corrigendum: Interleukin 33/ST2 Axis Components Are Associated to Desmoplasia, a Metastasis-Related Factor in Colorectal Cancer. [Front Immunol. 2019] In colorectal cancer (CRC), cancer-associated fibroblasts (CAFs) are the most abundant component from

the tumor microenvironment (TM). CAFs facilitate tumor progression by inducing angiogenesis, immune suppression and invasion, thus altering the organization/composition of the extracellular matrix (i.e., desmoplasia) and/or activating epithelial-mesenchymal transition (EMT). Soluble factors from the TM can also contribute to cell invasion through secretion of cytokines and recently, IL-33/ST2 pathway has gained huge interest as a protumor alarmin, promoting progression to metastasis by inducing changes in TM. Hence, we analyzed IL-33 and ST2 content in tumor and healthy tissue lysates and plasma from CRC patients. Tissue localization and distribution of these molecules was evaluated by immunohistochemistry (using localization reference markers α -smooth muscle actin or α -SMA and E-cadherin), and clinical/histopathological information was obtained from CRC patients. In vitro experiments were conducted in primary cultures of CAFs and normal fibroblasts (NFs) isolated from tumor and healthy tissue taken from CRC patients. Additionally, migration and proliferation analysis were performed in HT29 and HCT116 cell lines. It was found that IL-33 content increases in left-sided CRC patients with lymphatic metastasis, with localization in tumor epithelia associated with abundant desmoplasia. Although ST2 content showed similarities between tumor and healthy tissue, a decreased immunoreactivity was observed in left-sided tumor stroma, associated to metastasis related factors (advanced stages, abundant desmoplasia, and presence of tumor budding). A principal component analysis (including stromal and epithelial IL-33/ST2 and α -SMA immunoreactivity with extent of desmoplasia) allowed us to distinguish clusters of low, intermediate and abundant desmoplasia, with potential to develop a diagnostic signature with benefits for further therapeutic targets. IL-33 transcript levels from CAFs directly correlated with CRC cell line migration induced by CAFs conditioned media, with rhIL-33 inducing a mesenchymal phenotype in HT29 cells. These results indicate a role of IL-33/ST2 in tumor microenvironment, specifically in the interaction between CAFs and epithelial tumor cells, thus contributing to invasion and metastasis in left-sided CRC, most likely by activating desmoplasia.

NUTRITION. 2019 JAN;57:217-224. DOI: 10.1016/J.NUT.2018.05.031.

SARCOPENIA: THE NEED TO ESTABLISH DIFFERENT CUTOFF POINTS OF FAT-FREE MASS FOR THE CHILEAN POPULATION.

Wigodski S, Carrasco F, Bunout D, Barrera G, Hirsch S, de la Maza MP.

OBJECTIVES: International cutoff points for the diagnosis of sarcopenia are not applicable to the Chilean population due to previous evidence of a lower lean mass and strength in this population. Dual-energy x-ray absorptiometry is used to establish fat-free mass cutoff points to define sarcopenia in the Chilean population and analyze its association with handgrip strength in older adults. **METHODS:** Appendicular fat-free mass (AFFM) was calculated from 4062 dual-energy x-ray absorptiometries of healthy Chileans, ages 18 to 99 y. Possible cutoff points for sarcopenia were obtained using four methods: A) Normative, -2 standard deviation (SD) below mean AFFM/height² (AFFMI) of adults age <40 y; B) normative -1 SD, -1 SD under the average AFFMI of adults age <40 y; C) stratification, 25th percentile of the residual distribution obtained with the regression equation to predict AFFM in the entire sample; and D) percentage, -2 SD under the average skeletal muscle mass/total body mass of individuals age <40 y. Additionally, in a subsample of elderly subjects, the correlation between handgrip strength and the four calculated cutoff points was analyzed. **RESULTS:** Using the normative method, sarcopenia was defined as an AFFMI <6.4 kg/m² in men and <4.8 kg/m² in women and at -1 SD, the cutoff points were <7.5 kg/m² and <5.6 kg/m², respectively. With the stratification method, sarcopenia was defined as -1.33 kg and -1.05 kg of AFFM with respect to the expected value according to the regression equation in men and women, respectively. According to the percentage method, the cutoff points for sarcopenia were <30% and <22.9% in men and women, respectively. The concordance of the four methods was slight to moderate. Only the percentage method showed a progressive increase in the proportion of subjects with sarcopenia as age increased. The latter and the normative -1 DS predicted lower handgrip strength in elderly women, unlike the other diagnostic methods. For elderly men, only the normative -1 DS method predicted weaker handgrip strength. **CONCLUSIONS:** The AFFM of young Chileans is lower than that reported in Western countries but similar to Latin American data; therefore, the use of the traditional normative method would not be appropriate with -2 SD to establish cutoff points, and using -1 DS resulted in values that are higher than Baumgartner's. Stratification is advantageous because this method throws expected values of AFFM for each population; however, overdiagnosis of sarcopenia is a possibility and thus the method requires a representative sample. The percentage method is simple and showed the expected decrease of muscle mass with age, and also correlated well with handgrip strength in elderly women. Thus, this method represented our method of choice to detect sarcopenia.

AESTHET SURG J. 2019 NOV 25. PII: SJZ343. DOI: 10.1093/ASJ/SJZ343. [EPUB AHEAD OF PRINT]

IS BANNING TEXTURIZED IMPLANTS TO PREVENT BREAST IMPLANT-ASSOCIATED ANAPLASTIC LARGE CELL LYMPHOMA (BIA-ALCL) A RATIONAL DECISION? A META-ANALYSIS AND COST-EFFECTIVENESS STUDY.

Danilla SV, Jara RP, Miranda F, Bencina F, Aguirre M, Troncoso E, Erazo CA, Andrades PR, Sepulveda SL, Albornoz CR.

BACKGROUND: Breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) is an emergent disease that threatens patients with texturized breast implants. Major concerns about the safety of these implants are leading to global changes to restrict the use of this product. The principal alternative is to perform breast augmentation utilizing smooth implants, given the lack of association with BIA-ALCL. The implications and costs of this intervention are unknown. **OBJECTIVES:** This study determined the cost-effectiveness of smooth implants compared with texturized implants for breast augmentation surgery. **METHODS:** A tree decision model was utilized to analyze the cost-effectiveness. Model input parameters were derived from published sources. The capsular contracture (CC) rate was calculated

from a meta-analysis. Effectiveness measures were life years, avoided BIA-ALCL, avoided deaths, and avoided reoperations. A sensitivity analysis was performed to test the robustness of the model. RESULTS: For avoided BIA-ALCL, the incremental cost was \$18,562,003 for smooth implants over texturized implants. The incremental cost-effectiveness ratio (ICER) is negative for life years, avoided death, and avoided reoperations are negative. The sensitivity analysis reveals that to avoid one case of BIA-ALCL, the use of smooth implants would be cost-effective for a risk of developing BIA-ALCL equal to or higher than 1:196, and there is a probability of CC with smooth implants equal to or lower than 0.096. CONCLUSIONS: The use of smooth implants to prevent BIA-ALCL is not cost-effective. Banning texturized implants to prevent BIA-ALCL may involve additional consequences, which should be considered in light of higher CC rates and more reoperations associated with smooth implants than with texturized implants.

AESTHETIC PLAST SURG. 2019 AUG 20. DOI: 10.1007/S00266-019-01475-6.

HIGH-DEFINITION LIPOSCULPTURE: WHAT ARE THE COMPLICATIONS AND HOW TO MANAGE THEM?

Daniella S, Babaitis RA, Jara RP, Quispe DA, Andrades PR, Erazo CA, Albornoz CR, Sepulveda SL.

BACKGROUND: High-definition liposculpture is a novel surgical technique widely accepted among plastic surgeons. The aim of this article is to describe surgical outcomes with a special emphasis on complications in high-definition liposculpture patients. METHODS: An historical cohort of patients who underwent high-definition liposculpture from two senior surgeons was reviewed. Technique, patient selection criteria, preoperative marks and surgical outcomes are described. Postoperative complications are discussed. RESULTS: A total of 417 patients underwent high-definition liposculpture between 2015 and 2018. Primary liposuction and secondary liposuction were performed in 308 (74%) and 109 (26%), respectively. Combined surgeries were performed in 121 cases (29%). There were no systemic complications. Local complications included hyperpigmentation (n=276), seroma (n=125), nodular fibrosis (n=83), unsatisfactory definition in superficial liposuction areas (n=16), unnatural appearance of body contour (n=17), VASER-related burns (n=3) and Mondor's syndrome (n=2). Most patients (94%) were satisfied with the results. CONCLUSION: High-definition liposculpture is a body contouring technique that has shown excellent results. Despite non-serious complications were frequent, most complications were local and safely treated without affecting surgical outcome. To know these complications will help to recognize them earlier and to adjust patient expectation about the postoperative period. LEVEL OF EVIDENCE IV: This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

DEPARTAMENTO DE DERMATOLOGÍA

J ULTRASOUND MED. 2019 NOV 9. DOI: 10.1002/JUM.15164.

SEVENTY-MHZ ULTRASOUND DETECTION OF EARLY SIGNS LINKED TO THE SEVERITY, PATTERNS OF KERATIN FRAGMENTATION, AND MECHANISMS OF GENERATION OF COLLECTIONS AND TUNNELS IN HIDRADENITIS SUPPURATIVA.

Wortsman X, Calderon P, Castro A.

OBJECTIVES: To test the capability of 70-MHz ultrasound for detecting initial ultrasound signs of hidradenitis suppurativa (HS) linked to severity. METHODS: A cross-sectional study of the ultrasound images of patients with HS was conducted and compared with a healthy control group. Detection and identification of early subclinical ultrasound signs in the lesional and perilesional areas of the HS cases in comparison with the control group were performed. Statistical analyses included mean, dispersion measures, the Kruskal-Wallis test, and bivariate and multivariate ordered logistic regression studies. Significance was assessed at $P < .05$. RESULTS: A total of 139 patients with HS met the criteria and showed abnormalities of the hair follicles such as a curved shape, ballooning, and protrusion into pseudocysts, collections, or tunnels (donor of keratin sign). Significant increases in the sizes of the hair follicles and hair shafts were found in HS cases. The following ultrasound signs were significantly linked to severity: a connecting band between the base of adjacent hair follicles (bridge sign), a fragment of the hair shaft extruding through a dilated hair follicle (sword sign), and retained cylindrical fragments of keratin in the dermis. Two patterns of fragmentation of the keratin were detected: multifragment and cylindrical. CONCLUSIONS: Ultrasound can detect early HS signs that are significantly linked to severity and 2 types of fragmentation of the keratin, which could support the generation and perpetuation of the fluid collections and tunnels. These ultrasound signs can help prompt diagnosis and management, the development and testing of medications, and the measure of treatment outcomes in HS.

INT J DERMATOL. 2019 AUG;58 SUPPL 1:4-28. DOI: 10.1111/IJD.14471.

LATIN AMERICAN CLINICAL PRACTICE GUIDELINES ON THE SYSTEMIC TREATMENT OF PSORIASIS SOLAPSO - SOCIEDAD LATINOAMERICANA DE PSORIASIS (LATIN AMERICAN PSORIASIS SOCIETY).

Kogan N, Raimondo N, Gusic SE, Izcovich A, Abarca Duran JA, Barahona-Torres L, Blanco O, Quintana GB, Briones MC, Castro C, Castro Vargas EG, Crinti J, Diez de Medina JC, Franco M, Gómez M, Levrero VP, Martínez López JE, Valenzuela F.

This Clinical Practice Guideline on the systemic treatment of Psoriasis includes the recommendations elaborated by a panel of experts from the Latin American Psoriasis Society SOLAPSO, who assessed the quality of the available evidence using the GRADE system and the PICO process to guide the literature search. To answer each question, the experts discussed the results of randomized controlled

trials, observational studies and metanalysis evaluating the interventions identified (non-biologics, biologics and phototherapy) in different populations of patients with moderate to severe plaque-psoriasis, which was summarized in Tables ad-hoc. The main end-points considered to assess efficacy were PASI 50, 75, 90 and 100, PGA 0-1 and significant improvement of health-related quality of life. Specific adverse events, either severe or leading to treatment interruption, were also evaluated. The 31 recommendations included in this CPG follow the structure proposed by GRADE: direction (for or against) and strength (strong or weak). The goal of this CPG is to improve the management of patients with psoriasis by recommending interventions of proved benefit and providing a reference standard for the treating physician. Adhering to the contents of this CPG does not guarantee therapeutic success. The final decision on the specific treatment is the responsibility of the physician based on the individual circumstances and considering the values, the preferences and the opinions of the patient or caregivers.

AN BRAS DERMATOL. 2019 SEP - OCT;94(5):582-585. DOI: 10.1016/J.ABD.2019.09.002.

GRANULOMATOUS PIGMENTED PURPURIC DERMATOSIS: REPORT OF A LATIN-AMERICAN CASE WITH BLASCHKOID DISTRIBUTION.
Carvajal D, Quiroz C, Morales C, Fernández J.

pigmented purpuric dermatosis clinically manifests as hyperpigmented maculae and petechiae, predominantly on the lower extremities. Histopathologically, it is characterized by a lymphocytic infiltrate in the upper dermis, extravasated erythrocytes, and hemosiderin deposits. There is an infrequent variant called granulomatous pigmented purpuric dermatosis, which histologically is characterized by the presence of non-necrotizing granulomas associated with the classic findings of other pigmented purpuric dermatoses. It more frequently affects middle-aged women of Asian origin, and predominantly on the lower extremities. The authors present the case of a female patient with granulomatous pigmented purpuric dermatosis on the lower extremities with blaschkoid distribution.

DERMATOL THER (HEIDELB). 2019 MAR;9(1):5-18. DOI: 10.1007/S13555-018-0279-5.

CLINICAL GOALS AND BARRIERS TO EFFECTIVE PSORIASIS CARE.

Strober BE, van der Walt JM, Armstrong AW, Bourcier M, Carvalho AVE, Chouela E, Cohen AD, de la Cruz C, Ellis CN, Finlay AY, Gottlieb AB, Gudjonsson JE, Iversen L, Kleyn CE, Leonardi CL, Lynde CW, Ryan C, Theng CT, Valenzuela F, *et al*

Engaging global key opinion leaders, the International Psoriasis Council (IPC) held a day-long roundtable discussion with the primary purpose to discuss the treatment goals of psoriasis patients and worldwide barriers to optimal care. Setting clear expectations might ultimately encourage undertreated psoriasis patients to seek care in an era in which great gains in therapeutic efficacy have been achieved. Here, we discuss the option for early treatment of all categories of psoriasis to alleviate disease impact while emphasizing the need for more focused attention for psoriasis patients with mild and moderate forms of this autoimmune disease. In addition, we encourage policy changes to keep pace with the innovative therapies and clinical science and highlight the demand for greater understanding of treatment barriers in resource-poor countries.

BR J RADIOL. 2019 MAR;92(1095):20180904. DOI: 10.1259/BJR.20180904.

THE CLINICAL VALUE OF IMAGING IN PRIMARY CUTANEOUS LYMPHOMAS: ROLE OF HIGH RESOLUTION ULTRASOUND AND PET-CT.
Mandava A, Koppula V, Wortsman X, Catalano O, Alfageme F.

BACKGROUND: Primary cutaneous lymphoma is a rare extranodal non-Hodgkin's lymphoma confined to the skin. The data on the imaging findings of primary cutaneous lymphomas are largely lacking and the current diagnosis is based on clinical and histopathological examination. With the advances in dermatological ultrasound and molecular imaging, newer perspectives in the evaluation of cutaneous lymphomas are available. OBJECTIVE: To review and describe the imaging findings in patient's with the diagnosis of primary cutaneous lymphoma. METHODS: A multicentric, retrospective observational study was undertaken in four countries to review the high resolution ultrasonography (HRUS) and fluorine 18-fludeoxyglucose positron emission tomography-computed tomography (PET-CT) imaging findings. RESULTS: We had 41 patients, Female:Male 1:4.1; mean age, 57 years; range, 13-94 years. High resolution ultrasonography of the primary cutaneous lesions revealed thickening of the dermis in all the cases and the lesions were hypoechoic without any calcifications or central necrosis. The sonographic appearances of the lesions were categorised into focal infiltrative, nodular, pseudonodular, and diffusely infiltrative patterns. Nodular and pseudonodular lesions were predominant in B cell lymphomas, while diffusely infiltrative lesions were more common in T-cell lymphomas. On colour Doppler imaging, the lesions were hypervascular. Whole body 18F-fludeoxyglucose PET-CT imaging of the patients revealed increased uptake of the metabolite in the lesions. CONCLUSION: Sonographic patterns based on high resolution ultrasonography provide early clues to the non-invasive diagnosis of primary cutaneous lymphomas and PET-CT is the recommended modality of imaging for staging and follow-up. ADVANCES IN KNOWLEDGE: High resolution ultrasound with colour Doppler and PET-CT imaging are complimentary to the clinical diagnosis of primary cutaneous lymphomas.

INT J WOMENS DERMATOL. 2019 MAR 21;5(3):183-186. DOI: 10.1016/J.IJWD.2019.03.002.

MALIGNANT ACANTHOSIS NIGRICANS AS A PARANEOPLASTIC MANIFESTATION OF METASTATIC BREAST CANCER.
Arellano J, Iglesias P, Suarez C, Corredoira Y, Schnettler K.

Malignant acanthosis nigricans is a rare paraneoplastic syndrome, usually associated with a gastric adenocarcinoma and less frequently with other neoplasms. In general, its appearance indicates a poor prognosis with a survival of < 2 years. We describe the case of a

40-year-old patient who presented with generalized cutaneous thickening that had a velvety appearance, was rapidly progressing, and involved right axillary adenopathy. Skin and nipple biopsy yielded results consistent with acanthosis nigricans, and palpable adenopathy biopsy results were compatible with mammary adenocarcinoma (human epidermal growth factor receptor 2 positive and estrogen and progesterone receptor negative) without a detectable primary tumor. This case of malignant acanthosis nigricans is presented because of the importance of its early recognition as a paraneoplastic syndrome and its relation with mammary adenocarcinoma, an association infrequently reported in the literature.

DEPARTAMENTO DE MEDICINA

ENDOCRINOLOGÍA Y DIABETES

REV MED CHIL. 2019 MAY;147(5):668-672. DOI: 10.4067/S0034-98872019000500668.

[AUTOIMMUNE PANCREATITIS ASSOCIATED WITH DIABETES MELLITUS. REPORT OF ONE CASE].

Pinto K E, Vargas R C, Gómez G P, Durruty A P, López S G.

Autoimmune pancreatitis is uncommon, responds to steroids and is usually associated with diabetes mellitus. We report a 73 year-old male who, two months after a diagnosis of diabetes mellitus, presented with obstructive jaundice and weight loss. Abdominal magnetic resonance imaging was suggestive of an autoimmune pancreatitis and serum IgG4 was 339 mg/dl (normal range 3-201). The patient was treated with prednisone 40 mg/day with a good clinical and laboratory response. During outpatient care, the dose of prednisone was tapered.

GASTROENTEROLOGÍA

REV MED CHIL. 2019 JUN;147(6):751-754. DOI: 10.4067/S0034-98872019000600751.

[PRIMARY MALIGNANT HEPATIC TUMORS OTHER THAN HEPATOCARCINOMA OR CHOLANGIOPAPILLOM. A SERIES OF CASES].

Araneda G, Poniachik R, Freundlich A, Carreño L, Poniachik J.

BACKGROUND: There are several types of primary malignant hepatic tumors (PMHT) other than hepatocellular carcinoma (HCC) and cholangiocarcinoma (CC): they are infrequent and poorly known. Imaging studies could help characterize the lesions and may guide the diagnosis. However, the definitive diagnosis of PMHT is made by pathology. **AIM:** To review a registry of liver biopsies performed to diagnose hepatic tumors. **PATIENTS AND METHODS:** Review of a pathology registry of liver biopsies performed for the diagnosis of liver tumors. Among these, 25 patients aged 57 ± 17 years, 60% males, in whom a liver tumor other than a HCC or CC was diagnosed, were selected for review. The medical records of these patients were reviewed to register their clinical characteristics, imaging and the pathological diagnosis performed during surgery and/ or with the percutaneous liver biopsy. **RESULTS:** Ten patients (40%) had neuroendocrine tumors, six (24%) had a lymphoma and four (16%) had hepatic hemangioendothelioma. Angiosarcoma and sarcomatoid carcinoma were diagnosed in one patient each. In 22 patients (88%), neither clinical features nor imaging studies gave the correct diagnosis. Four patients (16%) had chronic liver disease. The most frequent symptoms were weight loss in 28% and abdominal pain in 24%. **CONCLUSIONS:** The most common PMHT other than HCC and CC were neuroendocrine tumors and lymphomas. Imaging or clinical features were not helpful to reach the correct diagnosis.

PLOS ONE. 2019 JUN 6;14(6):E0217684. DOI: 10.1371/JOURNAL.PONE.0217684.

PRIMARY INFECTION BY PNEUMOCYSTIS INDUCES NOTCH-INDEPENDENT CLARA CELL MUCIN PRODUCTION IN RAT DISTAL AIRWAYS.

Méndez A, Rojas DA, Ponce CA, Bustamante R, Beltrán CJ, Toledo J, García-Angulo VA, Henríquez M, Vargas SL.

Clara cells are the main airway secretory cells able to regenerate epithelium in the distal airways through transdifferentiating into goblet cells, a process under negative regulation of the Notch pathway. Pneumocystis is a highly prevalent fungus in humans occurring between 2 and 5 months of age, a period when airways are still developing and respiratory morbidity typically increases. Pneumocystis induces mucus hyperproduction in immunocompetent host airways and whether it can stimulate Clara cells is unknown. Markers of Clara cell secretion and Notch1 activation were investigated in lungs of immunocompetent rats at 40, 60, and 80 days of age during Pneumocystis primary infection with and without Valproic acid (VPA), a Notch inducer. The proportion of rats expressing mucin increased in Pneumocystis-infected rats respect to controls at 60 and 80 days of age. Frequency of distal airways Clara cells was maintained while mRNA levels for the mucin-encoding genes Muc5B and Muc5ac in lung homogenates increased 1.9 and 3.9 times at 60 days of infection ($P = 0.1609$ and $P = 0.0001$, respectively) and protein levels of the Clara cell marker CC10 decreased in the Pneumocystis-infected rats at 60 and 80 days of age ($P = 0.0118$ & $P = 0.0388$). CC10 and Muc5b co-localized in distal airway epithelium of Pneumocystis-infected rats at day 60. Co-localization of Muc5b and Ki67 as marker of mitosis in distal airways was not observed suggesting that Muc5b production by Clara cells was independent of mitosis. Notch levels remained similar and no transnucleation of activated Notch associated to Pneumocystis infection was detected. Unexpectedly, mucus was greatly increased at day 80 in Pneumocystis-infected rats receiving VPA suggesting that a Notch-independent mechanism was triggered. Overall, data suggests a Clara to goblet cell transdifferentiation mechanism induced by Pneumocystis and independent of Notch.

ANN HEPATOL. 2019 MAR - APR;18(2):325-330. DOI: 10.1016/J.AOHEP.2018.11.001.

PRIORITIZATION FOR LIVER TRANSPLANTATION USING THE MELD SCORE IN CHILE: INEQUITIES GENERATED BY MELD EXCEPTIONS: A COLLABORATION BETWEEN THE CHILEAN LIVER TRANSPLANT PROGRAMS, THE PUBLIC HEALTH INSTITUTE AND THE NATIONAL TRANSPLANT COORDINATOR.

Díaz LA, Norero B, Lara B, Robles C, Elgueta S, Humeres R, Poniachik J, Silva G, Wolff R, Innocenti F, Rojas JL, Zapata R8, Hunter B, Álvarez S, Cancino A, Ibarra J, Rius M, González S, Calabrán L, Pérez RM.

INTRODUCTION AND AIM: The MELD score has been established as an efficient and rigorous prioritization system for liver transplant (LT). Our study aimed to evaluate the effectiveness of the MELD score as a system for prioritization for LT, in terms of decreasing the dropout rate in the waiting list and maintaining an adequate survival post-LT in Chile. **MATERIALS AND METHODS:** We analyzed the Chilean Public Health Institute liver transplant registry of candidates listed from October 15th 2011 to December 31st 2014. We included adult candidates (>15 years old) listed for elective cadaveric LT with a MELD score of 15 or higher. Statistical analysis included survival curves (Kaplan-Meier), log-rank statistics and multivariate logistic regression. **RESULTS:** 420 candidates were analyzed. Mean age was 53.6±11.8 years, and 244 were men (58%). Causes of LT included: Liver cirrhosis without exceptions (HC) 177 (66.4%); hepatocellular carcinoma (HCC) 111 (26.4%); cirrhosis with non-HCC exceptions 102 (24.3%) and non-cirrhotic candidates 30 (7.2%). LT rate was 43.2%. The dropout rate was 37.6% at 1-year. Even though the LT rate was higher, the annual dropout rate was significantly higher in cirrhotic candidates (without exceptions) compared with cirrhotics with HCC, and non-HCC exceptions plus non-cirrhotic candidates (47.9%; 37.2% and 24.2%, respectively, with $p=0.004$). Post-LT survival was 84% per year, with no significant differences between the three groups ($p=0.95$). **CONCLUSION:** Prioritization for LT using the MELD score system has not decreased the dropout rate in Chile (persistent low donor's rate). Exceptions generate inequities in dropout rate, disadvantaging patients without exceptions.

ANN HEPATOL. 2019 SEP 10. PII: S1665-2681(19)32213-6. DOI: 10.1016/J.AOHEP.2019.06.012.

LIVER TRANSPLANTATION IN ACUTE LIVER FAILURE DUE TO HEPATITIS B. TWO CLINICAL CASES.

Sedano R, Castro L, Venegas M, Miranda J, Hurtado C, Poniachik J, Brahm J.

Hepatitis B virus (HBV) related acute liver failure (ALF) is uncommon in our region, and there is limited HBV literature regarding the optimal management of these cases. In this article, we report two clinical cases of young men who have sex with men (MSM), both developed severe acute hepatitis caused by HBV, progressed to ALF and afterward required liver transplantation. Antiviral post-transplant treatment included entecavir without Hepatitis B Immunoglobulin (HBIG), and immunosuppression therapy with steroids, tacrolimus, and mycophenolate. Serologic follow-up showed early Hepatitis B surface Antigen (HBsAg) seroconversion, undetectable HBV viral load, and positive Anti-HBs titers. During later follow-up, Anti-HBs titers gradually fell (<10IU/L after six months), with normal liver function. **DISCUSSION:** In cases of HBV-related ALF, the liver develops a robust immune response, leading to, an early undetectable viral load and seroconversion, with loss of HBsAg, and the appearance of Anti-HBs as a result of the inflammatory response. The management varies depending on whether this is a de novo acute infection or a reactivation of a previous chronic infection. In both cases, the use of antiviral therapy is recommended, with entecavir or tenofovir, among others, but the use of specific HBIG is supported only in ALF related to chronic HBV infection. The optimal length of the antiviral therapy after liver transplantation is still under discussion. **CONCLUSION:** These cases of HBV related ALF with an early HBsAg seroconversion demonstrates the relevance of requesting IgM antibody against hepatitis B core antigen (anti-HBc IgM) for the etiological study of ALF with negative HBsAg. Usage of HBIG does not seem essential during the post-transplantation period in these cases.

GENÉTICA

EUR J HUM GENET. 2019 NOV 4. DOI: 10.1038/S41431-019-0485-3.

FURTHER DELINEATION OF NEUROPSYCHIATRIC FINDINGS IN TATTON-BROWN-RAHMAN SYNDROME DUE TO DISEASE-CAUSING VARIANTS IN DNMT3A: SEVEN NEW PATIENTS.

Tenorio J, Alarcón P, Arias P, Dapía I, García-Miñaur S, Palomares Bralo M, Campistol J, Climent S, Valenzuela I, Ramos S, Monseny AM, Grondona FL, Botet J, Serrano M, Solís M, Santos-Simarro F, Álvarez S, Teixidó-Tura G, Fernández Jaén A, Gordo G, Bardón Rivera MB, Nevado J, Hernández A2, Cigudosa JC, Ruiz-Pérez VL, Tizzano EF; SOGRI Consortium, Lapunzina P.

Tatton-Brown-Rahman (TBRS) syndrome is a recently described overgrowth syndrome caused by loss of function variants in the DNMT3A gene. This gene encodes for a DNA methyltransferase 3 alpha, which is involved in epigenetic regulation, especially during embryonic development. Somatic variants in DNMT3A have been widely studied in different types of tumors, including acute myeloid leukemia, hematopoietic, and lymphoid cancers. Germline gain-of-function variants in this gene have been recently implicated in microcephalic dwarfism. Common clinical features of patients with TBRS include tall stature, macrocephaly, intellectual disability (ID), and a distinctive facial appearance. Differential diagnosis of TBRS comprises Sotos, Weaver, and Malan Syndromes. The majority of these disorders present other clinical features with a high clinical overlap, making necessary a molecular confirmation of the clinical diagnosis. We here describe seven new patients with variants in DNMT3A, four of them with neuropsychiatric disorders, including schizophrenia and psychotic behavior. In addition, one of the patients has developed a brain tumor in adulthood. This patient has also cerebral atrophy, aggressive behavior, ID, and abnormal facial features. Clinical evaluation of this group of patients should include a complete neuropsychiatric assessment together with psychological support in order to

detect and manage abnormal behaviors such as aggressiveness, impulsivity, and attention deficit-hyperactivity disorder. TBRS should be suspected in patients with overgrowth, ID, tall stature, and macrocephaly, who also have some neuropsychiatric disorders without any genetic defects in the commonest overgrowth disorders. Molecular confirmation in these patients is mandatory.

AM J MED GENET A. 2019 JUN;179(6):893-895. DOI: 10.1002/AJMG.A.61139.

MANDIBULOACRAL DYSPLASIA WITH TYPE B LIPODYSTROPHY IN A PATIENT FROM CHILE.

Alarcón PI, Mujica I, Sanz P, García CJ, Gilgenkrantz S.

We report the first case of mandibuloacral dysplasia with type B lipodystrophy (MADB) in Chile, South America. MADB is a very rare illness, characterized by short stature, mandibular hypoplasia, acro-osteolysis in hands, feet and clavicles, lipodystrophy, changes in skin pigments and skin calcinosis at knees and hands. Diagnosis was confirmed by molecular study that showed two compound heterozygous variants in ZMPSTE24 gene, c.1085dup p.(Leu362Phefs*19) and c.794A>G p.(Asn265Ser). This article could help in establishing the correlation between genotype and phenotype of this disorder, comparing with other cases previously described.

CLIN GENET. 2019 JUN;95(6):726-731. DOI: 10.1111/CGE.13504.

MRX93 SYNDROME (BRWD3 GENE): FIVE NEW PATIENTS WITH NOVEL MUTATIONS.

Tenorio J, Alarcón P, Arias P, Ramos FJ, Campistol J, Climent S, García-Miñaur S, Dapía I, Hernández A, Nevado J, Solís M, Ruiz-Pérez VL; Sogri Consortium, Lapunzina P.

Overgrowth syndromes (OGS) comprise a heterogeneous group of disorders whose main characteristic is that either the weight, height, or head circumference are above the 97th centile or 2 to 3 SD above the mean for age and sex. Additional features, such as facial dysmorphism, developmental delay or intellectual disability (ID), congenital anomalies, neurological problems and an increased risk of neoplasia are usually associated with OGS. Genetic analysis in patients with overlapping clinical features is essential, to distinguish between two or more similar conditions, and to provide appropriate genetic counseling and recommendations for follow up. In the present paper, we report five new patients (from four unrelated families) with an X-linked mental retardation syndrome with overgrowth (XMR93 syndrome), also known as XLID-BRWD3-related syndrome. The main features of these patients include ID, macrocephaly and dysmorphic facial features. XMR93 syndrome is a recently described disorder caused by mutations in the Bromodomain and WD-repeat domain-containing protein 3 (BRWD3) gene. This article underscores the importance of genetic screening by exome sequencing for patients with OGS and ID with unclear clinical diagnosis, and expands the number of reported individuals with XMR93 syndrome, highlighting the clinical features of this unusual disease.

INFECTOLOGÍA

VACCINE. 2019 JUL 26;37(32):4646-4650. DOI: 10.1016/J.VACCINE.2019.06.069.

CHILE'S NATIONAL ADVISORY COMMITTEE ON IMMUNIZATION (CAVEI): EVIDENCE-BASED RECOMMENDATIONS FOR PUBLIC POLICY DECISION-MAKING ON VACCINES AND IMMUNIZATION.

Dabanch J, González C, Cerda J, Acevedo J, Calvo M, Díaz E, Endeiza M, Inostroza J, Rodríguez J, Saldaña A, Santillana S, El Omeiri N, Bastías M.

A National Immunization Technical Advisory Group (NITAG) provides independent, evidence-based recommendations to the Ministry of Health for immunization programmes and policy formulation. In this article, we describe the structure, functioning and work processes of Chile's NITAG (CAVEI) and assess its functionality, quality of work processes and outputs, and integration of the committee into the Ministry of Health policy process using the Assessment tool for National Immunization Technical Advisory Groups. Among its strengths, CAVEI's administrative and work plasticity allows it to respond in a timely manner to the Ministry of Health's requests and proactively raise subjects for review. Representation of multiple areas of expertise within the committee makes CAVEI a robust and balanced entity for the development of evidence-based comprehensive recommendations. High ranking profile of the Secretariat structure furthers CAVEI's competences in policymaking and serves as a bridge between the committee and international initiatives in the field of immunizations.

REV CHILENA INFECTOL. 2019 JUN;36(3):253-264. DOI: 10.4067/S0716-10182019000300253.

[CHANGES IN PRESCRIPTIONS AND ANTIBIOTIC CONSUMPTION AFTER THE IMPLEMENTATION OF RECOMMENDATIONS FOR USE: EXPERIENCE IN A UNIVERSITY HOSPITAL].

Ávila F, Luppi M, Gaete P, Rivas A, Silva F, Olivares R.

BACKGROUND: Nowadays about half of antibiotic prescriptions are inadequate, increasing bacterial resistance. Both cephalosporins and fluoroquinolones are associated with this phenomenon: increase of β -lactamase producing bacteria and Clostridioides difficile infections, which is why regulatory agencies seek to rationalize their use. AIM: To evaluate the effect of use recommendations on the proportion of inadequate prescriptions of ceftriaxone and fluoroquinolones. METHODS: A prospective and interventional study was developed, comparing the quality and quantity of use of ceftriaxone and fluoroquinolones before and after the implementation of use recommendations for treatments of infectious diseases acquired at the community. The outcomes were: proportion of inadequate prescriptions and defined

daily dose (DDD). Data were analyzed using the Chi-square test, Fisher's correction and Student's test. RESULTS: A total of 206 patients were evaluated, a 35% decrease in inadequate prescriptions, a decline in the consumption of ceftriaxone and levofloxacin, and a significant increase in the use of ampicillin/ sulbactam was observed. CONCLUSIONS: The implementation of use recommendations based on scientific evidence and local susceptibility allowed to reduce the proportion of inadequate prescriptions and to reduce de consumption of ceftriaxone and fluoroquinolones.

INMUNOLOGÍA

ALLERGY. 2019 JUL;74(7):1219-1236. DOI: 10.1111/ALL.13701.

ARIA PHARMACY 2018 "ALLERGIC RHINITIS CARE PATHWAYS FOR COMMUNITY PHARMACY": AIRWAYS ICPS INITIATIVE (EUROPEAN INNOVATION PARTNERSHIP ON ACTIVE AND HEALTHY AGEING, DG CONNECT AND DG SANTÉ) POLLAR (IMPACT OF AIR POLLUTION ON ASTHMA AND RHINITIS) GARD DEMONSTRATION PROJECT.

Bosnic-Anticevich S, Costa E, Menditto E, Lourenço O, Novellino E, Bialek S, Briedis V, Guzmán MA, *et al.*

Pharmacists are trusted health care professionals. Many patients use over-the-counter (OTC) medications and are seen by pharmacists who are the initial point of contact for allergic rhinitis management in most countries. The role of pharmacists in integrated care pathways (ICPs) for allergic diseases is important. This paper builds on existing studies and provides tools intended to help pharmacists provide optimal advice/interventions/strategies to patients with rhinitis. The Allergic Rhinitis and its Impact on Asthma (ARIA)-pharmacy ICP includes a diagnostic questionnaire specifically focusing attention on key symptoms and markers of the disease, a systematic Diagnosis Guide (including differential diagnoses), and a simple flowchart with proposed treatment for rhinitis and asthma multimorbidity. Key prompts for referral within the ICP are included. The use of technology is critical to enhance the management of allergic rhinitis. However, the ARIA-pharmacy ICP should be adapted to local healthcare environments/situations as regional (national) differences exist in pharmacy care.

ALLERGOL IMMUNOPATHOL (MADR). 2019 MAY - JUN;47(3):282-288. DOI: 10.1016/J.ALLER.2018.10.003.

TREATMENT, OUTCOMES AND COSTS OF ASTHMA EXACERBATIONS IN CHILEAN CHILDREN: A PROSPECTIVE MULTICENTER OBSERVATIONAL STUDY.

Herrera AM, Brand P, Cavada G, Koppmann A, Rivas M, Mackenney J, Sepúlveda H, Wevar ME, Cruzat L, Soto S, Pérez MA, León A, Contreras I, Alvarez C, Walker B, Flores C, Lezana V, Garrido C, Herrera ME, Rojas *et al.*

OBJECTIVE: To describe potential regional variations in therapies for severe asthma exacerbations in Chilean children and estimate the associated health expenditures. METHODS: Observational prospective cohort study in 14 hospitals over a one-year period. Children five years of age or older were eligible for inclusion. Days with oxygen supply and pharmacological treatments received were recorded from the clinical chart. A basic asthma hospitalization basket was defined in order to estimate the average hospitalization cost for a single patient. Six months after discharge, new visits to the Emergency Room (ER), use of systemic corticosteroids and adherence to the controller treatment were evaluated. RESULTS: 396 patients were enrolled. Patients from the public health system and from the north zone received significantly more days of oxygen, systemic corticosteroids and antibiotics. Great heterogeneity in antibiotic use among the participating hospitals was found, from 0 to 92.3% (ICC 0.34, 95% CI 0.16-0.52). The use of aminophylline, magnesium sulfate and ketamine varied from 0 to 36.4% between the different Pediatric Intensive Care Units (ICC 0.353, 95% CI 0.010-0.608). The average cost per inpatient was of \$1910 USD. 290 patients (73.2%) completed the follow-up six months after discharge. 76 patients (26.2%) were not receiving any controller treatment and nearly a fourth had new ER visits and use of systemic corticosteroids due to new asthma exacerbations. CONCLUSIONS: Considerable practice variation in asthma exacerbations treatment was found among the participating hospitals, highlighting the poor outcome of many patients after hospital discharge, with an important health cost.

MEDICINA INTERNA

ANN HEPATOL. 2019 MAY - JUN;18(3):518-535. DOI: 10.1016/J.AOHEP.2019.04.005.

ALCOHOL-RELATED LIVER DISEASE: CLINICAL PRACTICE GUIDELINES BY THE LATIN AMERICAN ASSOCIATION FOR THE STUDY OF THE LIVER (ALEH).

Arab JP, Roblero JP, Altamirano J, Bessone F, Chaves Araujo R, Higuera-De la Tijera F, Restrepo JC, Torre A, Urzua A, Simonetto DA, Abalde JG, Méndez-Sánchez N, Contreras F, Lucey MR, Shah VH, Cortez-Pinto H, Bataller R.

Alcohol-related liver disease (ALD) is a major cause of advanced chronic liver disease in Latin-America, although data on prevalence is limited. Public health policies aimed at reducing the alarming prevalence of alcohol use disorder in Latin-America should be implemented. ALD comprises a clinical-pathological spectrum that ranges from steatosis, steatohepatitis to advanced forms such as alcoholic hepatitis (AH), cirrhosis and hepatocellular carcinoma. Besides genetic factors, the amount of alcohol consumption is the most important risk factor for the development of ALD. Continuous consumption of more than 3 standard drinks per day in men and more than 2 drinks per day in women increases the risk of developing liver disease. The pathogenesis of ALD is only partially understood and recent translational studies have identified novel therapeutic targets. Early forms of ALD are often missed and most clinical attention is focused on AH, which is defined as an abrupt onset of jaundice and

liver-related complications. In patients with potential confounding factors, a transjugular biopsy is recommended. The standard therapy for AH (i.e. prednisolone) has not evolved in the last decades yet promising new therapies (i.e. G-CSF, N-acetylcysteine) have been recently proposed. In both patients with early and severe ALD, prolonged abstinence is the most efficient therapeutic measure to decrease long-term morbidity and mortality. A multidisciplinary team including alcohol addiction specialists is recommended to manage patients with ALD. Liver transplantation should be considered in the management of patients with end-stage ALD that do not recover despite abstinence. In selected cases, increasing number of centers are proposing early transplantation for patients with severe AH not responding to medical therapy.

MEDICINA NUCLEAR

J NUCL CARDIOL. 2019 AUG 13. DOI: 10.1007/S12350-019-01845-2.

DIASTOLIC DYSSYNCHRONY ASSESSMENT BY GATED MYOCARDIAL PERFUSION-SPECT IN SUBJECTS WHO UNDERWENT CARDIAC RESYNCHRONIZATION THERAPY.

Alexanderson-Rosas E, Espinola-Zavaleta N, Garcia EV, Peix A, Massardo T, Pabon LM, Antonio-Villa NE, Carvajal-Juarez I, Mesquita CT, Jimenez-Heffernan A, Patel C, Karthikeyan G, Kumar A, Butt S, Kalaivani M, Marin V, Morozova O, Paez D.

BACKGROUND: Left ventricular diastolic dyssynchrony (LVDD) can be assessed by gated myocardial perfusion single-photon emission computed tomography (GMP-SPECT). LVDD is an area of interest in subjects who underwent cardiac resynchronization therapy (CRT). The aim of this post hoc analysis was to assess the role of LVDD in subjects with CRT who were followed up at 6-month period. MATERIAL & METHODS: Left ventricular diastolic dyssynchrony was assessed by GMP-SPECT at baseline and after CRT procedure in 160 subjects from 10 different cardiological centers. CRT procedure was performed as per current guidelines. Outcomes were defined as improvement in ≥ 1 New York Heart Association (NYHA) class, left ventricular ejection fraction (LVEF) by 5%, and reduction in end-systolic volume (ESV) by 15% and 5% points in Minnesota Living with Heart Failure Questionnaire. LVDD was defined as diastolic phase standard deviation $\geq 40 \pm 14^\circ$. RESULTS: Improvement in NYHA functional class occurred in 105 (65.6%), LVEF in 74 (46.3%), decrease in ESV in 86 (53.8%), and Minnesota score in 85 (53.1%) cases. Baseline LV diastolic standard deviation was $53.53^\circ \pm 20.85$ and at follow-up $40.44^\circ \pm 26.1283$; ($P < 0.001$). LVDD was not associated with improvement in clinical outcomes at follow-up. CONCLUSION: CRT improves both systolic and diastolic dyssynchrony values at 6-month follow-up. LVDD at baseline is correlated with cardiac functionality at follow-up, but not with overall favorable clinical outcomes.

J NUCL CARDIOL. 2019 APR 11. DOI: 10.1007/S12350-019-01704-0.

EFFECT OF CARDIAC RESYNCHRONIZATION THERAPY ON SEPTAL PERFUSION AND SEPTAL THICKENING: ASSOCIATION WITH LEFT VENTRICULAR FUNCTION, REVERSE REMODELLING AND DYSSYNCHRONY.

Patel C, Kalaivani M, Karthikeyan G, Peix A, Kumar A, Massardo T, Jiménez-Heffernan A, Mesquita CT, Pabon M, Butt S, Alexanderson E, Marin V, Morozova O, Paez D, Garcia EV.

BACKGROUND: We evaluated the effect of cardiac resynchronization therapy (CRT) on septal perfusion and thickening at 6 months post implantation assessed on Tc99m-MIBI Gated myocardial perfusion SPECT (GMPS). We also studied the association of change in septal perfusion and thickening with primary outcome defined as at least one [improvement in ≥ 1 NYHA class, left ventricular ejection fraction (LVEF) by $\geq 5\%$, reduction of end-systolic volume (ESV) by $\geq 15\%$, and improvement ≥ 5 points in Minnesota living with heart failure questionnaire (MLHFQ)]. METHOD: One hundred and five patients underwent clinical and GMPS evaluation before and at 6 months post CRT. RESULT: Post CRT there was significant improvement in mean normalized septal perfusion uptake and in septal thickening (P value = 0.001, both). There was no significant relation between improvement in septal perfusion and primary outcome. However, improvement in septal thickening was statistically significant with favorable primary outcome ($P = 0.001$). There was no significant correlation between improvement of septal perfusion and improvement in LVEF, reduction in End diastolic volume (EDV), ESV, and Left ventricular Dyssynchrony (LVD). But, there was significant correlation between improvement of septal thickening and these parameters. CONCLUSION: Improvement in septal thickening was associated with reverse remodeling, improvement in LVEF, and reduction of LVD.

J NUCL CARDIOL. 2019 JAN 25. DOI: 10.1007/S12350-018-01589-5.

VALUE OF INTRAVENTRICULAR DYSSYNCHRONY ASSESSMENT BY GATED-SPECT MYOCARDIAL PERFUSION IMAGING IN THE MANAGEMENT OF HEART FAILURE PATIENTS UNDERGOING CARDIAC RESYNCHRONIZATION THERAPY (VISION-CRT).

Peix A, Karthikeyan G, Massardo T, Kalaivani M, Patel C, Pabon LM, Jiménez-Heffernan A, Alexanderson E, Butt S, Kumar A, Marin V, Mesquita CT, Morozova O, Paez D, Garcia EV.

BACKGROUND: Placing the left ventricular (LV) lead in a viable segment with the latest mechanical activation (vSOLA) may be associated with optimal cardiac resynchronization therapy (CRT) response. We assessed the role of gated SPECT myocardial perfusion imaging (gSPECT MPI) in predicting clinical outcomes at 6 months in patients submitted to CRT. METHODS: Ten centers from 8 countries enrolled 195 consecutive patients. All underwent gSPECT MPI before and 6 months after CRT. The procedure was performed as per current guidelines, the operators being unaware of gSPECT MPI results. Regional LV dyssynchrony (Phase SD) and vSOLA were automatically determined using a 17 segment model. The lead was considered on-target if placed in vSOLA. The primary outcome was improvement in ≥ 1 of the following: ≥ 1 NYHA class, left ventricular ejection fraction (LVEF) by $\geq 5\%$, reduction in end-systolic volume by $\geq 15\%$, and ≥ 5

points in Minnesota Living With Heart Failure Questionnaire (MLHFQ). RESULTS: Sixteen patients died before the follow-up gSPECT MPI. The primary outcome occurred in 152 out of 179 (84.9%) cases. Mean change in LV phase standard deviation (PSD) at 6 months was 10.5°. Baseline dyssynchrony was not associated with the primary outcome. However, change in LV PSD from baseline was associated with the primary outcome (OR 1.04, 95% CI 1.01-1.07, P = .007). Change in LV PSD had an AUC of 0.78 (0.66-0.90) for the primary outcome. Improvement in LV PSD of 4° resulted in the highest positive likelihood ratio of 7.4 for a favorable outcome. In 23% of the patients, the CRT lead was placed in the vSOLA, and in 42% in either this segment or in a segment within 10° of it. On-target lead placement was not significantly associated with the primary outcome (OR 1.53, 95% CI 0.71-3.28). CONCLUSION: LV dyssynchrony improvement by gSPECT MPI, but not on-target lead placement, predicts clinical outcomes in patients undergoing CRT.

NEFROLOGÍA

REV MED CHIL. 2019 JUN;147(6):709-717. DOI: 10.4067/S0034-98872019000600709.

[PREGNANCY DURING CHRONIC HEMODIALYSIS. A SERIES OF CASES].

Fiedler Z Ú, Sanhueza V ME, Toro C L.

BACKGROUND: Pregnancies in women with end stage renal failure are uncommon. However, correction of anemia and improvement in dialysis techniques increases the rate of successful pregnancies. AIM: To describe a 16 years' experience treating pregnant women on hemodialysis and to analyze maternal-fetal outcomes. MATERIALS AND METHODS: Observational study of a dialysis center historical cohort in a university hospital, between 2001 and 2016. RESULTS: Thirteen pregnancies were found in 11 women aged 23 to 32 years, 77% on dialysis prior to pregnancy. Residual diuresis was 1,300 [625-1,575] mL in 24 hrs. The baseline hemoglobin was 9.0 [7.6-9.9] g/dL and 92% of patients did not use contraception. The pre-dialysis blood urea nitrogen was 34 [29-36] mg /dL. An ultrasound to confirm pregnancy was done in all. At 23 [14-25] weeks of pregnancy, dialysis hours were increased, reaching 24 [19.5-24.0] hours per week. The most common complications were severe arterial hypertension (54%), severe anemia (46%), polyhydramnios (31%) and severe intrauterine growth retardation (IUGR) (23%). The median time of pregnancy at delivery was 34 [29-34] weeks. Neonatal median hospitalization length was 4 [4-32] days, with 18% of neonatal deaths. CONCLUSIONS: Pregnancies in dialysis are no longer exceptional. Despite better maternal and fetal outcomes, morbidity and mortality remains higher than in the normal population, which makes multidisciplinary management essential.

J BONE MINER RES. 2019 OCT;34(10):1851-1861. DOI: 10.1002/JBMR.3761.

GLUCOCORTICOIDS DECREASE LONGITUDINAL BONE GROWTH IN PEDIATRIC KIDNEY TRANSPLANT RECIPIENTS BY STIMULATING THE FGF23/FGFR3 SIGNALING PATHWAY.

Delucchi Á, Toro L, Alzamora R, Barrientos V, González M, Andaur R, León P, Villanueva F, Galindo M, Las Heras F, Montecino M, Moena D, Lazcano A, Pinto V, Salas P, Reyes ML, Mericq V, Michea L.

Renal transplantation (RTx) is an effective therapy to improve clinical outcomes in pediatric patients with terminal chronic kidney disease. However, chronic immunosuppression with glucocorticoids (GCs) reduces bone growth and BMD. The mechanisms causing GC-induced growth impairment have not been fully clarified. Fibroblast growth factor 23 (FGF23) is a peptide hormone that regulates phosphate homeostasis and bone growth. In pathological conditions, FGF23 excess or abnormal FGF receptors (FGFR) activity leads to bone growth impairment. Experimental data indicate that FGF23 expression is induced by chronic GC exposure. Therefore, we hypothesize that GCs impair bone growth by increasing FGF23 expression, which has direct effects on bone growth plate. In a post hoc analysis of a multicentric randomized clinical trial of prepubertal RTx children treated with early GC withdrawal or chronic GC treatment, we observed that GC withdrawal was associated with improvement in longitudinal growth and BMD, and lower plasma FGF23 levels as compared with a chronic GC group. In prepubertal rats, GC-induced bone growth retardation correlated with increased plasma FGF23 and bone FGF23 expression. Additionally, GC treatment decreased FGFR1 expression whereas it increased FGFR3 expression in mouse tibia explants. The GC-induced bone growth impairment in tibiae explants was prevented by blockade of FGF23 receptors using either a pan-FGFR antagonist (PD173074), a C-terminal FGF23 peptide (FGF23180-205) which blocks the binding of FGF23 to the FGFR-Klotho complex or a specific FGFR3 antagonist (P3). Finally, local administration of PD173074 into the tibia growth plate ameliorated cartilage growth impairment in GC-treated rats. These results show that GC treatment partially reduces longitudinal bone growth via upregulation of FGF23 and FGFR3 expression, thus suggesting that the FGF23/Klotho/FGFR3 axis at the growth plate could be a potential therapeutic target for the management of GC-induced growth impairment in children.

J HYPERTENS. 2019 JUL;37(7):1482-1492. DOI: 10.1097/HJH.0000000000002067.

DENDRITIC CELLS ARE CRUCIAL FOR CARDIOVASCULAR REMODELING AND MODULATE NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN EXPRESSION UPON MINERALOCORTICOID RECEPTOR ACTIVATION.

Araos P, Prado C, Lozano M, Figueroa S, Espinoza A, Berger T, Mak TW, Jaisser F, Pacheco R, Michea L, Amador CA.

BACKGROUND: Adaptive immunity is crucial in cardiovascular and renal inflammation/fibrosis upon hyperactivation of mineralocorticoid receptor. We have previously demonstrated that dendritic cells can respond to mineralocorticoid receptor activation, and the neutrophil gelatinase-associated lipocalin (NGAL) in dendritic cells is highly increased during aldosterone (Aldo)/mineralocorticoid receptor-

dependent cardiovascular damage. However, the interrelationship among dendritic cells, target organs inflammation/fibrosis induced by mineralocorticoid receptor, and NGAL-dependence remains unknown. OBJECTIVE: We studied the role of dendritic cells in mineralocorticoid receptor-dependent tissue remodeling and whether NGAL can modulate the inflammatory response of dendritic cells after mineralocorticoid receptor activation. METHODS: Cardiovascular and renal remodeling induced by Aldo and high-salt diet [nephrectomy-Aldo-salt (NAS) model] were analyzed in CD11c.DOG mice, a model which allows dendritic cells ablation by using diphtheria toxin. In addition, in-vitro studies in NGAL-knock out dendritic cells were performed to determine the immunomodulatory role of NGAL upon Aldo treatment. RESULTS: The ablation of dendritic cells prevented the development of cardiac hypertrophy, perivascular fibrosis, and the overexpression of NGAL, brain natriuretic peptide, and two profibrotic factors induced by NAS: collagen 1A1 and connective tissue growth factor. We determined that dendritic cells were not required to prevent renal hypertrophy/fibrosis induced by NAS. Between different immune cells analyzed, we observed that NGAL abundance was higher in antigen-presenting cells, while in-vitro studies showed that mineralocorticoid receptor stimulation in dendritic cells favored NGAL and IL-23 expression (p19 and p40 subunits), which are involved in the development of fibrosis and the Th17-driven response, respectively. CONCLUSION: NGAL produced by dendritic cells may play a pivotal role in the activation of adaptive immunity that leads to cardiovascular fibrosis during mineralocorticoids excess.

AM J PHYSIOL RENAL PHYSIOL. 2019 APR 1;316(4):F624-F634. DOI: 10.1152/AJPRENAL.00398.2018.

L-NIL PREVENTS THE ISCHEMIA AND REPERFUSION INJURY INVOLVING TLR-4, GST, CLUSTERIN, AND NFAT-5 IN MICE.

Pasten C, Alvarado C, Rocco J, Contreras L, Aracena P, Liberona J, Suazo C, Michea L, Irrázabal CE.

On renal ischemia-reperfusion (I/R) injury, recruitment of neutrophils during the inflammatory process promotes local generation of oxygen and nitrogen reactive species, which, in turn, are likely to exacerbate tissue damage. The mechanism by which inducible nitric oxide synthase (iNOS) is involved in I/R has not been elucidated. In this work, the selective iNOS inhibitor L-N^G-L-Iminoethyl)lysine (L-NIL) and the NOS substrate L-arginine were employed to understand the role of NOS activity on the expression of particular target genes and the oxidative stress elicited after a 30-min of bilateral renal ischemia, followed by 48-h reperfusion in Balb/c mice. The main findings of the present study were that pharmacological inhibition of iNOS with L-NIL during an I/R challenge of mice kidney decreased renal injury, prevented tissue loss of integrity, and improved renal function. Several novel findings regarding the molecular mechanism by which iNOS inhibition led to these protective effects are as follows: 1) a prevention of the I/R-related increase in expression of Toll-like receptor 4 (TLR-4), and its downstream target, IL-1 β ; 2) reduced oxidative stress following the I/R challenge; noteworthy, this study shows the first evidence of glutathione S-transferase (GST) inactivation following kidney I/R, a phenomenon fully prevented by iNOS inhibition; 3) increased expression of clusterin, a survival autophagy component; and 4) increased expression of nuclear factor of activated T cells 5 (NFAT-5) and its target gene aquaporin-1. In conclusion, prevention of renal damage following I/R by the pharmacological inhibition of iNOS with L-NIL was associated with the inactivation of proinflammatory pathway triggered by TLR-4, oxidative stress, renoprotection (autophagy inactivation), and NFAT-5 signaling pathway.

ONCOLOGÍA

J KIDNEY CANCER VHL. 2019 MAR 5;6(1):1-7. DOI: 10.15586/JKCVHL.2019.114.

IS CYTOREDUCTIVE NEPHRECTOMY STILL A STANDARD OF CARE IN METASTATIC RENAL CELL CARCINOMA?

Renner A, Samtani S, Marín A, Burotto M.

Cytoreductive nephrectomy has been an integral part of management in metastatic renal cell carcinoma for patients with good performance status, based on the benefit shown by prospective trials in the interferon era and retrospective trials in the targeted therapies era. Clinical Trial to Assess the Importance of Nephrectomy (CARMENA), the first prospective phase III trial comparing a targeted agent alone (sunitinib) versus nephrectomy plus sunitinib, has been recently published, showing non-inferiority for the nephrectomy-sparing arm. In this article, we discuss the impact of nephrectomy including its immune-mediated effects, surgical morbidity and mortality, and the clinical data supporting the indications of nephrectomy in order to analyze the CARMENA trial in context, with the aim to identify optimal strategies for different patient populations in the metastatic setting.

J GLOB ONCOL. 2019 JUL;5:1-5. DOI: 10.1200/JGO.19.00142.

IMMUNE CHECKPOINT INHIBITOR DOSING: CAN WE GO LOWER WITHOUT COMPROMISING CLINICAL EFFICACY?

Renner A, Burotto M, Rojas C.

In just a few years, immune checkpoint inhibitors have dramatically changed the landscape in oncology, offering durable responses and improved survival for many patients across several tumor types. With more than 3,300 new agents in the immuno-oncology pipeline plus a wide array of combinations being studied, it seems this new era is just getting started. These advances come with a significant caveat: most of the world population does not have access to their benefits, because the yearly cost of a novel anticancer medication can routinely exceed \$100,000. There is a large amount of data showing that checkpoint inhibitors have significant activity at doses much lower than those currently approved. We review the evidence for reduced drug dosing as a strategy to increase the number of patients who can be treated and what would be needed to further validate this approach.

UNIDAD DEL DOLOR

FRONT IMMUNOL. 2019 MAY 28;10:1171. DOI: 10.3389/FIMMU.2019.01171.

REGULATION OF TOLEROGENTIC FEATURES ON DEXAMETHASONE-MODULATED MPLA-ACTIVATED DENDRITIC CELLS BY MYC.

García-González PA, Maggi J, Schinnerling K, Sepúlveda-Gutiérrez A, Soto L, Neira O, Mehdi AM, Nel HJ, Pesce B, Aravena O, Molina MC, Catalán D, Thomas R, Verdugo RA, Aguillón JC.

The potential of tolerogenic dendritic cells (tolDCs) to shape immune responses and restore tolerance has turned them into a promising therapeutic tool for cellular therapies directed toward immune regulation in autoimmunity. Although the cellular mechanisms by which these cells can exert their regulatory function are well-known, the mechanisms driving their differentiation and function are still poorly known, and the variety of stimuli and protocols applied to differentiate DCs toward a tolerogenic phenotype makes it even more complex to underpin the molecular features involved in their function. Through transcriptional profiling analysis of monocyte-derived tolDCs modulated with dexamethasone (Dex) and activated with monophosphoryl lipid A (MPLA), known as DM-DCs, we were able to identify MYC as one of the transcriptional regulators of several genes differentially expressed on DM-DCs compared to MPLA-matured DCs (M-DCs) and untreated/immature DCs (DCs) as revealed by Ingenuity Pathway Analysis (IPA) upstream regulators evaluation. Additionally, MYC was also amongst the most upregulated genes in DM-DCs, finding that was confirmed at a transcriptional as well as at a protein level. Blockade of transactivation of MYC target genes led to the downregulation of tolerance-related markers IDO1 and JAG1. MYC blockade also led to downregulation of PLZF and STAT3, transcription factors associated with immune regulation and inhibition of DC maturation, further supporting a role of MYC as an upstream regulator contributing to the regulatory phenotype of DM-DCs. On the other hand, we had previously shown that fatty acid oxidation, oxidative metabolism and zinc homeostasis are amongst the main biological functions represented in DM-DCs, and here we show that DM-DCs exhibit higher intracellular expression of ROS and Zinc compared to mature M-DCs and DCs. Taken together, these findings suggest that the regulatory profile of DM-DCs is partly shaped by the effect of the transcriptional regulation of tolerance-inducing genes by MYC and the modulation of oxidative metabolic processes and signaling mediators such as Zinc and ROS.

FRONT IMMUNOL. 2019 FEB 19;10:203. DOI: 10.3389/FIMMU.2019.00203.

HUMANIZED MOUSE MODELS OF RHEUMATOID ARTHRITIS FOR STUDIES ON IMMUNOPATHOGENESIS AND PRECLINICAL TESTING OF CELL-BASED THERAPIES.

Schinnerling K, Rosas C, Soto L, Thomas R, Aguillón JC.

Rodent models of rheumatoid arthritis (RA) have been used over decades to study the immunopathogenesis of the disease and to explore intervention strategies. Nevertheless, mouse models of RA reach their limit when it comes to testing of new therapeutic approaches such as cell-based therapies. Differences between the human and the murine immune system make it difficult to draw reliable conclusions about the success of immunotherapies. To overcome this issue, humanized mouse models have been established that mimic components of the human immune system in mice. Two main strategies have been pursued for humanization: the introduction of human transgenes such as human leukocyte antigen molecules or specific T cell receptors, and the generation of mouse/human chimera by transferring human cells or tissues into immunodeficient mice. Recently, both approaches have been combined to achieve more sophisticated humanized models of autoimmune diseases. This review discusses limitations of conventional mouse models of RA-like disease and provides a closer look into studies in humanized mice exploring their usefulness and necessity as preclinical models for testing of cell-based therapies in autoimmune diseases such as RA.

BANCO DE SANGRE

IMMUNOBIOLOGY. 2019 SEP;224(5):697-705. DOI: 10.1016/J.IMBIO.2019.05.011.

DEXAMETHASONE TURNS TUMOR ANTIGEN-PRESENTING CELLS INTO TOLEROGENTIC DENDRITIC CELLS WITH T CELL INHIBITORY FUNCTIONS.

Falcón-Beas C, Tittarelli A, Mora-Bau G, Tempio F, Pérez C, Hevia D, Behrens C, Flores I, Falcón-Beas F, Garrido P, Ascui G, Pereda C, González FE, Salazar-Onfray F, López MN.

BACKGROUND: Dendritic cells (DCs) are usually immunogenic, but they are also capable of inducing tolerance under anti-inflammatory conditions. Immunotherapy based on autologous DCs loaded with an allogeneic melanoma cell lysate (TRIMEL/DCs) induces immunological responses and increases melanoma patient survival. Glucocorticoids can suppress DC maturation and function, leading to a DC-mediated inhibition of T cell responses. **METHODS:** The effect of dexamethasone, a glucocorticoid extensively used in cancer therapies, on TRIMEL/DCs phenotype and immunogenicity was examined. **RESULTS:** Dexamethasone induced a semi-mature phenotype on TRIMEL/DC with low maturation surface marker expressions, decreased pro-inflammatory cytokine induction (IL-1 β and IL-12) and increased release of regulatory cytokines (IL-10 and TGF- β). Dexamethasone-treated TRIMEL/DCs inhibited allogeneic CD4⁺ T cell proliferation and cytokine release (IFN γ , TNF- α and IL-17). Co-culturing melanoma-specific memory tumor-infiltrating lymphocytes with dexamethasone-treated TRIMEL/DC inhibited proliferation and effector T cell activities, including cytokine secretion and anti-melanoma cytotoxicity. **CONCLUSIONS:** These findings suggest that dexamethasone repressed melanoma cell lysate-mediated DC maturation, generating a potent tolerogenic-like DC phenotype that inhibited melanoma-specific effector T cell activities. These results suggest that dexamethasone-induced immunosuppression may interfere with the clinical efficacy of DC-based melanoma vaccines, and must be taken into account for optimal design of cellular therapy against cancer.

LABORATORIO CLÍNICO

J CLIN MICROBIOL. 2019 AUG 26;57(9). PII: E00798-19. DOI: 10.1128/JCM.00798-19.

A MULTICENTER STUDY TO EVALUATE CEFTAROLINE BREAKPOINTS: PERFORMANCE IN AN AREA WITH HIGH PREVALENCE OF METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS SEQUENCE TYPE 5 LINEAGE.

Khan A, Rivas LM, Spencer M, Martinez R, Lam M, Rojas P, Porte L, Silva F, Braun S, Valdivieso F, Mv Lhauser M, Lafourcade M, Miller WR, García P, Arias CA, Munita JM.

Ceftaroline (CPT) is a broad-spectrum agent with potent activity against methicillin-resistant *Staphylococcus aureus* (MRSA). The sequence type 5 (ST5) Chilean-Cordobés clone, associated with CPT nonsusceptibility, is dominant in Chile, a region with high rates of MRSA infections. Here, we assessed the in vitro activity of CPT against a collection of MRSA isolates collected between 1999 and 2018 from nine hospitals (n = 320) and community settings (n = 41) in Santiago, Chile, and evaluated performance across testing methodologies. We found that our hospital-associated isolates exhibited higher CPT MIC distributions (MIC50 and MIC90 of 2 mg/liter) than the community isolates (MIC50 and MIC90 of 0.5 mg/liter), a finding that was consistent across time and independent of the culture source. High proportions (64%) of isolates were CPT nonsusceptible despite the absence of CPT use in Chile. Across methodologies, the Etest underestimated the MIC relative to the gold standard broth microdilution (BMD) test (MIC50 and MIC90 of 1 and 1.5 mg/liter, respectively). There was low (~51%) categorical agreement (CA) between Etest and BMD results across CLSI and EUCAST breakpoints. The recent revision of CLSI guidelines abolished "very major error" (VME) from the previous guidelines (81%), which perform similarly to the EUCAST guidelines. The level of concordance between CLSI and EUCAST for BMD testing and Etest was >95%. Disk diffusion performed poorly relative to BMD under CLSI (CA, 55%) and EUCAST (CA, 36%) guidelines. Comparison of EUCAST to CLSI for disk diffusion (with EUCAST used as the reference) showed low agreement (CA, 25%; VME, 70%). In summary, CPT-nonsusceptible MRSA are dominant in clinical settings in Chile. Our results provide data to support the reevaluation of CPT breakpoints and to improve agreement across methodologies and agencies.

FRONT MICROBIOL. 2019 FEB 4;10:104. DOI: 10.3389/FMICB.2019.00104.

IDENTIFICATION OF GENES INVOLVED IN BIOGENESIS OF OUTER MEMBRANE VESICLES (OMVs) IN SALMONELLA ENTERICA SEROVAR TYPHI. Nevermann J, Silva A, Otero C, Oyarzún DP, Barrera B, Gil F, Calderón IL, Fuentes JA.

Outer membrane vesicles (OMVs) are nano-sized proteoliposomes discharged from the cell envelope of Gram-negative bacteria. OMVs normally contain toxins, enzymes and other factors, and are used as vehicles in a process that has been considered a generalized, evolutionarily conserved delivery system among bacteria. Furthermore, OMVs can be used in biotechnological applications that require delivery of biomolecules, such as vaccines, remarking the importance of their study. Although it is known that *Salmonella enterica* serovar Typhi (*S. Typhi*), the etiological agent of typhoid fever in humans, delivers toxins (e.g., HlyE) via OMVs, there are no reports identifying genetic determinants of the OMV biogenesis in this serovar. In the present work, and with the aim to identify genes participating in OMV biogenesis in *S. Typhi*, we screened 15,000 random insertion mutants for increased HlyE secretion. We found 9 *S. Typhi* genes (generically called zzz genes) determining an increased HlyE secretion that were also involved in OMV biogenesis. The genes corresponded to *ompA*, *nlpI*, and *tolR* (envelope stability), *rfaE* and *waaC* (LPS synthesis), *yipP* (*envC*), *mrcB* (synthesis and remodeling of peptidoglycan), *degS* (stress sensor serine endopeptidase) and *hns* (global transcriptional regulator). We found that *S. Typhi* Δ zzz mutants were prone to secrete periplasmic, functional proteins with a relatively good envelope integrity. In addition, we showed that zzz genes participate in OMV biogenesis, modulating different properties such as OMV size distribution, OMV yield and OMV protein cargo.

UNIDAD PACIENTES CRÍTICOS

J THORAC DIS. 2019 JUL;11(7):3122-3135. DOI: 10.21037/JTD.2019.06.27.

LUNG MONITORING WITH ELECTRICAL IMPEDANCE TOMOGRAPHY: TECHNICAL CONSIDERATIONS AND CLINICAL APPLICATIONS.

Tomicic V, Cornejo R.

In recent years there has been substantial progress in the imaging evaluation of patients with lung disease requiring mechanical ventilatory assistance. This has been demonstrated by the inclusion of pulmonary ultrasound, positron emission tomography, electrical impedance tomography (EIT), and magnetic resonance imaging (MRI). The EIT uses electric current to evaluate the distribution of alternating current conductivity within the thoracic cavity. The advantage of the latter is that it is non-invasive, bedside radiation-free functional imaging modality for continuous monitoring of lung ventilation and perfusion. EIT can detect recruitment or derecruitment, overdistension, variation of poorly ventilated lung units (silent spaces), and pendelluft phenomenon in spontaneously breathing patients. In addition, the regional expiratory time constants have been recently explored.

REV MED CHIL. 2019;147(1):34-40. DOI: 10.4067/S0034-98872019000100034.

[REGISTRY OF PERIOPERATIVE CARDIAC ARRESTS IN A CLINICAL HOSPITAL IN THE PERIOD 2006-2017].

Aguirre C MM, Mayanz S S, Blanch Z A, Aranibar L H, Salazar T A, Roizen G G, Álvarez N MG, Izquierdo A C, Penna S A.

BACKGROUND: Perioperative cardiac arrest (PCA) is a rare but important event in the operating room. AIM: To describe PCA events at a Clinical Hospital in Santiago, Chile. MATERIAL AND METHODS: Registry of PCA that occurred in the operating room (OR) and during

procedures not carried out in the OR between September 2006 and November 2017. Precipitating events, type of anesthesia and results of resuscitation maneuvers were described. RESULTS: Eighty events (five outside of the OR) during 170,431 surgical procedures were recorded, resulting in an incidence of 4.4 events per 10,000 interventions. Hypotension/hypoperfusion was the most frequently found preexisting condition (42.5%). The main cause was the presence of preoperative complications (57.5%). Nineteen cases (23.8%) were attributable to anesthesia, with an incidence of 1.11 per 10,000 anesthetic procedures. Survival rate at hospital discharge was 52.5%. The figure for PCA caused by anesthesia was 84.2%. CONCLUSIONS: The incidence of PCA and its survival is similar to that reported abroad. In general, PCA has a better prognosis than other types of cardiac arrest, especially if it has an anesthetic cause.

ANTIMICROB RESIST INFECT CONTROL. 2019 JAN 5;8:3. DOI: 10.1186/S13756-018-0456-4.

ANTIMICROBIAL PROPERTIES OF A NOVEL COPPER-BASED COMPOSITE COATING WITH POTENTIAL FOR USE IN HEALTHCARE FACILITIES. Montero DA, Arellano C, Pardo M, Vera R, Gálvez R, Cifuentes M, Berasain MA, Gómez M, Ramírez C, Vidal RM.

BACKGROUND: Healthcare-associated infections (HAIs) have a major impact on public health worldwide. Particularly, hospital surfaces contaminated with bacterial pathogens are often the origin of both sporadic cases and outbreaks of HAIs. It has been demonstrated that copper surfaces reduce the microbial burden of high touch surfaces in the hospital environment. Here we report the antimicrobial characterization of a novel composite coating with embedded copper particles, named Copper Armour™. METHODS: The Copper Armour™ bactericidal activity was evaluated in in vitro assays against several bacterial pathogens, including *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Escherichia coli* O157:H7 and *Listeria monocytogenes*. Additionally, its antimicrobial properties were also evaluated in a pilot study over a nine-week period at an adult intensive care unit. For this, four high touch surfaces, including bed rails, overbed table, bedside table and IV Pole, were coated with Copper Armour™, and its microbial burden was determined over a nine-week period. RESULTS: Copper Armour™ coated samples showed an in vitro reduction in bacterial burden of >99.9% compared to control samples. Moreover, pilot study results indicate that Copper Armour™ significantly reduces the level of microbial contamination on high-touch surfaces in the hospital environment, as compared with standard surfaces. CONCLUSIONS: Based on its antimicrobial properties, Copper Armour™ is a novel self-sanitizing coating that exhibits bactericidal activity against important human pathogens and significantly reduces the microbial burden of hospital surfaces. This composite could be used as a self-sanitizing coating to complement infection control strategies in healthcare facilities.

AM J RESPIR CRIT CARE MED. 2019 MAR 1;199(5):603-612. DOI: 10.1164/RCCM.201805-0869OC.

NEAR-APNEIC VENTILATION DECREASES LUNG INJURY AND FIBROPROLIFERATION IN AN ACUTE RESPIRATORY DISTRESS SYNDROME MODEL WITH EXTRACORPOREAL MEMBRANE OXYGENATION.

Araos J, Alegria L, Garcia P, Cruces P, Soto D, Erranz B, Amthauer M, Salomon T, Medina T, Rodriguez F, Ayala P, Borzone GR, Meneses M, Damiani F, Retamal J, Cornejo R, Bugedo G, Bruhn A.

RATIONALE: There is wide variability in mechanical ventilation settings during extracorporeal membrane oxygenation (ECMO) in patients with acute respiratory distress syndrome. Although lung rest is recommended to prevent further injury, there is no evidence to support it. OBJECTIVES: To determine whether near-apneic ventilation decreases lung injury in a pig model of acute respiratory distress syndrome supported with ECMO. METHODS: Pigs (26-36 kg; n=24) were anesthetized and connected to mechanical ventilation. In 18 animals lung injury was induced by a double-hit consisting of repeated saline lavages followed by 2 hours of injurious ventilation. Then, animals were connected to high-flow venovenous ECMO, and randomized into three groups: 1) nonprotective (positive end-expiratory pressure [PEEP], 5 cm H₂O; V_t, 10 ml/kg; respiratory rate, 20 bpm), 2) conventional-protective (PEEP, 10 cm H₂O; V_t, 6 ml/kg; respiratory rate, 20 bpm), and 3) near-apneic (PEEP, 10 cm H₂O; driving pressure, 10 cm H₂O; respiratory rate, 5 bpm). Six other pigs were used as sham. All groups were maintained during the 24-hour study period. MEASUREMENTS AND MAIN RESULTS: Minute ventilation and mechanical power were lower in the near-apneic group, but no differences were observed in oxygenation or compliance. Lung histology revealed less injury in the near-apneic group. Extensive immunohistochemical staining for myofibroblasts and procollagen III was observed in the nonprotective group, with the near-apneic group exhibiting the least alterations. Near-apneic group showed significantly less matrix metalloproteinase-2 and -9 activity. Histologic lung injury and fibroproliferation scores were positively correlated with driving pressure and mechanical power. CONCLUSIONS: In an acute respiratory distress syndrome model supported with ECMO, near-apneic ventilation decreased histologic lung injury and matrix metalloproteinase activity, and prevented the expression of myofibroblast markers.

REV GASTROENTEROL MEX. 2019 APR - JUN;84(2):149-157. DOI: 10.1016/J.RGMX.2018.03.007.

EVALUATION OF GASTRIC MOTILITY THROUGH SURFACE ELECTROGASTROGRAPHY IN CRITICALLY ILL SEPTIC PATIENTS. COMPARISON OF METOCLOPRAMIDE AND DOMPERIDONE EFFECTS: A PILOT RANDOMIZED CLINICAL TRIAL.

Mancilla Asencio C, Gálvez-Arévalo LR, Tobar Almonacid E, Landskron-Ramos G, Madrid-Silva AM.

INTRODUCTION AND AIMS: Critically ill patients present with a broad spectrum of gastrointestinal motility disorders that affect the digestive tract. Our aim was to compare the effect of two prokinetic drugs on gastric electrical rhythm in critically ill septic patients, measured through surface electrogastrography (EGG). MATERIAL AND METHODS: A prospective triple-blinded randomized study was conducted on 36 patients admitted to the intensive care unit (ICU) with the diagnosis of septic shock. They were randomized to receive

metoclopramide or domperidone. We assessed dominant frequency (DF), percentage distribution over time, and dominant power (DP), which represents the strength of contraction, before and after administration of the study drugs. RESULTS: Reliable electrogastrograms were achieved in all patients. In relation to the distribution of DF over time, 64% of patients had dysrhythmia, the mean baseline DF was 2.9 cpm, and the mean DP was 56.5 μ v. After drug administration, 58% of the patients had dysrhythmia, the mean DF increased to 5.7 cpm ($P < .05$), and the DP did not change (57.4 μ v²). There were no significant differences between drugs. In the metoclopramide group, the baseline DF was 2.1 cpm and the baseline DP was 26.1 μ v². The post-drug values increased to 5.4 cpm and 34.1 μ v², respectively. In the domperidone group, the baseline DF was 3.7 cpm and the baseline DP was 86.9 μ v². After drug administration, the DF increased to 6.1 cpm and the DP decreased to 83.5 μ v². CONCLUSIONS: Both metoclopramide and domperidone similarly increased the DF of gastric pacemaker activity and improved gastric motility by restoring a normogastric pattern. Gastric dysmotility is frequent in septic patients.

DEPARTAMENTO DE NEUROLOGÍA Y NEUROCIRUGÍA

J ALZHEIMERS DIS. 2019;67(1):381-392. DOI: 10.3233/JAD-180771.

NEUROPSYCHIATRIC SYMPTOMS IN ALZHEIMER'S DISEASE ARE THE MAIN DETERMINANTS OF FUNCTIONAL IMPAIRMENT IN ADVANCED EVERYDAY ACTIVITIES.

Delgado C, Vergara RC, Martínez M, Musa G, Henríquez F, Slachevsky A.

BACKGROUND: Neuropsychiatric symptoms and cognitive impairment are independent contributors of functional impairment in activities of daily living (ADL) in Alzheimer's disease (AD) patients. ADL could be divided according to its complexity in three subdomains: basic (BADL), instrumental (IADL), and advanced (a-ADL). OBJECTIVE: Studying the cognitive and neuropsychiatric determinants of BADL, IADL, and a-ADL in normal cognitive elders and AD patients. METHODS: 144 subjects were graduated using the clinical dementia rating (CDR) in CDR=0, n=52 (control group) and 92 AD patients CDR=0.5, n=34 and CDR=1&2, n=58. They were assessed with measures of cognitive performance and neuropsychiatric symptoms that were included in regression models to measure the best predictors for each ADL subdomain at every CDR status. RESULTS: AD patients were significantly older, and had significantly more severe functional impairment, neuropsychiatric symptoms, and cognitive decline than controls. The best predictors of functional impairment in controls and CDR=0.5 AD patients were neuropsychiatric symptoms; in the CDR 0.5 patients, apathy severity was the most important determinant of IADL and a-ADL impairment. While in the CDR 1&2 AD patients, cognitive impairment was the principal determinant of functional impairment, being memory the best determinant of IADL and a-ADL impairment, while global cognition was of BADL impairment. CONCLUSIONS: The contribution of cognitive impairment and neuropsychiatric symptoms varied according to the subdomain of ADL, and the CDR. In very mild AD and controls the neuropsychiatric symptoms are the best predictors of more complex ADL impairment, while cognitive impairment is more important at mild to moderate states of AD.

J NEUROL NEUROSURG PSYCHIATRY. 2019 MAY;90(5):576-585. DOI: 10.1136/JNNP-2018-319578.

MUSCLE MRI IN A LARGE COHORT OF PATIENTS WITH OCULOPHARYNGEAL MUSCULAR DYSTROPHY.

Alonso-Jimenez A, Kroon RHMJM, Alejaldre-Monforte A, Nuñez-Peralta C, Horlings CGC, van Engelen BGM, Olivé M, González L, Verges-Gil E, Paradas C, Márquez C, Garibaldi M, Gallano P, Rodríguez MJ, Gonzalez-Quereda L, Dominguez Gonzalez C, Vissing , Fornander F, Eismum AV, García-Sobrino T, Pardo J, García-Figueiras R, Muelas N, Vilchez JJ, Kapetanovic S, Tasca G, Monforte M, Ricci E, Gomez MT, Bevilacqua JA *et al*

BACKGROUND AND OBJECTIVE: Oculopharyngeal muscular dystrophy (OPMD) is a genetic disorder caused by an abnormal expansion of GCN triplets within the PABPN1 gene. Previous descriptions have focused on lower limb muscles in small cohorts of patients with OPMD, but larger imaging studies have not been performed. Previous imaging studies have been too small to be able to correlate imaging findings to genetic and clinical data. METHODS: We present cross-sectional, T1-weighted muscle MRI and CT-scan data from 168 patients with genetically confirmed OPMD. We have analysed the pattern of muscle involvement in the disease using hierarchical analysis and presented it as heatmaps. Results of the scans were correlated with genetic and clinical data. RESULTS: Fatty replacement was identified in 96.7% of all symptomatic patients. The tongue, the adductor magnus and the soleus were the most commonly affected muscles. Muscle pathology on MRI correlated positively with disease duration and functional impairment. CONCLUSIONS: We have described a pattern that can be considered characteristic of OPMD. An early combination of fat replacement in the tongue, adductor magnus and soleus can be helpful for differential diagnosis. The findings suggest the natural history of the disease from a radiological point of view. The information generated by this study is of high diagnostic value and important for clinical trial development.

NEUROLOGIA. 2019 JUL - AUG;34(6):376-385. DOI: 10.1016/J.NRL.2017.01.013.

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. OBJECTIVE: 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: amnesic mild cognitive impairment (aMCI; n=24), non-amnesic 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.

FRONT NEUROL. 2019 JUL 24;10:788. DOI: 10.3389/FNEUR.2019.00788.

PROSPECTIVE ASSESSMENT OF NO EVIDENCE OF DISEASE ACTIVITY-4 STATUS IN EARLY DISEASE STAGES OF MULTIPLE SCLEROSIS IN ROUTINE CLINICAL PRACTICE.

Guevara C, Garrido C, Martinez M, Farias GA, Orellana P, Soruco W, Alarcón P, Diaz V, Silva C, Kempton MJ, Barker G, de Grazia J.

Background: In relapsing-remitting multiple sclerosis, no evidence of disease activity-3 (NEDA-3) is defined as no relapses, no disability progression and no MRI activity. NEDA-4 status is defined as meeting all NEDA-3 criteria plus having an annualized brain volume loss (a-BVL) of $\leq 0.4\%$. Prospective real-world studies presenting data on NEDA-4 are scarce. Objective: To determine the proportion of patients failing to meet one or more NEDA-4 criteria and the contribution of each component to this failure. Methods: Forty-eight patients were followed for 12 months. Structural image evaluation, using normalization, of atrophy was used to assess a-BVL. Results: The patients had a mean age of 33.0 years (range 18-57), disease duration of 1.7 years (0.4-4) and Expanded Disability Status Scale score of 1.3 (0-4); 71% were women. All patients were on disease-modifying therapies. During follow-up, 21% of the patients had at least one relapse, 21% had disability progression, 8% had new T2 lesions, and 10% had gadolinium-enhanced lesions. Fifty-eight percent (28/48) achieved NEDA-3 status. a-BVL of $>0.4\%$ was observed in 52% (25/48). Only 29% (14/48) achieved NEDA-4 status. Conclusion: a-BVL is a good marker to detect subclinical disease activity. a-BVL is parameter to continue investigating for guiding clinical practice in relapsing-remitting multiple sclerosis.

FRONT AGING NEUROSCI. 2019 APR 26;11:97. DOI: 10.3389/FNAGI.2019.00097.

CINGULATE CORTEX ATROPHY IS ASSOCIATED WITH HEARING LOSS IN PRESBYCUSIS WITH COCHLEAR AMPLIFIER DYSFUNCTION.

Belkhiria C, Vergara RC, San Martín S, Leiva A, Marcenaro B, Martinez M, Delgado C, Delano PH.

Erratum in

Erratum: Cingulate Cortex Atrophy Is Associated With Hearing Loss in Presbycusis With Cochlear Amplifier Dysfunction. [Front Aging Neurosci. 2019] Age-related hearing loss is associated with cognitive decline and has been proposed as a risk factor for dementia. However, the mechanisms that relate hearing loss to cognitive decline remain elusive. Here, we propose that the impairment of the cochlear amplifier mechanism is associated with structural brain changes and cognitive impairment. Ninety-six subjects aged over 65 years old (63 female and 33 male) were evaluated using brain magnetic resonance imaging, neuropsychological and audiological assessments, including distortion product otoacoustic emissions as a measure of the cochlear amplifier function. All the analyses were adjusted by age, gender and education. The group with cochlear amplifier dysfunction showed greater brain atrophy in the cingulate cortex and in the parahippocampus. In addition, the atrophy of the cingulate cortex was associated with cognitive impairment in episodic and working memories and in language and visuoconstructive abilities. We conclude that the neural abnormalities observed in presbycusis subjects with cochlear amplifier dysfunction extend beyond core auditory network and are associated with cognitive decline in multiple domains. These results suggest that a cochlear amplifier dysfunction in presbycusis is an important mechanism relating hearing impairments to brain atrophy in the extended network of effortful hearing.

ACTA NEUROPATHOL COMMUN. 2019 JAN 5;7(1):3. DOI: 10.1186/S40478-018-0655-5.

'DUSTY CORE DISEASE' (DUCD): EXPANDING MORPHOLOGICAL SPECTRUM OF RYR1 RECESSIVE MYOPATHIES.

Garibaldi M, Rendu J, Brocard J, Lacene E, Fauré J, Brochier G, Beuvin M, Labasse C, Madelaine A, Malfatti E, Bevilacqua JA, Lubieniecki F, Monges S, Taratuto AL, Laporte J, Marty I, Antonini G, Romero NB.

Several morphological phenotypes have been associated to RYR1-recessive myopathies. We recharacterized the RYR1-recessive morphological spectrum by a large monocentric study performed on 54 muscle biopsies from a large cohort of 48 genetically confirmed patients, using histoenzymology, immunohistochemistry, and ultrastructural studies. We also analysed the level of RyR1 expression in patients' muscle biopsies. We defined "dusty cores" the irregular areas of myofibrillar disorganisation characterised by a reddish-purple

granular material deposition with uneven oxidative stain and devoid of ATPase activity, which represent the characteristic lesion in muscle biopsy in 54% of patients. We named Dusty Core Disease (DuCD) the corresponding entity of congenital myopathy. Dusty cores had peculiar histological and ultrastructural characteristics compared to the other core diseases. DuCD muscle biopsies also showed nuclear centralization and type1 fibre predominance. Dusty cores were not observed in other core myopathies and centronuclear myopathies. The other morphological groups in our cohort of patients were: Central Core (CCD: 21%), Core-Rod (C&R:15%) and Type1 predominance "plus" (T1P+:10%). DuCD group was associated to an earlier disease onset, a more severe clinical phenotype and a lowest level of RyR1 expression in muscle, compared to the other groups. Variants located in the bridge solenoid and the pore domains were more frequent in DuCD patients. In conclusion, DuCD is the most frequent histopathological presentation of RYR1-recessive myopathies. Dusty cores represent the unifying morphological lesion among the DuCD pathology spectrum and are the morphological hallmark for the recessive form of disease.

MUSCLE NERVE. 2019 APR;59(4):436-444. DOI: 10.1002/MUS.26403.

DISEASE DURATION AND DISABILITY IN DYSFERLINOPATHY CAN BE DESCRIBED BY MUSCLE IMAGING USING HEATMAPS AND RANDOM FORESTS. Gómez-Andrés D, Díaz J, Munell F, Sánchez-Montañez Á, Pulido-Valdeolivas I, Suazo L, Garrido C, Quijano-Roy S, Bevilacqua JA.

INTRODUCTION: The manner in which imaging patterns change over the disease course and with increasing disability in dysferlinopathy is not fully understood. METHODS: Fibroadipose infiltration of 61 muscles was scored based on whole-body MRI of 33 patients with dysferlinopathy and represented in a heatmap. We trained random forests to predict disease duration, Motor Function Measure dimension 1 (MFM-D1), and modified Rankin scale (MRS) score based on muscle scoring and selected the most important muscle for predictions. RESULTS: The heatmap delineated positive and negative fingerprints in dysferlinopathy. Disease duration was related to infiltration of infraspinatus, teres major-minor, and supraspinatus muscles. MFM-D1 decreased with higher infiltration of teres major-minor, triceps, and sartorius. MRS related to infiltration of vastus medialis, gracilis, infraspinatus, and sartorius. DISCUSSION: Dysferlinopathy shows a recognizable muscle MRI pattern. Fibroadipose infiltration in specific muscles of the thigh and the upper limb appears to be an important marker for disease progression. Muscle Nerve 59:436-444, 2019.

ARQ NEUROPSIQUIATR. 2019 JUL 29;77(7):470-477. DOI: 10.1590/0004-282X20190073.

OBSERVATIONS FROM A NATIONWIDE VIGILANCE PROGRAM IN MEDICAL CARE FOR SPINAL MUSCULAR ATROPHY PATIENTS IN CHILE.

Alvarez K, Suarez B, Palomino MA, Hervias C, Calcagno G, Martínez-Jallie M, Lozano-Arango A, Lillo S, Haro M, Cortés F, Pantoja S, Chahin A, Orellana P, Bevilacqua JA, Bertini E, Castiglioni C.

METHODS: Spinal muscular atrophy (SMA) has gained much attention in the last few years because of the approval of the first intrathecal treatment for this neurodegenerative disease. Latin America needs to develop the demographics of SMA, timely access to diagnosis, and appropriate following of the standards of care recommendations for patients. These are essential steps to guide health policies. This was a descriptive study of a cohort of SMA patients from all over Chile. We analyzed the clinical, motor functional, and social data, as well as the care status of nutritional, respiratory and skeletal conditions. We also measured the SMN2 copy number in this population. RESULTS: We recruited 92 patients: 50 male; 23 SMA type-1, 36 SMA type-2 and 33 SMA type-3. The median age at genetic diagnosis was 5, 24 and 132 months. We evaluated the SMN2 copy number in 57 patients. The SMA type-1 patients were tracheostomized and fed by gastrostomy in a 69.6 % of cases, 65% of SMA type-2 patients received nocturnal noninvasive ventilation, and 37% of the whole cohort underwent scoliosis surgery. CONCLUSION: Ventilatory care for SMA type-1 is still based mainly on tracheostomy. This Chilean cohort of SMA patients had timely access to genetic diagnosis, ventilatory assistance, nutritional support, and scoliosis surgery. In this series, SMA type-1 is underrepresented, probably due to restrictions in access to early diagnosis and the high and early mortality rate.

DEPARTAMENTO DE OBSTETRICIA Y GINECOLOGÍA

EUR J PREV CARDIOL. 2019 AUG 18:2047487319868545. DOI: 10.1177/2047487319868545.

EXERCISE-INDUCED CARDIO-PULMONARY REMODELLING IN ENDURANCE ATHLETES: NOT ONLY THE HEART ADAPTS.

Domenech-Ximenes B, Garza MS, Prat-González S, Sepúlveda-Martínez Á, Crispi F, Perea RJ, Garcia-Alvarez A, Sitges M.

BACKGROUND: The cumulative effects of intensive endurance exercise may induce a broad spectrum of right ventricular remodelling. The mechanisms underlying these variable responses have been scarcely explored, but may involve differential pulmonary vasculature adaptation. Our aim was to evaluate right ventricular and pulmonary circulation in highly trained endurance athletes. METHODS: Ninety-three highly trained endurance athletes (>12h training/week at least during the last five years; age: 36 ± 6 years; 52.7% male) and 72 age- and gender-matched controls underwent resting cardiovascular magnetic resonance imaging to assess cardiac dimensions and function, as well as pulmonary artery dimensions and flow. Pulmonary vascular resistance (PVR) was estimated based on left ventricular ejection fraction and pulmonary artery flow mean velocity. Resting and exercise Doppler echocardiography was also performed in athletes to estimate pulmonary artery pressure. RESULTS: Athletes showed larger biventricular and biatrial sizes, slightly reduced systolic biventricular function, increased pulmonary artery dimensions and reduced pulmonary artery flow velocity as compared with controls in both genders

($p < 0.05$), which resulted in significantly higher estimated PVR in athletes as compared with controls (2.4 ± 1.2 vs. 1.7 ± 1.1 ; $p < 0.05$). Substantially high estimated PVR values (> 4.2 WU) were found in seven of the 93 (9.3%) athletes: those exhibiting an enlarged pulmonary artery (indexed area cm^2/m^2 : 4.8 ± 0.6 vs. 3.9 ± 0.6 , $p < 0.05$), a decreased pulmonary artery distensibility index (%: 43.0 ± 15.2 vs. 62.0 ± 17.4 , $p < 0.05$) and a reduced right ventricular ejection fraction (%: 49.3 ± 4.5 vs. 53.6 ± 4.6 , $p < 0.05$). CONCLUSIONS: Exercise-induced remodelling involves, besides the cardiac chambers, the pulmonary circulation and is associated with an increased estimated PVR. A small subset of athletes exhibited substantial increase of estimated PVR related to pronounced pulmonary circulation remodelling and reduced right ventricular systolic function.

GYNECOL OBSTET INVEST. 2019;84(3):237-241. DOI: 10.1159/000493477.

CHORIONIC BUMP: AN EARLY ULTRASOUND MARKER FOR ADVERSE OBSTETRIC OUTCOME.

Silva MC, Sepúlveda-Martínez A, Guíñez R, Haya MT, Parra-Cordero M.

BACKGROUND/AIMS: To assess the perinatal outcome of pregnancies with chorionic bump detected at the first trimester of pregnancy. METHODS: This was a nested case-control study of pregnancies with chorionic bump identified at the first trimester ultrasound that was performed from October 2014 and October 2016. The control group consisted of the following 5 unaffected pregnancies after each case. From the first trimester ultrasound, maternal and perinatal characteristics were obtained and stored in a dedicated database. The primary outcome was defined as the presence of an alive new-born. Secondary outcome was defined as the presence of a composite adverse obstetric outcome. RESULTS: Eleven first trimester pregnancies affected by a chorionic bump and 55 controls were identified. The primary outcome was observed in 72.7 and 89.1% of chorionic bump and controls respectively ($p = 0.2$). The secondary outcome was observed in 45.5% of pregnancies with a chorionic bump versus 12.7% in the unaffected group ($p = 0.01$). First trimester uterine artery Doppler demonstrated a non-significant trend to be higher in the chorionic bump group. CONCLUSIONS: The presence of a chorionic bump is associated with a significant higher risk of adverse perinatal outcome.

ARQ NEUROPSIQUIATR. 2019 JUL 29;77(7):470-477. DOI: 10.1590/0004-282X20190073.

OBSERVATIONS FROM A NATIONWIDE VIGILANCE PROGRAM IN MEDICAL CARE FOR SPINAL MUSCULAR ATROPHY PATIENTS IN CHILE.

Alvarez K, Suarez B, Palomino MA, Hervias C, Calcagno G, Martínez-Jalilie M, Lozano-Arango A, Lillo S, Haro M, Cortés F, Pantoja S, Chahin A, Orellana P, Bevilacqua JA, Bertini E, Castiglioni C.

METHODS: Spinal muscular atrophy (SMA) has gained much attention in the last few years because of the approval of the first intrathecal treatment for this neurodegenerative disease. Latin America needs to develop the demographics of SMA, timely access to diagnosis, and appropriate following of the standards of care recommendations for patients. These are essential steps to guide health policies. This was a descriptive study of a cohort of SMA patients from all over Chile. We analyzed the clinical, motor functional, and social data, as well as the care status of nutritional, respiratory and skeletal conditions. We also measured the SMN2 copy number in this population. RESULTS: We recruited 92 patients: 50 male; 23 SMA type-1, 36 SMA type-2 and 33 SMA type-3. The median age at genetic diagnosis was 5, 24 and 132 months. We evaluated the SMN2 copy number in 57 patients. The SMA type-1 patients were tracheostomized and fed by gastrostomy in a 69.6 % of cases, 65% of SMA type-2 patients received nocturnal noninvasive ventilation, and 37% of the whole cohort underwent scoliosis surgery. CONCLUSION: Ventilatory care for SMA type-1 is still based mainly on tracheostomy. This Chilean cohort of SMA patients had timely access to genetic diagnosis, ventilatory assistance, nutritional support, and scoliosis surgery. In this series, SMA type-1 is underrepresented, probably due to restrictions in access to early diagnosis and the high and early mortality rate.

ULTRASOUND OBSTET GYNECOL. 2019 MAY;53(5):623-629. DOI: 10.1002/UOG.20119.

TRANSGENERATIONAL TRANSMISSION OF SMALL-FOR-GESTATIONAL AGE.

Sepúlveda-Martínez Á, Rodríguez-López M, Paz Y Miño F, Casu G, Crovetto F, Gratacós E, Crispi F.

OBJECTIVE: To evaluate the transgenerational transmission of small-for-gestational age (SGA). METHODS: This was a cohort study of a random sample of 2043 offspring delivered between 1975 and 1993 at Hospital Sant Joan de Déu in Barcelona. Exclusion criteria were multiple pregnancy, aneuploidy or genetic syndrome, major birth defects, severe mental disease and macrosomia. Eligible individuals were contacted and those with at least one offspring were included in the study. Participants were classified according to the presence of SGA (defined as birth weight < 10 th percentile) at birth. Multiple regression analysis was used to determine the presence of SGA or placenta-mediated disease (defined as the presence of SGA, pre-eclampsia, gestational hypertension and/or placental abruption) in the following generation. RESULTS: Of 623 individuals who agreed to participate, 152 (72 born SGA and 80 born appropriate-for-gestational age (AGA)) were reported to have at least one child. Descendants of SGA individuals presented with a lower birth-weight percentile (median, 26 (interquartile range (IQR), 7-52) vs 43 (IQR, 19-75); $P < 0.001$) and a higher prevalence of SGA (40.3% vs 16.3%; $P = 0.001$) and placenta-mediated disease (43.1% vs 17.5%; $P = 0.001$) than did the offspring of AGA individuals. After adjustment for confounding variables, parental SGA background was associated with an almost three-fold increased risk of subsequent SGA or any placenta-mediated disease in the following generation. This association was stronger in SGA mothers than in SGA fathers. CONCLUSIONS: Our data provide evidence suggesting a transgenerational transmission of SGA, highlighting the importance of public health strategies for preventing intrauterine growth impairment.

BJOG. 2019 JAN;126(2):291-298. DOI: 10.1111/1471-0528.15246.

POSTNATAL PERSISTENCE OF FETAL CARDIOVASCULAR REMODELLING ASSOCIATED WITH ASSISTED REPRODUCTIVE TECHNOLOGIES: A COHORT STUDY.

Valenzuela-Alcaraz B, Serafini A, Sepulveda-Martínez A, Casals G, Rodríguez-López M, García-Otero L, Cruz-Lemini M, Bijmens B, Sitges M, Balasch J, Gratacós E, Crispi F.

OBJECTIVE: To assess the postnatal persistence of fetal cardiovascular remodelling associated with assisted reproductive technologies (ART) in children at 3 years of age. DESIGN: A cohort study of children conceived by ART. SETTING: Maternal-Fetal Medicine Unit, Hospital Clinic Barcelona, Spain. POPULATION SAMPLE: Eighty singleton pregnancies conceived by ART and 80 spontaneously conceived (controls) followed from fetal life up to childhood. METHODS: Cardiovascular evaluation was performed at 3 years of corrected age, including echocardiography, carotid intima-media (cIMT) by ultrasound, and blood pressure. MAIN OUTCOME MEASURES: Postnatal persistence of cardiovascular changes in children conceived by ART. RESULTS: Compared with controls, children conceived by ART showed larger atria (right atrial area: control 4.9 cm² (0.9) versus ART 5.5 cm² (0.9), $P < 0.001$), more globular ventricles (right ventricular sphericity index: control mean 1.8 (SD 0.5) versus ART 1.6 (0.2), $P < 0.001$), and signs of systolic (tricuspid annular plane systolic excursion: control 18 mm (2) versus ART 16 mm (3), $P < 0.001$) and diastolic dysfunction (isovolumic relaxation time: control 68 ms (12) versus ART 79 ms (12), $P < 0.001$). ART children also presented increased systolic blood pressure (control 90 mmHg (6) versus ART 94 mmHg (5), $P < 0.003$) and cIMT (control 0.52 μ m (0.14) versus ART 0.60 μ m (0.16), $P < 0.001$) as compared with those spontaneously conceived. CONCLUSIONS: Cardiovascular changes previously reported in ART fetuses persist postnatally at 3 years of age. These results underscore the importance of future studies for assessing the long-term cardiovascular health associated with ART. TWEETABLE ABSTRACT: Cardiovascular changes described in fetuses conceived by ART, persist in children at 3 years of age.

J OBSTET GYNAECOL RES. 2019 JAN;45(1):104-112. DOI: 10.1111/JOG.13809.

FIRST TRIMESTER SCREENING FOR PRETERM AND TERM PRE-ECLAMPSIA BY MATERNAL CHARACTERISTICS AND BIOPHYSICAL MARKERS IN A LOW-RISK POPULATION.

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

AIM: To develop a combined predictive model for preterm and term pre-eclampsia (PE) during the first trimester of pregnancy. METHODS: This investigation was a nested case-control study in singleton pregnancies at the Maternal-Fetal Medicine Unit, University of Chile Hospital. A priori risks for preterm and term PE were calculated by multivariate logistic regression analyses. Biophysical markers were log₁₀-transformed and expressed as multiples of the median. A multivariate logistic regression analysis was used to estimate a combined predictive model of preterm and term PE. Detection rates at different cut-off points were determined by a receiver operator curve analysis of a posteriori risks. RESULTS: First trimester mean arterial pressure and uterine artery Doppler pulsatility index were significantly higher in women who develop PE than in the unaffected group. The detection rate of preterm PE based on maternal characteristics and biophysical markers was 72% at a 10% false-positive rate, corresponding to a cut-off risk of 1 in 50. The detection rate for term PE was 30% at a 10% false-positive rate. CONCLUSION: Preterm PE can be predicted by a combination of maternal characteristics and biophysical markers. However, first trimester screening is less valuable for term PE.

FETAL DIAGN THER. 2019 DEC 10:1-12. DOI: 10.1159/000503228.

NOMOGRAMS OF FETAL RIGHT VENTRICULAR FRACTIONAL AREA CHANGE BY 2D ECHOCARDIOGRAPHY.

Guirado L, Crispi F, Soveral I, Valenzuela-Alcaraz B, Rodríguez-López M, García-Otero L, Torres X, Sepúlveda-Martínez Á, Escobar-Díaz MC, Martínez JM, Friedberg MK, Gratacós E, Gómez O.

OBJECTIVES: Fetal right ventricular (RV) function assessment is challenging due to the RV geometry and limitations of in utero assessment. Postnatally, 2D echocardiographic RV fractional area change (FAC) is used to assess RV global systolic function by calculating the percentage of change in RV area from systole to diastole. Reports on FAC are scarce in prenatal life, and nomograms throughout pregnancy are not available. Our aims were (1) to study prenatal RV FAC feasibility and reproducibility and (2) to construct nomograms for RV FAC and end-diastolic (ED) and end-systolic (ES) RV areas from 18 to 41 weeks of gestation. METHODS: Prospective cohort study including 602 low-risk singleton pregnancies undergoing a fetal echocardiography from 18 to 41 weeks of gestation. RV ED and ES areas were measured following standard recommendations for ventricular dimensions and establishing strict landmarks to identify the different phases of the cardiac cycle. RV FAC was calculated as: $([ED \text{ area} - ES \text{ area}] / ED \text{ area}) \times 100$. RV FAC intra- and inter-observer reproducibility was evaluated in 45 fetuses by calculating the intraclass correlation coefficient (ICC). Parametric regressions were tested to model each parameter against gestational age (GA) and estimated fetal weight (EFW). RESULTS: RV areas and FAC were successfully obtained in ~99% of fetuses with acceptable reproducibility throughout gestation (RV ED area inter-observer ICC [95% CI] 0.96 [0.93-0.98], RV ES area 0.97 [0.94-0.98], and FAC 0.69 [0.44-0.83]). Nomograms were constructed for RV ED and ES areas and FAC. RV areas showed a quadratic and logarithmic increase with GA and EFW, respectively. In contrast, RV FAC showed a slight quadratic decrease throughout gestation (mean RV FAC ranged from 36% at 18 weeks of gestation [10-90th centiles: 25-47%, respectively] to 29% at 41 weeks [10-90th centiles: 18-40%, respectively]). The best models for RV areas and FAC were a second-

degree polynomial. CONCLUSIONS: RV FAC is a feasible and reproducible parameter to assess RV global systolic function in fetal life. We provide reference ranges adjusted by GA and EFW that can be used as normal references for the assessment of RV function in prenatal conditions.

FETAL DIAGN THER. 2019 JAN 4;1-12. DOI: 10.1159/000494838.

NOMOGRAMS OF FETAL CARDIAC DIMENSIONS AT 18-41 WEEKS OF GESTATION.

García-Otero L, Gómez O, Rodríguez-López M, Torres X, Soveral I, Sepúlveda-Martínez Á, Guirado L, Valenzuela-Alcaraz B, López M, Martínez JM, Gratacós E, Crispi F.

OBJECTIVE: There is a need for standardized reference values for cardiac dimensions in prenatal life. The objective of the present study was to construct nomograms for fetal cardiac dimensions using a well-defined echocardiographic methodology in a low-risk population. METHODS: This is a prospective cohort study including 602 low-risk singleton pregnancies undergoing a standardized fetal echocardiography to accurately assess fetal cardiac, ventricular, and atrial dimensions. Parametric regressions were tested to model each measurement against gestational age from 18 to 41 weeks of gestation. RESULTS: Nomograms were constructed for fetal cardiac dimensions (transverse and longitudinal diameters and areas) of the whole heart, atria, and ventricles, as well as myocardial wall thicknesses. All dimensions showed a progressive increase with gestational age. The best model for most parameters was a second-degree linear polynomial. Fetal cardiac, ventricular, and atrial diameters and areas were successfully obtained in 98.6% of the fetuses, while myocardial wall thicknesses could be obtained in 96.5% of the population. The results showed excellent interobserver and intraobserver reproducibility (intraclass correlation coefficient, ICC > 0.811 and ICC > 0.957, respectively). CONCLUSIONS: We provide standardized and comprehensively evaluated reference values for fetal cardiac morphometric parameters across gestation in a low-risk population. These no nograms would enable the early identification of different patterns of fetal cardiac remodeling.

J MATERN FETAL NEONATAL MED. 2019 JUL;32(14):2319-2327. DOI: 10.1080/14767058.2018.1432041.

COMPARISON OF 2D VERSUS M-MODE ECHOCARDIOGRAPHY FOR ASSESSING FETAL MYOCARDIAL WALL THICKNESS.

Sepúlveda-Martínez A, García-Otero L, Soveral I, Guirado L, Valenzuela-Alcaraz B, Torres X, Rodríguez-Lopez M, Gratacos E, Gómez O, Crispi F.

OBJECTIVE: M-mode and 2D have been proposed for evaluating fetal myocardial thickness. However, studies comparing the performance of both modalities are lacking. We aimed to compare 2D versus M-mode reproducibility for assessing myocardial wall thicknesses. METHODS: A prospective study including 45 healthy fetuses from low-risk pregnancies evaluated between 18 and 41 weeks of gestation. Left and right ventricular free-wall and septal myocardial thicknesses were measured at end-diastole (ED) and end-systole (ES) in transverse 4-chamber view using 2D and M-mode. Intra- and interobserver reproducibility was evaluated by the concordance correlation coefficient (CCC). Both techniques were compared by t-test of the CCC. RESULTS: 2D and M-mode demonstrated excellent and similar intraobserver repeatability, with the best concordance in ES septal thickness (M-mode CCC 0.956 versus 2D-mode CCC 0.914). Interobserver reproducibility demonstrated also a high concordance, optimal in ES left ventricular free wall (M-mode 0.925 versus 2 D 0.855). Comparison of both techniques demonstrated a high concordance in all measurements, except for ED septal thickness with better reproducibility using M-mode (CCC 0.954 versus 0.847, $p = .017$). CONCLUSIONS: 2D and M-mode can be used in a reproducible manner for measuring fetal myocardial thickness, with a slightly better performance of M-mode for assessing ED septal wall thickness.

LABORATORIO DE ENDOCRINOLOGÍA Y BIOLOGÍA DE LA REPRODUCCIÓN

CANCERS (BASEL). 2019 DEC 7;11(12). PII: E1970. DOI: 10.3390/CANCERS11121970.

NGF-ENHANCED VASCULOGENIC PROPERTIES OF EPITHELIAL OVARIAN CANCER CELLS IS REDUCED BY INHIBITION OF THE COX-2/PGE2 SIGNALING AXIS.

Garrido MP, Hurtado I, Valenzuela-Valderrama M, Salvatierra R, Hernández A, Vega M, Selman A, Quest AFG, Romero C.

Epithelial ovarian cancer (EOC) is a lethal gynecological neoplasia characterized by extensive angiogenesis and overexpression of nerve growth factor (NGF). Here, we investigated the mechanism by which NGF increases vascular endothelial growth factor (VEGF) expression and the vasculogenic potential of EOC cells, as well as the contribution of the cyclooxygenase 2/prostaglandin E2 (COX-2/PGE2) signaling axis to these events. EOC biopsies and ovarian cell lines were used to determine COX-2 and PGE2 levels, as well as those of the potentially pro-angiogenic proteins c-MYC (a member of the Myc transcription factors family), survivin, and β -catenin. We observed that COX-2 and survivin protein levels increased during EOC progression. In the EOC cell lines, NGF increased the COX-2 and PGE2 levels. In addition, NGF increased survivin, c-MYC, and VEGF protein levels, as well as the transcriptional activity of c-MYC and β -catenin/T-cell factor/lymphoid enhancer-binding factor (TCF-Lef) in a Tropomyosin receptor kinase A (TRKA)-dependent manner. Also, COX-2 inhibition prevented the NGF-induced increases in these proteins and reduced the angiogenic score of endothelial cells stimulated with conditioned media from EOC cells. In summary, we show here that the pro-angiogenic effect of NGF in EOC depends on the COX-2/PGE2 signaling axis. Thus, inhibition COX-2/PGE2 signaling will likely be beneficial in the treatment of EOC.

FRONT ONCOL. 2019 SEP 19;9:913. DOI: 10.3389/FONC.2019.00913.

ANGIOGENESIS IN GYNECOLOGICAL CANCERS: ROLE OF NEUROTROPHINS.

Garrido MP, Torres I, Vega M, Romero C.

Angiogenesis, or generation of new blood vessels from other pre-existing, is a key process to maintain the supply of nutrients and oxygen in tissues. Unfortunately, this process is exacerbated in pathologies such as retinopathies and cancers with high angiogenesis as ovarian cancer. Angiogenesis is regulated by multiple systems including growth factors and neurotrophins. One of the most studied angiogenic growth factors is the vascular endothelial growth factor (VEGF), which is overexpressed in several cancers. It has been recently described that neurotrophins could regulate angiogenesis through direct and indirect mechanisms. Neurotrophins are a family of proteins that include nerve growth factor (NGF), brain-derived growth factor (BDNF), and neurotrophins 3 and 4/5 (NT 3, NT 4/5). These molecules and their high affinity receptors (TRKs) regulate the development, maintenance, and plasticity of the nervous system. Furthermore, it was recently described that they display essential functions in non-neuronal tissues, such as reproductive organs among others. Studies have shown that several types of cancer overexpress neurotrophins such as NGF and BDNF, which might contribute to tumor progression and angiogenesis. Besides, in recent years the FDA has approved the use of pharmacologic inhibitors of pan-TRK receptors in patients with TRKs fusion-positive cancers. In this review, we discuss the mechanisms by which neurotrophins stimulate tumor progression and angiogenesis, with emphasis on gynecological cancers.

AM J PHYSIOL ENDOCRINOL METAB. 2019 DEC 24. DOI: 10.1152/AJPENDO.00162.2019.

THE INSULIN SENSITIZER MECHANISM OF MYO-INOSITOL IS ASSOCIATED TO AMPK ACTIVATION AND GLUT-4 EXPRESSION IN HUMAN ENDOMETRIAL CELLS EXPOSED TO A PCOS ENVIRONMENT.

Cabrera-Cruz H, Oróstica L, Plaza-Parrochia F, Torres-Pinto I, Romero C, Vega M.

Polycystic Ovary Syndrome (PCOS), is an endocrine-metabolic disorder characterized by hyperandrogenism and ovulatory dysfunction but also obesity and hyperinsulinemia. These characteristics induce an insulin-resistant state in tissues as endometrium, affecting its reproductive functions. Myo-inositol (MYO) is an insulin-sensitizer compound used in PCOS patients; however, its insulin-sensitizer mechanism is unclear. To understand the relationship of MYO with insulin action in endometrial cells, SMIT-1 (MYO-transporter) and MYO effect on protein-levels related to insulin pathway were evaluated. SMIT-1 was assessed in endometrial tissue from women with normal-weight, obesity, insulin-resistance and PCOS; additionally, using an in-vitro model of human endometrial cells exposed to environment resembling hyperinsulinic-obese-PCOS, MYO effect was evaluated on p-AMPK and GLUT-4 levels and glucose uptake by western blot, immunocytochemistry and confocal microscopy, respectively. SMIT-1 was detected in endometrial tissue from all groups and decreased in PCOS and obesity ($p < 0.05$ vs normal-weight). In in-vitro model, PCOS conditions decreased p-AMPK levels being restored with MYO ($p < 0.05$). The diminished GLUT-4 protein levels promoted by PCOS environment were restored by MYO through SMIT-1 and p-AMPK-dependent mechanism ($p < 0.05$). Also, MYO restored glucose uptake in cells under PCOS condition through a p-AMPK-dependent mechanism. Finally, these results were similar to those obtained with metformin treatment in the same in-vitro conditions. Consequently, MYO could be a potential insulin-sensitizer by its positive effects in insulin-resistant tissues as PCOS-endometrium, acting through SMIT-1, provoking AMPK activation and elevated GLUT-4 levels and consequently, increasing glucose uptake by human endometrial cells. Therefore, MYO may be used as an effective option in insulin-resistant PCOS women.

J ENDOCRINOL. 2019 JAN 1. PII: JOE-18-0520.R1. DOI: 10.1530/JOE-18-0520.

METFORMIN IMPROVES OVARIAN INSULIN SIGNALING ALTERATIONS CAUSED BY FETAL PROGRAMMING.

Heber MF, Ferreira SR, Abruzzese GA, Raices T, Pignataro OP, Vega M, Motta AB.

Insulin resistance is the decreased ability of insulin to mediate metabolic actions. In the ovary, insulin controls ovulation and oocyte quality. Alterations in ovarian insulin signaling pathway could compromise ovarian physiology. Here, we aimed to investigate the effects of fetal programming on ovarian insulin signaling and evaluate the effect of metformin treatment. Pregnant rats were hyperandrogenized with testosterone and female offspring born to those dams were employed; at adulthood, prenatally hyperandrogenized (PH) offspring presented two phenotypes: irregular ovulatory (PHiov) and anovulatory (PHanov). Half of each group was orally treated with metformin. Metformin treatment improved the estrous cyclicity in both PH groups. Both PH groups showed low mRNA levels of IR, IRS1 and Glut4. IRS2 was decreased only in PHanov. Metformin upregulated the mRNA levels of some of the mediators studied. Protein expression of IR, IRS1/2 and GLUT4 was decreased in both PH groups. In PHiov, metformin restored the expression of all the mediators, whereas, in PHanov, metformin restored only that of IR and IRS1/2. IRS1 phosphorylation was measured in tyrosine residues, which activates the pathway, and in serine residues, which impairs insulin action. PHiov presented high IRS1 phosphorylation on tyrosine and serine residues, whereas PHanov showed high serine phosphorylation and low tyrosine phosphorylation. Metformin treatment lowered serine phosphorylation only in PHanov rats. Our results suggest that PHanov rats have a defective insulin action, partially restored with metformin. PHiov rats had less severe alterations, and metformin treatment was more effective in this phenotype.

DEPARTAMENTO DE ORTOPEDIA Y TRAUMATOLOGÍA

J AM ACAD ORTHOP SURG GLOB RES REV. 2019 NOV 27;3(11). PII: E10.5435. DOI: 10.5435/JAAOSGLOBAL-D-19-00139.

A NOVEL APPROACH TO LOWER-LIMB AXIAL ALIGNMENT ANALYSIS: A CT STUDY.

Barahona M, Guzman M, Barrientos C, Zamorano A, Palet M, Infante C, Hinzpeter J.

To analyze the torsion of the lower extremities in a healthy cohort and to determine the contribution of different segments of the femur and tibia to the torsion of both bones. **METHODS:** In this cross-sectional study, 32 patients with nonjoint or bone-related symptoms were analyzed by CT angiography. Lower-limb torsion, femoral torsion, proximal femoral torsion, femoral shaft torsion, distal femoral torsion, tibial torsion, proximal tibial torsion, and distal tibial torsion were measured. **RESULTS:** The median total limb torsion was 25° external torsion, with the median femoral torsion being -9° and the median tibial torsion 30°. Both femoral metaphyses had internal torsion, with the internal torsion of the proximal metaphysis being approximately three times greater than that of the distal femoral metaphysis. The shaft was found to compensate with an external torsion of approximately two-thirds of the internal torsion of both femoral metaphyses. The proximal metaphysis of the tibia accounted for approximately one-third of the external torsion, with the segment from the distal to the tibial tubercle accounting for the remaining two-thirds of the tibial torsion. **CONCLUSIONS:** The diaphysis and distal metaphysis are the major contributors to external torsion of the tibia, whereas the proximal metaphysis is the major contributor to the internal torsion of the femur.

CUREUS. 2019 AUG 25;11(8):E5480. DOI: 10.7759/CUREUS.5480.

ACUTE SURGERY VS. NON-UNION SURGERY OF DISPLACED MIDSHAFT CLAVICLE FRACTURES: A CASE-CONTROL STUDY.

Marsalli M, Rojas JT, Barahona M.

Introduction There is a lack of information about the results of surgical treatment and complications in midshaft clavicle fracture non-unions. Our hypothesis was that there is no difference in functional outcomes between the surgical treatment of an acute displaced middle-third clavicle fracture and the surgical treatment of a chronic symptomatic non-union of a displaced middle-third clavicle fracture. **Methods** This was a case-control study. Fourteen cases were considered with a displaced midshaft clavicle fracture, initially treated non-surgically, but which developed symptomatic non-union and required surgical treatment. The control group was a cohort of 18 patients with a displaced midshaft clavicle fracture, who had surgical treatment in an acute setting (<3 weeks). Our cases had a median follow-up of 77 months and were retrospectively analyzed. All those in the control group had a 12-month prospective follow-up evaluation. The variables measured were Constant score, time to discharge to work, and bone union rate. **Results** The median Constant score at final follow-up for surgically treated non-unions was 87.5 (control group 84.5, $p > 0.05$). The median time to complete return to work was 3.2 months in the control group and 9.7 months in the case group ($p=0.001$). Hundred percent of those patients who were initially treated with surgery had bone union without other treatment. Two out of 14 cases required a second surgery with a plate and bone graft to achieve bone union. **Conclusion** Symptoms from displaced midshaft clavicular fracture non-unions are due to related pain and dysfunctional deficits that result from displacement and shortening. According to our study, patients with a displaced midshaft clavicle fracture non-union who needed surgery achieved similar functional results as compared to patients treated in an acute setting for a displaced midshaft clavicle fracture. The median time to discharge and return to work was more than doubled in the non-union surgery group.

FOOT ANKLE INT. 2019 APR;40(4):475-483. DOI: 10.1177/1071100718820341.

KNOTLESS MODIFIED ARTHROSCOPIC-BROSTRÖM TECHNIQUE FOR ANKLE INSTABILITY.

Pellegrini MJ, Sevillano J, Ortiz C, Giza E, Carcuro G.

Instability is a common sequela after repeated ankle sprains. When nonoperative treatment fails, open lateral ligament complex repair and reinforcement with the inferior extensor retinaculum has been the gold standard procedure. The recent advancements in arthroscopic techniques have created comparable biomechanical and functional results to open procedures. The authors' modification to the standard arthroscopic technique permits ligament approximation to the distal fibula over a larger surface area, using knotless anchors to avoid the need of an accessory portal and limit potential suture knot-related complications. **Level of Evidence:** Level V, expert opinion.

INJURY. 2019 DEC;50(12):2312-2317. DOI: 10.1016/J.INJURY.2019.10.007.

POSTERIOR PILON FRACTURE: EPIDEMIOLOGY AND SURGICAL TECHNIQUE.

Chaparro F, Ahumada X, Urbina C, Lagos L, Vargas F, Pellegrini M, Barahona M, Bastias C.

OBJECTIVES: To review a case series of patients with posterior pilon variant fracture using a novel approach, focusing on demographic data, injury pattern, surgical results based on computed tomography (CT) scan, and short-term complications. **DESIGN:** Consecutive case series. **SETTING:** Level I trauma center. **PATIENTS/PARTICIPANTS:** Twenty-five patients with posterior pilon fracture. **INTERVENTION:** Posterior pilon fracture open reduction and internal fixation. **MAIN OUTCOME MEASUREMENTS:** Parameters measured included age, sex, type of fracture, surgical technique, anatomical reduction, and complications. **RESULTS:** Twenty-five patients sustained a posterior pilon fracture, accounting for 13.4% of all operatively treated ankle fractures with median follow-up of 21.7 months. The average age of patients was 42 years (22-62);

19/25 (76%) were female, and 6/25 (24%) were male. A modified posteromedial approach was used in 18/25 (72%) patients. Persistent syndesmotic instability was present in 11/25 (44%) patients after posterior malleolar stabilization. Quality of reduction was assessed under CT scan in 19 patients, with 15/19 (78.9%) having anatomic reduction. We report 2/25 (8%) patients with early wound problems and 7/25 (20%) with short-term complications during follow-up. CONCLUSION: Posterior pilon variant fracture appears to be less common than previously reported. Most fractures can be satisfactorily treated through a modified posteromedial approach. Albeit obtaining posterior malleolar fracture rigid fixation, syndesmotic instability was more prevalent than expected. The short-term complication rate was low.

FOOT ANKLE SURG. 2019 DEC;25(6):812-818. DOI: 10.1016/J.FAS.2018.10.004.

CHRONIC DELTOID LIGAMENT INSUFFICIENCY REPAIR WITH INTERNAL BRACE™ AUGMENTATION.

Pellegrini MJ, Torres N, Cuchacovich NR, Huertas P, Muñoz G, Carcuro GM.

BACKGROUND: Patients with chronic deltoid ligament insufficiency (CDLI) present a challenging situation. Although numerous procedures have been described, optimal treatment is still a matter of debate. While the treatment armamentarium ranges from simple ligament repair to complex reconstructions with or without realignment osteotomies, direct repair augmented with an Internal Brace™ device appears to be an attractive intermediate option. We investigated functional outcomes and complications in patients with CDLI operated on using Internal Brace™ augmentation. METHODS: A prospective study was conducted. Patients were included if they presented medial ankle pain and/or giving way, exhibited asymmetric flexible hindfoot valgus, failed conservative treatment, and had a positive MRI evaluated by an independent radiologist. Patients with stage IV flatfoot deformity, neuropathy and/or inflammatory arthritis were excluded. CDLI was confirmed intraoperatively with the arthroscopic drive-through sign. Patients were evaluated preoperatively and postoperatively using FAAM, SF-36 and grade of satisfaction. Paired t-tests were used to assess FAAM and SF-36 scores variation. RESULTS: Thirteen patients met inclusion criteria. No patient was lost to follow-up, with a mean follow-up time of 13.5 months (range 6-21). Preoperative FAAM and SF-36 scores improved from 58.7 to 75.3 and from 60.2 to 84.4 postoperatively, respectively ($p < .01$). Two implant failures were observed, with no apparent compromise of construct stability. No patient was re-operated. CONCLUSIONS: Our results suggest that deltoid ligament repair with Internal Brace™ augmentation in patients with CDLI is a reliable option with good functional outcomes and high satisfaction grade in short term follow-up.

FOOT ANKLE SURG. 2019 JUN;25(3):272-277. DOI: 10.1016/J.FAS.2017.11.005.

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

Bastias 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. LEVEL OF EVIDENCE: IV (Case Series).

KNEE SURG RELAT RES. 2019 JUN 1;31(2):143-146. DOI: 10.5792/KSRR.18.053.

TREATMENT OF OSTEOCHONDRITIS DISSECANS OF THE KNEE WITH AUTOLOGOUS ILIAC BONE GRAFT AND HYALURONIC ACID SCAFFOLD.

Hinzpeter J, Zamorano A, Barahona M, Campos P.

Osteochondritis dissecans (OCD) is a condition that corresponds to an idiopathic focal lesion affecting the subchondral bone with possible compromise of the stability of the adjacent cartilage. Treatment depends on the size of the lesion, cartilage stability, and the physal status. The case reported is about an 18-year-old male patient who complained of suffering from knee pain for a period of ten months. Magnetic resonance imaging (MRI) revealed a lesion of 2 cm² in the medial femoral condyle that compromised the subchondral bone, compatible with OCD. He underwent surgery that consisted of filling the subchondral defect with an iliac crest autograft and sealing the defect with a hyaluronic acid scaffold. At the 12-month follow-up, the MRI shows complete healing and the patient has resumed sports activities. Management with autologous iliac crest graft and hyaluronic acid scaffold represents an effective alternative treatment for OCD.

FOOT ANKLE SURG. 2019 OCT 31. PII: S1268-7731(19)30177-8. DOI: 10.1016/J.FAS.2019.10.007.

CROSS-CULTURAL ADAPTATION AND VALIDATION OF THE FOOT AND ANKLE OUTCOME SCORE (FAOS) INTO SPANISH (CHILE).

Pellegrini MJ, Poniachik R, Nuñez A, Escudero MI, Carcuro G, Cortes AA.

PURPOSE: To adapt and validate the English version of the Foot and Ankle Outcome Score (FAOS) into Spanish FAOS-CL, following the WHO

guidelines. METHODS: A cross-sectional study including 318 outpatients with non-traumatic conditions. Validity, acceptability and internal consistency including correlations with the Medical Outcome Study Short Form 36 are reported. RESULTS: The preliminary version resulted from the forward and back-translation and a pilot administration. Validation response rate was 99.22%. Substantial ceiling effects were observed for Symptoms and ADL and floor effect for QoL sub-scales. The FAOS-CL had excellent internal consistency (Cronbach's $\alpha = 0.98$). The principal component analysis gave five factors explaining the 72.6% of the variance. The FAOS-CL items significantly correlate with their sub-scales. FAOS-CL sub-scales significantly correlated with SF-36 components and subcomponents. CONCLUSION: The first Spanish version of the FAOS was generated. Culturally adapted and validated with high reliability capable of evaluating different foot and ankle conditions.

J SURG ORTHOP ADV. 2019 SUMMER;28(2):132-136.

ISOLATED SUBTALAR ARTHRODESIS FOR AVASCULAR NECROSIS OF THE TALUS.

Dekker TJ, Pellegrini MJ, Schiff AP, Easley ME, DeOrio JK, Nunley JA, Adams SB.

Isolated subtalar arthrodesis has been attempted in talar avascular necrosis (AVN) patients to preserve the tibiotalar joint and potential revascularization. This article reports the efficacy of isolated subtalar arthrodesis in the setting of AVN. A retrospective review of subtalar arthrodeses was performed on a cohort of 12 patients with talar AVN who underwent subtalar arthrodesis. The primary outcome was radiographic fusion with secondary outcomes of subsequent procedures, recurrent pain, and perioperative complications. Radiographic fusion of subtalar arthrodesis occurred in 12 of 12 patients. Five of six patients with traumatic etiology went on to have secondary procedures. One of six patients with atraumatic etiology underwent a secondary procedure for advancement of tibiotalar arthritis. In the setting of atraumatic talar AVN, this small cohort demonstrates that isolated subtalar arthrodesis is a safe and reliable procedure with high fusion rates and low need for secondary procedures. (Journal of Surgical Orthopaedic Advances 28(2):132-136, 2019).

CASE REP ORTHOP. 2019 DEC 5;2019:8374709. DOI: 10.1155/2019/8374709.

SUCCESSFUL SELECTIVE EMBOLIZATION FOR RECURRENT HEMARTHROSIS AFTER KNEE ARTHROPLASTY.

Barrientos C, Barahona M, Cermenati T, Wulf R, Hinzpeter J.

Knee replacement has demonstrated to be a cost-effective treatment for severe knee osteoarthritis. Nevertheless, perioperative complications may occur, including recurrent hemarthrosis reaching an incidence between 0.3 and 1.6%. Success rate after conservative treatment has been reported to be above 80%, but in case of recurrence, computed tomography angiography, magnetic resonance angiography, and Doppler ultrasound have been used to conduct the diagnosis. Arthroscopy or selective embolization is used for treatment depending on the etiology of the bleeding. Open surgery is performed in the rare cases of failure of the above alternatives. The patient consulted seven months after total knee arthroplasty with sudden pain in the medial side of the knee. Infection was ruled out, and arthrocentesis shows hemarthrosis. Successful selective embolization of medial superior and lateral superior genicular artery was performed. After two years, the patients report 92 points in the Forgotten joint score, 0 in Womac pain, 1 in Womac stiffness, and 3 in Womac functional score.

CASE REP ORTHOP. 2019 SEP 11;2019:1893042. DOI: 10.1155/2019/1893042.

RETROGRADE INTRAMEDULLARY NAIL FIXATION FOR DEROTATIONAL FEMORAL OSTEOTOMY FOR RECURRENT FEMOROPATELLAR INSTABILITY.

Barahona M, Zamorano A, Barrientos C, Guzmán M, Sato Y, Hinzpeter J.

Axial alignment of the femur and tibia is often misdiagnosed in patients with patellofemoral stability problems. Femoral torsion is critical for patellofemoral biomechanics, so it must be evaluated in every patient before the plan of surgery is decided. This case describes a femoral derotational osteotomy due to excessive internal torsion of the femur fixed with a retrograde femoral nail. This type of fixation provides a biomechanical advantage compared to plates. At the two-year follow-up, the patient achieved excellent results, reaching a functional score of 91 points on the Lysholm scale. Derotational femoral osteotomy should be considered in patellofemoral pathology, and a retrograde femoral nail is a valid fixation method for this surgery.

FOOT ANKLE INT. 2019 SEP;40(9):997-1006. DOI: 10.1177/1071100719849084.

TOTAL ANKLE ARTHROPLASTY SURVIVAL AND RISK FACTORS FOR FAILURE.

Escudero MI, Le V, Barahona M, Symes M, Wing K, Younger A, Veljkovic A, Penner M.

BACKGROUND: Total ankle arthroplasty (TAA) is an increasingly selected treatment for end-stage ankle arthritis; however, failure and revision of the tibial and talar components remains an issue. Although multiple risk factors have been shown to contribute to early component revision, no study has looked at combining such risk factors into a predictive model that could potentially decrease revision rates and improve implant survival. This study aimed to develop a predictive model for TAA failure based on patient characteristics, patient-reported outcomes (PROs), and immediate postoperative radiographs. METHODS: A retrospective review of a single-site ankle arthritis database was conducted. All patients with current-generation ankle replacements including the Hintegra and Infinity prostheses implanted between 2004 and 2015 and with complete postoperative radiographs taken between 6 and 12 weeks postoperatively were included. Eight coronal and sagittal radiographic parameters were assessed and performed twice by 2 independent orthopedic surgeons

on included TAAs. These radiographic parameters were then analyzed in association with patient demographics and PRO. Advanced statistical methods including survival analysis were used to construct a predictive model for TAA survival. A total of 107 patients were included and analyzed with a median clinical follow-up of 49 months (minimum 24 months). RESULTS: A predictive model was created, with 4 parameters identified as being statistically associated with TAA metal-component revision: diabetes mellitus, poor baseline Ankle Osteoarthritis Scale (AOS) score, excessively dorsiflexed talar component, and an anteriorly/posteriorly translated talus relative to the tibial axis. The presence of 3 parameters predicted TAA survival of 0.60 whereas presence of all 4 parameters predicted survival of only 0.13 in the period studied. CONCLUSION: Our predictive model is based on a combination of patient factors, PROs, and radiographic TAA alignment. We believe it can be used by surgeons to predict failure in their TAA patients, thereby optimizing postoperative outcomes by improving patient selection and modifiable outcome-specific parameters. LEVEL OF EVIDENCE: Level III, retrospective cohort study using prospectively collected data.

FOOT ANKLE SURG. 2019 JUN;25(3):390-397. DOI: 10.1016/J.FAS.2018.02.007. EPUB 2018 FEB 16.

TIBIOTALOCALCANEAL ARTHRODESIS WITH DISTAL TIBIAL ALLOGRAFT FOR MASSIVE BONE DEFICITS IN THE ANKLE.

Escudero MI, Poggio D, Alvarez F, Barahona M, Vivar D, Fernandez A.

BACKGROUND: The purpose of this study was to assess the outcomes of distal tibial structural allograft to obtain a stable TTC fusion. METHODS: Retrospectively, ten patients were carried out with a minimum one year follow-up. The median age was 72 (33-81). The median BMI was 28 (24-33). Indications for TTC arthrodesis included failed total ankle arthroplasty (n=7 patients), prior nonunion (n=2 patients), and a trauma injury. RESULTS: Union rate was 80%. The median initial height of the distal tibial allograft was 19mm (14-24mm). In seven cases the allograft did not lose height. The AOFAS score median was 69 (31-84). SF-12 median physical component was 39 (30-53), and 59 (23-62) for mental component. The VAS median was 2 (0-8). CONCLUSIONS: TTC using distal tibial allograft shows a lower rate of collapse than other structural grafts and provides a fusion rate higher or in accordance with the literature. LEVEL OF EVIDENCE: Level IV, retrospective case series.

DEPARTAMENTO DE PSIQUIATRÍA Y SALUD MENTAL

FRONT PSYCHIATRY. 2019 OCT 3;10:716. DOI: 10.3389/FPSYT.2019.00716.

INITIATING CHANGE OF PEOPLE WITH CRIMINAL JUSTICE INVOLVEMENT THROUGH PARTICIPATION IN A DRAMA PROJECT: AN EXPLORATORY STUDY.

Mundt AP, Marín P, Gabrysch C, Sepúlveda C, Roumeau J, Heritage P.

Introduction: Innovative and interdisciplinary approaches are needed to improve mental health and psychosocial outcomes of people with criminal justice involvement and their families. Aim of the study was to assess effects of the participation in a theatre project on the mental health problems of people with criminal justice involvement and relatives. Methods: We conducted structured diagnostic interviews and in-depth qualitative interviews with five participants performing Shakespeare's Richard III in Chile. Three participants had been imprisoned prior to the project, and two were the parents of a person who died in a prison fire. Qualitative interviews followed a topic guide. Data were transcribed, and a six-phase approach for thematic analysis of the data was used. Results: Substance use disorder or major depression was identified in all the participants. Participation in the theatre project was experienced by the respondents as having a positive effect on the mental health conditions. The research registered the positive experiences of role identification, emotional expression, commitment with group processes, improved skills to socially interact, to be heard by the general public and society, and positive perceptions of the audience (including relatives). Discussion: The study raises the possibility that there may be improvements of depression and substance use problems through the participation of people with criminal justice involvement in a drama project. Wider scale research is recommended on the possible effects. The approach may be an alternative to psychotherapy and medication for some individuals.

FRONT PSYCHIATRY. 2019 AUG 14;10:570. DOI: 10.3389/FPSYT.2019.00570.

MEASURING PRIMARY HEALTH CARE CLINICIANS' SKILLS FOR DEPRESSION MANAGEMENT.

Martínez P, Rojas G, Martínez V, Marín R, Cornejo JP, Gómez V.

Introduction: Primary health care clinicians play an important role in the management of depression. Thus, it is very important to have a valid and reliable assessment of the competences needed to manage depression in primary health care, with the use of clinical simulation providing such an opportunity. Objective: The present study describes the assessment of primary health care clinicians' depression-related skills through a series of objective structured clinical examination stations. Material and Methods: Clinicians from multi-professional teams for the management of depression at two primary health care clinics in Santiago, Chile, went through seven objective structured clinical examination stations, lasting 10 to 20min each, to assess their depression-related skills. The clinical and communicative skills measured were in accordance with clinical guidelines. Standardized patients portrayed cases usually encountered in clinical practice, while expert raters evaluated clinicians' performance with standardized checklists. Results: Psychosocial clinicians performed better than biomedical clinicians in the assessed skills. The most notable results were as follows: a high level of accomplishment in the relationship with patient,

medical anamnesis, health checkup, and lab test requests; heterogeneous performance in patient management according to screening results, feedback to the patient, and registration in clinical records; and major deficiencies in the differential diagnosis of bipolar disorder. Discussion: The objective structured clinical examinations administered provided an opportunity to perform an in-depth examination of the depression-related skills of primary health care clinicians, where flaws in the screening and diagnosis procedures used by biomedical clinicians were detected. Given the significant involvement of these types of clinicians in depression management, undergraduate-level and continuing health education opportunities are needed.

PLOS ONE. 2019 MAR 14;14(3):E0213711. DOI: 10.1371/JOURNAL.PONE.0213711.

MENTAL DISORDERS AND MENTAL HEALTH SYMPTOMS DURING IMPRISONMENT: A THREE-YEAR FOLLOW-UP STUDY.

Gabrysch C, Fritsch R, Priebe S, Mundt AP.

BACKGROUND: Data on the course of mental disorders during imprisonment are scarce. Longitudinal studies from high-income Western countries point to improvements of symptoms over time. The aim of the present study was to assess mental disorders and symptoms three years after baseline evaluation at imprisonment and to determine predictors of change in a South American prison context. METHODS: Consecutively admitted prisoners in Santiago de Chile were assessed at intake and reassessed after three years using the Mini International Neuropsychiatric Interview and the Symptom-Check-List 90 Revised (SCL-90-R). The global severity index (GSI) was calculated with standard deviations (SD) and compared using paired t-tests. The prevalence of mental disorders at baseline and at follow-up were compared using McNemar tests. Analyses of variance were conducted to evaluate whether prespecified socio-demographic variables and disorders at baseline predicted symptom change at follow-up. RESULTS: 73 (94%) out of 78 prisoners participated. The prevalence of major mental illnesses was lower at follow-up: 47 (64%) at intake vs. 23 (32%) at follow-up had major depression ($p < 0.001$); 22 (30%) at intake vs. 10 (14%) at follow-up had psychosis ($p = 0.008$). The mean GSI improved from 1.97 (SD 0.65) at intake to 1.16 (SD 0.82) at follow-up ($p < 0.001$). Depression at baseline ($F = 9.39$; [Formula: see text] = 0.137; $\beta = -0.67$; $p = 0.003$) and working or studying during imprisonment ($F = 10.61$; [Formula: see text] = 0.152; $\beta = -0.71$; $p = 0.002$) were associated with strong improvement of the GSI at follow-up, whereas psychosis at intake was associated with relatively small symptom improvement ($F = 12.11$; [Formula: see text] = 0.17; $\beta = 0.81$; $p = 0.001$). CONCLUSIONS: In a resource poor prison context in South America, mental health symptoms and disorders improve considerably over three years during imprisonment. This applies especially to people with depression at intake. Offers to work or study during imprisonment may improve mental health outcomes.

FRONT PUBLIC HEALTH. 2019 DEC 20;7:391. DOI: 10.3389/FPUBH.2019.00391.

IMPROVING MENTAL HEALTH CARE IN DEVELOPING COUNTRIES THROUGH DIGITAL TECHNOLOGIES: A MINI NARRATIVE REVIEW OF THE CHILEAN CASE.

Rojas G, Martínez V, Martínez P, Franco P, Jiménez-Molina Á.

The uneven distribution of mental health resources contributes to the burden of mental disorders in vulnerable groups, especially in developing countries. Internet-based interventions and digital technologies can contribute to reducing the gap between high prevalence of mental disorders, demand for treatment, and access to mental health care, thereby reducing inequities in mental health. This mini review summarizes the current state of the field of e-mental health research in Chile, showing its progress, limitations, and challenges. Internet-based interventions are at an early stage of development in Chile. The interventions included are heterogeneous in terms of participants (e.g., secondary students, patients, healthcare professionals) and contexts (e.g., rural, urban, schools, primary health care), aims, and modalities (e.g., website, online games). While these studies confirmed the feasibility of Internet-based interventions, the shortage of studies on effectiveness and cost-effectiveness makes it difficult to disseminate and scale up these Internet-based programs. However, the growing amount of knowledge accumulated in the Chilean context could guide practices in other developing countries for supporting the mental health of underserved populations.

FRONT PSYCHIATRY. 2019 SEP 13;10:664. DOI: 10.3389/FPSYT.2019.00664.

INTERNET-BASED INTERVENTIONS FOR THE PREVENTION AND TREATMENT OF MENTAL DISORDERS IN LATIN AMERICA: A SCOPING REVIEW.

Jiménez-Molina Á, Franco P, Martínez V, Martínez P, Rojas G, Araya R.

Background: There is a huge gap in the treatment of mental disorders in Latin America, especially among socioeconomically disadvantaged groups. Given the sharp increase in Internet access and the rapid penetration of smartphones in the region, the use of Internet-based technologies might potentially contribute to overcoming this gap and to provide more widely distributed and low-cost mental health care in a variety of contexts. Methods: We conducted a scoping review of the literature in order to systematically map the existing evidence on use of Internet-based interventions for prevention, treatment, and management of mental disorders across Latin American countries, as well as to identify existing gaps in knowledge. Six electronic databases were searched for published papers (PubMed, Embase, CINAHL, Web of Science, SciELO, and CENTRAL). Results: After the eligibility assessment, we identified 22 Internet-based studies carried out in Latin America for prevention, treatment, education, or facilitating self-management of mental disorders. Included studies mainly targeted depression ($n =$

11), substance misuse (n = 6), anxiety (n = 3), and mental health literacy for education and health professionals (n = 2). Most studies were undertaken in Brazil (n = 6), Mexico (n = 5), and Chile (n = 4). Only 3 studies were randomized controlled trials (RCTs), 4 were pilot RCTs, and 15 were naturalistic, acceptability, or feasibility studies. The three RCTs identified showed disparate results, but overall, there are challenges to face. Better results are seen in the short-term (postintervention or after 3 months), but most studies do not explore outcomes for long enough (follow-up after 6 or 12 months). Most of the feasibility and pilot studies showed reasonably good acceptability for a wide range of strategies but difficulties to engage and retain participants for long enough or adhering to established protocols. Conclusion: This study shows that Internet-based interventions for the prevention and treatment of mental disorders are growing rapidly in Latin America, but there are few studies on effectiveness and cost effectiveness, making it difficult to provide the evidence needed to justify scaling up these interventions.

FRONT PSYCHIATRY. 2019 JUL 30;10:552. DOI: 10.3389/FPSYT.2019.00552. ECOLLECTION 2019.

COMPUTER-ASSISTED COGNITIVE-BEHAVIORAL THERAPY TO TREAT ADOLESCENTS WITH DEPRESSION IN PRIMARY HEALTH CARE CENTERS IN SANTIAGO, CHILE: A RANDOMIZED CONTROLLED TRIAL.

Martínez V, Rojas G, Martínez P, Gaete J, Zitzko P, Vöhringer PA, Araya R.

Introduction: Evidence from developed countries shows the efficacy of computer-assisted cognitive-behavioral therapy (cCBT) in addressing adolescent depression in home and/or school settings. This paper presents the results of a randomized controlled trial (RCT) of a brief therapist-guided cCBT intervention for adolescent depression in resource-constrained primary health care (PHC) settings. Material and methods: A multicenter, two-arm parallel-group, individually RCT with a 1:1 allocation ratio assigned 216 depressed adolescents (aged 15-19) attending four PHC centers in a low-income municipality of Santiago, Chile, to receive eight weekly face-to-face therapist-guided cCBT sessions by study therapists (N = 108), or to receive an enhanced usual care (EUC) intervention by trained PHC psychologists, encouraged to adhere to the national clinical guidelines for the management of depression (N = 108). Both groups received pharmacotherapy concordant with these guidelines. The primary outcome was the Beck Depression Inventory (BDI) at 4 months post-randomization, to assess depressive symptoms. BDI at 6 months post-randomization was a secondary outcome. Additional measures included patients' compliance, and satisfaction with different treatment components, at 6 months post-randomization. Main Results: The adjusted difference in mean BDI score between groups was -3.75 (95% CI -6.23 to -1.28; p = 0.003) at 4 months post-randomization. At 6 months post-randomization, the adjusted difference in mean BDI score between groups was -2.31 (95% CI -4.89 to 0.27; p = 0.078). The effect size was small-to-medium at 4 months post-randomization, d = 0.39 (0.12 to 0.67), and small and non-significant at 6 months post-randomization d = 0.29 (-0.00 to 0.59). Adolescents in the experimental treatment group were significantly more satisfied with treatment, with the PHC centers' facilities, with the psychological care received, and with non-professional staff than those in the comparator treatment group. Discussion: A brief therapist-guided cCBT eight-session intervention improves the response of depressed adolescents attending PHC centers at 4 months post-randomization. At 6 months post-randomization, the differences of between groups were not significant. Future research may focus on exploring strategies to sustain and increase response.

TRIALS. 2019 MAY 14;20(1):268. DOI: 10.1186/S13063-019-3310-Y.

VIDEO FEEDBACK INTERVENTION TO ENHANCE PARENTAL REFLECTIVE FUNCTIONING IN PRIMARY CAREGIVERS OF INPATIENT PSYCHIATRIC CHILDREN: PROTOCOL FOR A RANDOMIZED FEASIBILITY TRIAL.

Leyton F, Olhaberry M, Alvarado R, Rojas G, Dueñas LA, Downing G, Steele H.

BACKGROUND: Children requiring hospitalization for psychiatric care have serious disorders, high use of psychotropic medication, and frequent readmissions. The development and implementation of therapies focused on incorporating primary caregivers or attachment figures is necessary for working with children with severe psychiatric disorders. Mentalization or parental reflective functioning (PRF) is the ability of parents to understand their children's behaviors as an expression of internal emotional states and act accordingly to help them regulate their emotions; in this way mentalizing is a key component of sensitive parenting. Video-assisted therapies have proven to be effective in promoting change in parent-child relationships. The majority of studies have been carried out with mothers of pre-school children and in an outpatient setting. Video intervention therapy (VIT) is a flexible manualized therapy, which allows the intervention to be individualized to the context where it is applied, according to the needs and resources of the people who participate in it. The objective of the study is to evaluate the feasibility and acceptability of applying VIT to improve the PRF of the parents as primary carers of children hospitalized in a psychiatric service. METHODS: This is a pilot randomized, single-masked (outcome assessor) study with a qualitative component. It will involve a block randomization procedure to generate a 2:1 allocation (with more people allocated to the intervention arm). The intervention consists of four modules; every module has both one video-recorded play session and one VIT session per week. People assigned to the control group will receive treatment as usual plus weekly play sessions. Feasibility and acceptability of the study will be quantitatively and qualitatively assessed. Evaluation of the caregivers will include assessments of PRF, wellbeing and personality structure; assessments of children will include parent-ratings and clinician-ratings of symptomatology and general functioning. After every video feedback (VF) session, PRF, the caregiver's wellbeing and children's general functioning will be reassessed. DISCUSSION: This study will contribute to the currently scarce evidence on how to provide family attachment-based interventions in a child inpatient psychiatric unit. It will also inform the design and implementation of a future randomized clinical trial.

INT J MENT HEALTH SYST. 2019 APR 3;13:21. DOI: 10.1186/S13033-019-0276-9.

ENHANCING MENTAL HEALTH RESEARCH CAPACITY: EMERGING VOICES FROM THE NATIONAL INSTITUTE OF MENTAL HEALTH (NIMH) GLOBAL HUBS.

da Silva ATC, Hanlon C, Susser E, Rojas G, Claro HG, Quayle J, Habtamu K, Burrone MS, Cavalcanti MT, Sharma M, Schneider M, Adhikari RP, van de Water T, Mohammed Y, Ordóñez AE, Seedat S.

BACKGROUND: Emerging researchers in low- and middle-income countries (LMIC) face many barriers, including inadequacies in funding, international exposure and mentorship. In 2012, the National Institute of Mental Health (NIMH) funded five research hubs aimed at improving the research core for evidence-based mental health interventions, enhancing research skills in global mental health, and providing capacity building (CB) opportunities for early career investigators in LMIC. In this paper emerging researchers contextualize their experiences. **CASE PRESENTATION:** Each of the five hubs purposively selected an emerging researcher who had experienced more than one hub-related CB opportunity and actively participated in hub-related clinical trial activities. The five 'voices' were invited to contribute narratives on their professional backgrounds, CB experience, challenges and successes as an emerging mental health researcher, and suggestions for future CB activities. These narratives are presented as case studies. CB activities provided broader learning opportunities for emerging researchers. Benefits included the receipt of research funding, hands-on training and mentorship, as well as exposure to networks and collaborative opportunities on a global scale. To overcome ongoing challenges of access to funding, mentoring, networking and global exposure, the emerging voices recommend making mentorship and training opportunities available to a wider range of emerging mental health researchers. **CONCLUSIONS:** Investing in CB is not enough to ensure sustainability and leave a legacy unless it is accompanied by ongoing mentorship and international exposure. Financial investment in building research capacity, promotion of mentorship and supervision, and international networking are essential to yield well-prepared young investigators in LMIC as experienced by these rising stars. Governments and policymakers should prioritize educational policies to support the continuous development and international engagement of emerging researchers. This can advance strategies to deal with one of most important and costly problems faced by healthcare systems in LMIC: the mental health treatment gap.

PSYCHOL MED. 2019 SEP 23:1-9. DOI: 10.1017/S0033291719002320.

CHARACTERIZING DSM-5 AND ICD-11 PERSONALITY DISORDER FEATURES IN PSYCHIATRIC INPATIENTS AT SCALE USING ELECTRONIC HEALTH RECORDS.

Barroilhet SA, Pellegrini AM, McCoy TH, Perlis RH.

BACKGROUND: Investigation of personality traits and pathology in large, generalizable clinical cohorts has been hindered by inconsistent assessment and failure to consider a range of personality disorders (PDs) simultaneously. **METHODS:** We applied natural language processing (NLP) of electronic health record notes to characterize a psychiatric inpatient cohort. A set of terms reflecting personality trait domains were derived, expanded, and then refined based on expert consensus. Latent Dirichlet allocation was used to score notes to estimate the extent to which any given note reflected PD topics. Regression models were used to examine the relationship of these estimates with sociodemographic features and length of stay. **RESULTS:** Among 3623 patients with 4702 admissions, being male, non-white, having a low burden of medical comorbidity, being admitted through the emergency department, and having public insurance were independently associated with greater levels of disinhibition, detachment, and psychoticism. Being female, white, and having private insurance were independently associated with greater levels of negative affectivity. The presence of disinhibition, psychoticism, and negative affectivity were each significantly associated with a longer stay, while detachment was associated with a shorter stay. **CONCLUSIONS:** Personality features can be systematically and scalably measured using NLP in the inpatient setting, and some of these features associate with length of stay. Developing treatment strategies for patients scoring high in certain personality dimensions may facilitate more efficient, targeted interventions, and may help reduce the impact of personality features on mental health service utilization.

DEPARTAMENTO DE OTORRINOLARINGOLOGÍA

HEAR RES. 2019 MAR 1;373:10-22. DOI: 10.1016/J.HEARES.2018.12.002.

P27KIP1 DOWN-REGULATION AS ACHIEVED BY TWO CLINICALLY FEASIBLE MEANS DID NOT INDUCE PROLIFERATION OF SUPPORTING CELLS IN THE RAT NEONATAL COCHLEA IN VIVO.

Silva SA, Maass JC.

In mammals, the cochlear sensory epithelium becomes quiescent early during development. After the first postnatal week, there is no cell replacement or proliferation, and severe damage leads to permanent deafness. Supporting cells' trans-differentiation has been suggested as a way to regenerate cochlear hair cells after damage. However, they are also needed for proper functionality. Cdkn1b (p27Kip1) participates in the cochlear terminal mitosis state achieved during development. Its expression is maintained in adult supporting cells and its postnatal deletion has induced cochlear proliferation in vitro and in vivo. Therefore, its manipulation has been proposed as a feasible way to induce proliferation of supporting cells after birth. Nevertheless, the literature is scarce regarding feasible methods to directly decrease p27Kip1 in the clinical domain. The effects of p27Kip1 knockdown using viral vectors are not completely elucidated and no pharmacological approaches

to decrease p27Kip1 in the cochlea have been tested in vivo before. This study explores the ability of p27Kip1 messenger knockdown and pharmacological transcriptional inhibition to induce proliferation of supporting cells in the P0 neonatal rat cochlea in vivo. Respectively, lentiviral vectors transducing shRNA against p27Kip1 were administered into the scala media or Alsterpaullone 2-Cyanoethyl into the round window niche. Cell markers and gene expression were assessed through immunostaining and qRT-PCR. Despite both methods significantly decreasing p27Kip1 expression in vivo, signs of toxicity in the organ of Corti were not found; however, relevant proliferation was not found either. Finally, cochlear damage was added to increase the response in vitro, achieving only a mild to moderate proliferation induction. We conclude that our approaches were not able to stimulate the recall of supporting cell proliferation despite significantly decreased p27Kip1 levels in vivo. Considering the evaluation of the cochlea at a very responsive stage, we propose that the level of isolated modification of p27Kip1 expression in living mammals achievable through these approaches is insufficient to induce proliferation of supporting cells. Future proliferation induction experiments in the cochlea should study other methods and genes.

PLOS ONE. 2019 JAN 7;14(1):E0208939. DOI: 10.1371/JOURNAL.PONE.0208939.

OSCILLATORY INFRASONIC MODULATION OF THE COCHLEAR AMPLIFIER BY SELECTIVE ATTENTION.

Dragicevic CD, Marcenaro B, Navarrete M, Robles L, Delano PH.

Evidence shows that selective attention to visual stimuli modulates the gain of cochlear responses, probably through auditory-cortex descending pathways. At the cerebral cortex level, amplitude and phase changes of neural oscillations have been proposed as a correlate of selective attention. However, whether sensory receptors are also influenced by the oscillatory network during attention tasks remains unknown. Here, we searched for oscillatory attention-related activity at the cochlear receptor level in humans. We used an alternating visual/auditory selective attention task and measured electroencephalographic activity simultaneously to distortion product otoacoustic emissions (a measure of cochlear receptor-cell activity). In order to search for cochlear oscillatory activity, the otoacoustic emission signal, was included as an additional channel in the electroencephalogram analyses. This method allowed us to evaluate dynamic changes in cochlear oscillations within the same range of frequencies (1-35 Hz) in which cognitive effects are commonly observed in electroencephalogram works. We found the presence of low frequency (<10 Hz) brain and cochlear amplifier oscillations during selective attention to visual and auditory stimuli. Notably, switching between auditory and visual attention modulates the amplitude and the temporal order of brain and inner ear oscillations. These results extend the role of the oscillatory activity network during cognition in neural systems to the receptor level.

REV MED CHIL. 2019 FEB;147(2):221-230. DOI: 10.4067/S0034-98872019000200221.

[HIGH INTENSITY INTERVAL TRAINING IN TEENAGERS].

Abarzúa V J, Viloff C W, Bahamondes V J, Olivera P Y, Poblete-Aro C, Herrera-Valenzuela T, Oliva C, García-Díaz DF.

This review analyzes the effects of high intensity interval training (HIIT) on muscle and cardiovascular fitness and body composition in teenagers. A search was carried out in international databases, finding 145 papers and selecting five for analysis. In all the reviewed manuscripts, peak oxygen uptake improved after HIIT. In the three manuscripts that measured muscle strength, it also increased. We conclude that HIIT improves muscle strength and cardiovascular fitness in school age children. A 12 weeks protocol with three 12-minute sessions per week would be ideal.

DEPARTAMENTO DE UROLOGÍA

REV INT ANDROL. 2019 NOV 25. PII: S1698-031X(19)30059-7. DOI: 10.1016/J.ANDROL.2019.07.002.

[PENILE PROSTHESES: DESCRIPTION OF A SERIES OF IMPLANTS WITH AND WITHOUT DILATATION OF THE CORPORA CAVERNOSA].

Fleck-Lavergne D, Marconi M, Mercado-Campero A, Hidalgo JP, Marchant F, Palma-Ceppi C.

INTRODUCTION: Penile prosthesis (PP) implantation is the treatment of choice for refractory erectile dysfunction (ED). They show a high satisfaction rate (75%-100%) and a complication rate that varies between 2.1% and 28.8%. The standard surgical technique includes dilatation of the corpora cavernosa (CC) prior to the insertion of the cylinders. This step takes time and is critical for the occurrence of complications. The aim of this study is to describe the results of a series of PP implanted using the techniques with and without dilatation of the CC. **MATERIALS AND METHODS:** One-hundred and 20 patients with refractory ED in whom a PP was implanted by 2 surgeons in different centers. Comorbidities, operative characteristics, satisfaction and postoperative complications were evaluated. **RESULTS:** The average age was 61±9.6 years. The most prevalent comorbidities were: history of radical prostatectomy, high-blood pressure and diabetes mellitus. Forty-two malleable and 78 hydraulic prostheses were implanted. Eleven patients had a previous PP. The median operative time was 70minutes (35-140). The satisfaction reported was 95.8%. Ten patients presented complications. In the group in which the surgery was performed without dilatation of the CC (n=80), the operative time was shorter (62.5minutes [35-105] versus 90minutes [60-140] respectively, p<0.0001). There was no difference in complications (p=0.73) or levels of satisfaction (p=0.196) when comparing the technique with and without dilatation of the CC. **CONCLUSION:** In our series, a shorter operative time was observed with the technique without dilatation of the CC, but there were no differences in complications. A prospective and randomized study is required to make a stronger recommendation regarding to dilatation of the CC.

INT BRAZ J UROL. 2019 JUL-AUG;45(4):798-806. DOI: 10.1590/S1677-5538.IBJU.2018.0556.

VOIDING SYMPTOMS OBTAINED BY OPEN VERSUS DIRECTED ANAMNESIS AS PREDICTORS OF VOIDING DYSFUNCTION IN WOMEN.

Valdevenito JP, Flores J, Rojas RG, Manriquez V, Arribillaga L, de Benito J.

OBJECTIVES: To determine the differences between voiding symptoms obtained by open anamnesis (VS-Open) versus voiding symptoms obtained by directed anamnesis (VSDirected) to predict voiding dysfunction in women. **MATERIALS AND METHODS:** Retrospective study of women with prior anti-incontinence surgery evaluated during 5 years. In a standardized clinical history taking, each patient was asked to answer question number five of the UDI-6 questionnaire ("Do you experience any difficulty emptying your bladder?"). If the answer was positive, the following voiding symptoms spontaneously described by the patient were documented: slow urine stream, straining to void, intermittent stream and feeling of incomplete bladder emptying, which were considered VS-Open. If the answer to this question was negative or if the patient had not reported the four voiding symptoms, she was asked in a directed manner about the presence of each of them, which were considered VS-Directed. Voiding dysfunction was considered the presence of a maximum flow ≤ 12 mL/s and/or a postvoid residual > 100 mL. **RESULTS:** Ninety-one women are analyzed. Eighteen patients presented voiding dysfunction (19.8%), There was a statistical association between voiding dysfunction and the presence of any VS-Open ($p = 0.037$) and straining to void obtained by open anamnesis ($p = 0.013$). Sensitivity, specificity, PPV, NPV, positive likelihood ratio and negative likelihood ratio, respectively, were 44.4% and 27.8%, 80.8% and 94.5%, 36.3% and 55.6%, 85.5% and 84.1%, 2.324 and 5.129, and 0.686 and 0.764. There was no statistical association between voiding dysfunction and VS-Directed. **CONCLUSIONS:** VS-Open may predict better voiding dysfunction than VS-Directed in women.

PHARMACOGENET GENOMICS. 2019 SEP;29(7):159-166. DOI: 10.1097/FPC.0000000000000379.

THE ROLE OF PHASE I AND II GENETIC POLYMORPHISMS, SMOKING, ALCOHOL AND CANCER FAMILY HISTORY, IN THE RISK OF DEVELOPING TESTICULAR CANCER.

Roco A, Lavanderos A, Cayún JP, Acevedo C, Celedón C, Rubilar JC, Sandoval C, Cerpa L, García-Martín E, Agúndez JA, Esguevillas G, Amo G, Canepa A, Cerda B, Peña K, Cáceres DD, Varela NM, Quiñones LA.

BACKGROUND: Testicular cancer (TCa) is a malignant tumor with highest incidence and mortality rates in Chile. The genes coding for cytochrome P450, glutathione-S-transferases (GSTs), and UDP glucuronyl transferases (UGT) participate in the biotransformation and detoxification of xenobiotics. Mutations in these genes have been associated with a high incidence of various types of cancer and an increased risk of presenting adverse reactions to drugs. **OBJECTIVE:** The aim of this study was to relate the presence of genetic polymorphisms in cytochrome P450 1A1 (CYP1A1), CYP3A4, GSTM1, GSTP1, GSTT1, and UGT1A1 genes and nongenetic factors with the risk of developing TCa. **METHODS:** A total of 276 volunteers from the Chilean general population and 251 Chilean TCa patients were recruited for the study. Genotypic analyses were performed using qPCR and PCR-RFLP. **RESULTS:** Variant alleles found to increase the risk of developing TCa were CYP1A1*2C (rs1048943), GSTP1 (rs1695), and GSTT1null, especially when in conjunction with a cancer family history and/or a smoking habit. The results of the multivariate analysis showed that the presence of variant alleles of GSTP1 (rs1695) together with a smoking habit and a family history of cancer accounted for a 15.9% risk of developing TCa in the Chilean population. CYP1A1*2C, GSTM1null, GSTT1null, and GSTP1 (rs1695) are statistically related to the risk of appearance of TCa, alone or associated with nongenetic factors. **CONCLUSION:** Therefore, phase I and II variant alleles might be useful in evaluating susceptibility to TCa in the studied population.

REV INT ANDROL. 2019 AUG 24. PII: S1698-031X(19)30056-1. DOI: 10.1016/J.ANDROL.2019.04.004.

MACROZOOSPERMIA ASSOCIATED WITH MUTATIONS OF AURKC GENE: FIRST CASE REPORT IN LATIN AMERICA AND LITERATURE REVIEW.

Ortega V, Oyanedel J, Fleck-Lavergne D, Horta F, Mercado-Campero A, Palma-Cepi C.

A Chilean 35-year-old male patient with a history of primary infertility made an appointment at the Unit of Reproductive Medicine at Clínica Las Condes, Santiago, Chile. Multiple semen analyses revealed abnormal sperm morphology as the most prevalent finding. Multiflagellated and macrocephalic spermatozoa were observed and indicated a possible macrozoospermic phenotype. The constant presence of abnormal sperm morphology led the scope of the study to include Aurora Kinase C (AURKC) gene sequencing. The patient was diagnosed with a homozygous mutation of this gene. The mutation was detected in exon 6, type c.744C>G+/- (PY248*) variant. As previously described in the Human Gene Mutation Database (HGMD), this pathogenic variant is associated with macrozoospermia. Although this mutation is not the most frequently observed, it is the first of its kind reported in Latin America.

FRONT PHARMACOL. 2019 MAR 8;10:206. DOI: 10.3389/FPHAR.2019.00206. ECOLLECTION 2019.

ASSOCIATION STUDY AMONG CANDIDATE GENETIC POLYMORPHISMS AND CHEMOTHERAPY-RELATED SEVERE TOXICITY IN TESTICULAR CANCER PATIENTS.

Lavanderos MA, Cayún JP, Roco Á, Sandoval C, Cerpa L, Rubilar JC, Cerro R, Molina-Mellico S, Celedón C, Cerda B, García-Martín E, Agúndez JAG, Acevedo C, Peña K, Cáceres DD, Varela NM, Quiñones LA.

Testicular cancer is one of the most commonly occurring malignant tumors in young men with fourfold higher rate of incidence and threefold higher mortality rates in Chile than the average global rates. Surgery is the initial line of treatment for testicular cancers, and is generally followed by chemotherapy, usually with combinations of bleomycin, etoposide, and cisplatin (BEP). However, the adverse effects of chemotherapy vary

significantly among individuals; therefore, the present study explored the association of functionally significant allelic variations in genes related to the pharmacokinetics/pharmacodynamics of BEP and DNA repair enzymes with chemotherapy-induced toxicity in BEP-treated testicular cancer patients. We prospectively recruited 119 patients diagnosed with testicular cancer from 2010 to 2017. Genetic polymorphisms were analyzed using PCR and/or qPCR with TaqMan @probes. Toxicity was evaluated based on the Common Terminology Criteria for Adverse Events, v4.03. After univariate analyses to define more relevant genetic variants ($p < 0.2$) and clinical conditions in relation to severe (III-IV) adverse drug reactions (ADRs), stepwise forward multivariate logistic regression analyses were performed. As expected, the main severe ADRs associated with the non-genetic variables were hematological (neutropenia and leukopenia). Univariate statistical analyses revealed that patients with ERCC2 rs13181 T/G and/or CYP3A4 rs2740574 A/G genotypes are more likely to develop alopecia; patients with ERCC2 rs238406 C/C genotype may develop leukopenia, and patients with GSTT1-null genotype could develop lymphocytopenia (III-IV). Patients with ERCC2 rs1799793 A/A were at risk of developing severe anemia. The BLMH rs1050565 G/G genotype was found to be associated with pain, and the GSTP1 G/G genotype was linked infection ($p < 0.05$). Multivariate analysis showed an association between specific ERCC1/2 genotypes and cumulative dose of BEP drugs with the appearance of severe leukopenia and/or febrile neutropenia. Grades III-IV vomiting, nausea, and alopecia could be partly explained by the presence of specific ERCC1/2, MDR1, GSTP1, and BLMH genotypes ($p < 0.05$). Hence, we provide evidence for the usefulness of pharmacogenetics as a tool for predicting severe ADRs in testicular cancer patients treated with BEP chemotherapy.

SERVICIO DE ANATOMÍA PATOLÓGICA

AN BRAS DERMATOL. 2019 MAR-APR;94(2):224-226. DOI: 10.1590/ABD1806-4841.20198032.

BULLOUS PEMPHIGOID ASSOCIATED WITH PSORIASIS: A GOOD RESPONSE TO METHOTREXATE.

Vargas P, Giacaman P, Fernández J, Morales C.

Psoriasis has been associated with various autoimmune diseases, however, its relation to bullous diseases is infrequent. Of these, bullous pemphigoid appears as the main associated entity, even though both conditions differ considerably in demographic and clinical aspects. We report the case of a 42-year-old female patient, with long-standing psoriasis who consulted due to the exacerbation of psoriatic plaques associated with generalized bullous lesions on the skin and oral mucosa, with one-week duration. With clinical signs and histopathological findings compatible with bullous pemphigoid associated with psoriasis, we decided to treat her with methotrexate 10mg a week. The patient had an excellent response after two months of treatment.

ACTAS DERMOSIFILIOGR. 2019 MAY;110(4):303-307. DOI: 10.1016/J.AD.2017.09.029.

HYPERVASCULAR PSEUDONODULAR PLAQUE-LIKE ULTRASOUND MORPHOLOGY IN ANGIOLYMPHOID HYPERPLASIA.

Wortsman X, Yagnam M, Carreño L.

Angiolymphoid hyperplasia with eosinophilia (ALHE) is a benign vascular proliferation characterized by solitary or multiple angiomatous lesions. It is most common in young or middle-aged women, and the lesions typically affect the head and neck, showing a particular predilection for the periauricular region. The differential diagnosis in patients with ALHE is broad and includes both benign and malignant conditions. We report on a series of cases of periauricular ALHE in which ultrasound imaging revealed an hypervascular, pseudonodular and plaque-like morphology with clinical and histologic correlations. It also evidenced vascular communication between lesions that appeared to be separate on clinical examination. Familiarity with such ultrasound presentations could help to improve diagnostic accuracy and facilitate disease monitoring in patients with ALHE.

GENE. 2019 MAR 1;687:228-237. DOI: 10.1016/J.GENE.2018.11.037.

DICKKOPF-1 REDUCES HYPERTROPHIC CHANGES IN HUMAN CHONDROCYTES DERIVED FROM BONE MARROW STEM CELLS.

Rojas A, Mardones R, Pritzker K, van Wijnen AJ, Galindo MA, Las Heras F.

The in vitro process of chondrogenic differentiation of mesenchymal stem cells (MSCs) induces a pre-apoptotic hypertrophic phenotype, guided by the active status of the WNT/ β -catenin pathway. To achieve a stable chondrocyte phenotype for cartilage tissue engineering, it is necessary to gain a better understanding of specific genes that regulate the cartilage tissue phenotype. RNA sequencing (RNA-seq) analysis of tissue samples from bone, cartilage, growth plate and muscle show that Dickkopf-1 (DKK1), a natural WNT canonical signaling inhibitor, is expressed in cartilage tissue. This observation reinforces the concept that inhibition of the WNT/ β -catenin pathway is critical for preventing avoid chondrocyte hypertrophy in vitro. We used two doses of DKK1 in a pellet cell culture system to inhibit the terminal differentiation of chondrocytes derived from bone marrow mesenchymal stem cells (MSCs). Bone marrow MSCs were cultured in chondrogenic induction medium with 50 and 200 ng/ml of DKK1 for 21 days. The highest doses of DKK1 reduce β -catenin expression and nuclear localization at day 21, concomitant with reduced expression and activity of hypertrophy markers collagen type X (COL10A1) and alkaline phosphatase (ALPL), thus decreasing the pre-hypertrophic chondrocyte population. Furthermore, DKK1 stimulated expression of collagen type II (COL2A1) and glycosaminoglycans (GAGs), which represent healthy articular cartilage markers. We conclude that exogenous DKK1 impedes chondrocyte progression into a prehypertrophic stage and stimulates expression of healthy articular cartilage markers by blocking the WNT/ β -catenin pathway. Hence, DKK1 may promote a mature healthy articular cartilage phenotype and facilitate cartilage tissue engineering for joint repair.

COMITÉ INFECCIONES INTRAHOSPITALARIAS

INT J INFECT DIS. 2019 APR;81:28-30. DOI: 10.1016/J.IJID.2019.01.051.

INTRODUCTION OF NDM-1 AND OXA-370 FROM BRAZIL INTO CHILE IN STRAINS OF KLEBSIELLA PNEUMONIAE ISOLATED FROM A SINGLE PATIENT. Carrasco-Anabalón S, Conceição Neto CO, D'Alincourt Carvalho-Assef AP, Lima CA, Cifuentes M, Silva F, Barrera B, Domínguez M, González-Rocha G, Bello-Toledo H.

Carbapenemase-producing Enterobacteriaceae have rapidly disseminated worldwide and can colonize patients in healthcare centers. As in Chile the first isolations of NDM-1 and OXA-370 carbapenemases were related with a patient arriving from Brazil, the genetic relatedness of Klebsiella pneumoniae strains producers of these enzymes and isolated in both countries was assessed. PFGE analyses revealed that the isolates were clonally related, illustrating how travel contributes to the spread of multidrug-resistant microorganisms. In addition, the occurrence of three different carbapenemases in three different K. pneumoniae strains isolated from a single patient is described.

CENTRO INVESTIGACIÓN CLÍNICA AVANZADA

J ALZHEIMERS DIS. 2019 DEC 9. DOI: 10.3233/JAD-190839.

INVERSE RELATIONSHIP BETWEEN ALZHEIMER'S DISEASE AND CANCER: HOW IMMUNE CHECKPOINTS MIGHT EXPLAIN THE MECHANISMS UNDERLYING AGE-RELATED DISEASES.

Rogers NK, Romero C, San Martín CD, Ponce DP, Salech F, López MN, Gleisner A, Tempio F, Behrens MI.

Alzheimer's disease (AD) is the most prevalent neurodegenerative disease in the adult population. There is evidence of an inverse epidemiological relationship between AD and cancer, another prevalent age-related disease. This has led to hypothesize that there could be a common biological mechanism, deregulated in opposite directions that might explain the phenomenon of mutual protection. The immunological system and its regulatory checkpoints are good candidates to explain why having survived a cancer could protect from developing AD. During cancerous growth, the neoplastic cells induce immune tolerance to block the host's immunity system that would prevent tumor growth. This has led to the development of drugs that block distinct immune checkpoints, such as Programmed Death 1 (PD-1) and its major ligand PD-L1, that have shown great promise in treating diverse types of cancer. We propose that in those individuals who survived a cancer, the immune system is left in a state of diminished tolerance or proinflammatory systemic milieu, after its successful attempt to fight the cancer, that protects them from developing AD.

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REMIFENTANIL-INDUCED SECONDARY HYPERALGESIA IS NOT PREVENTED BY PREOPERATIVE ACETAZOLAMIDE ADMINISTRATION IN PATIENTS UNDERGOING TOTAL THYROIDECTOMY: A RANDOMIZED CONTROLLED TRIAL.

Gutiérrez R, Contreras F, Blanch A, Bravo D, Egaña JI, Rappoport D, Cabané P, Rodríguez F, Penna A.

PURPOSE: Acute administration of remifentanyl may lead to opioid-induced hyperalgesia (OIH). Studies in mice suggest that OIH is mediated by impaired anionic homeostasis in spinal lamina I neurons due to a down-regulation of the K⁺-Cl⁻ co-transporter KCC2, which was reverted using acetazolamide (ACTZ), a carbonic anhydrase inhibitor. We propose that ACTZ prevents remifentanyl-mediated OIH in humans. **PATIENTS AND METHODS:** We conducted a randomized, double-blind, placebo-controlled clinical trial between December 2016 and September 2018. Patients were randomly allocated to receive ACTZ (250 mg of ACTZ 2 h before surgery) or placebo. To detect hyperalgesia, mechanical pain threshold (MPT) were measured before and after surgery using hand-held von Frey filaments in the forearm. Anesthesia was maintained with remifentanyl at a target effect site of 4.5 ± 0.5 ng/mL, and sevoflurane at an end-tidal concentration of 0.8 MAC corrected for age. **RESULTS:** In total, 47 patients completed the study. Both groups were comparable in the baseline characteristics and intraoperative variables. Baseline MPT were similar in both groups. However, MPT in the forearm significantly diminished in the time in both groups. Finally, postoperative pain and morphine consumption were similar between groups. **CONCLUSION:** Both groups developed remifentanyl-mediated OIH at 12-18 h after surgery. However, ACTZ did not prevent the MPT reduction in patients undergoing total thyroidectomy.

J GERONTOL A BIOL SCI MED SCI. 2019 JUN 18;74(7):1043-1051. DOI: 10.1093/GERONA/GLX248.

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, I Behrens M, 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 polymerase chain reaction. 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.

SERVICIO DE OFTALMOLOGÍA

FRONT IMMUNOL. 2019 APR 15;10:772. DOI: 10.3389/FIMMU.2019.00772.

INNATE IMMUNE CELLS' CONTRIBUTION TO SYSTEMIC LUPUS ERYTHEMATOSUS.

Herrada AA, Escobedo N, Iruretagoyena M, Valenzuela RA, Burgos PI, Cuitino L, Llanos C.

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by the presence of autoantibodies against nuclear antigens, immune complex deposition, and tissue damage in the kidneys, skin, heart and lung. Because of the pathogenic role of antinuclear antibodies and autoreactive T cells in SLE, extensive efforts have been made to demonstrate how B cells act as antibody-producing or as antigen-presenting cells that can prime autoreactive T cell activation. With the discovery of new innate immune cells and inflammatory mediators, innate immunity is emerging as a key player in disease pathologies. Recent work over the last decade has highlighted the importance of innate immune cells and molecules in promoting and potentiating SLE. In this review, we discuss recent evidence of the involvement of different innate immune cells and pathways in the pathogenesis of SLE. We also discuss new therapeutic targets directed against innate immune components as potential novel therapies in SLE.

OPHTHALMIC GENET. 2019 APR;40(2):91-98. DOI: 10.1080/13816810.2019.1571615.

CLINICAL FEATURES AND POSSIBLE FOUNDER MUTATION OF THE 8BP DUPLICATION MUTATION IN THE SLC4A11 GENE CAUSING CORNEAL DYSTROPHY AND PERCEPTIVE DEAFNESS IN THREE SOUTH AMERICAN FAMILIES.

Romero PT, Donoso R, López P, Miranda A, Rodríguez L, Chrzanowsky D, Asenjo MS, Burgos G, Villegas P, Desir J, Moya G, Herrera LM.

BACKGROUND: Corneal Dystrophy and Perceptive Deafness (CDPD) or Harboyan syndrome is an autosomal recessive rare disorder, characterized by congenital corneal opacities and progressive sensorineural hearing loss, which usually begins after the second decades of life. This study reports the ophthalmic, audiological and genetic features, in five CDPD affected patients from three Chilean families. **MATERIALS AND METHODS:** Five individuals affected with CDPD from three unrelated Chilean families were clinically and genetically examined. To evaluate a putative founder mutation 7 SNPs were analyzed in the three families, an Argentinian patient (carrier of the same mutation previously reported) and 87 Chilean controls. **RESULTS:** The ophthalmic symptoms in the five patients were bilateral and symmetric, starting before one year of age, and visual acuity varied from 0.1 to 0.3. In all cases, hearing loss began over 8 years old. The sequence of the 19 exons of SLC4A11 gene of all the affected patients exhibited homozygous eight nucleotide sequence duplication (c.2233_2240dup TATGACAC, p.(Ile748Metfs*5)) at the end of exon 16. All the affected patients of the three families were homozygous for a haplotype composed of five SNPs and covering 4,1 Mb. The same haplotype was present in one allele of the heterozygous Argentinean patient and has a frequency of 2.76% in Chilean population. **CONCLUSIONS:** The five CDPD patients were homozygous for the same mutation in the SLC4A11 gene. Haplotype analysis of all the affected, including the case reported from Argentina was in accordance with a founder mutation.

INT OPHTHALMOL. 2019 JUL;39(7):1451-1458. DOI: 10.1007/S10792-018-0958-3.

EFFECTIVENESS OF SAMPLING METHODS EMPLOYED FOR ACANTHAMOEBA KERATITIS DIAGNOSIS BY CULTURE.

Muiño L, Rodrigo D, Villegas R, Romero P, Peredo DE, Vargas RA, Liempi D, Osuna A, Jercic MI.

PURPOSE: This retrospective, observational study was designed to evaluate the effectiveness of the sampling methods commonly used for the collection of corneal scrapes for the diagnosis of Acanthamoeba keratitis (AK) by culture, in terms of their ability to provide a positive result. **METHODS:** A total of 553 samples from 380 patients with suspected AK received at the Parasitology Section of the Public Health Institute of Chile, between January 2005 and December 2015, were evaluated. A logistic regression model was used to determine the correlation between the culture outcome (positive or negative) and the method for sample collection. The year of sample collection was also included in the analysis as a confounding variable. **RESULTS:** Three hundred and sixty-five samples (27%) from 122 patients (32.1%) were positive by culture. The distribution of sample types was as follows: 142 corneal scrapes collected using a modified bezel needle (a novel method developed by a team of Chilean corneologists), 176 corneal scrapes obtained using a scalpel, 50 corneal biopsies, 30 corneal swabs, and 155 non-biological materials including contact lens and its paraphernalia. Biopsy provided the highest likelihood ratio for a positive result by culture (1.89), followed by non-biological materials (1.10) and corneal scrapes obtained using a modified needle (1.00). The lowest likelihood ratio was estimated for corneal scrapes obtained using a scalpel (0.88) and cotton swabs (0.78). **CONCLUSION:** Apart from biopsy, optimum corneal samples for the improved diagnosis of AK can be obtained using a modified bezel needle instead of a scalpel, while cotton swabs are not recommended.

SERVICIO DE EMERGENCIA

EMERG MICROBES INFECT. 2019;8(1):486-502. DOI: 10.1080/22221751.2019.1595985.

CUMULATIVE ACQUISITION OF PATHOGENICITY ISLANDS HAS SHAPED VIRULENCE POTENTIAL AND CONTRIBUTED TO THE EMERGENCE OF LEE-NEGATIVE SHIGA TOXIN-PRODUCING ESCHERICHIA COLI STRAINS.

Montero DA, Canto FD, Velasco J, Colello R, Padola NL, Salazar JC, Martin CS, Oñate A, Blanco J, Rasko DA, Contreras C, Puente JL, Scheutz F, Franz E, Vidal RM.

Shiga toxin-producing *Escherichia coli* (STEC) are foodborne pathogens causing severe gastroenteritis, which may lead to hemolytic uremic syndrome. The Locus of Enterocyte Effacement (LEE), a Pathogenicity Island (PAI), is a major determinant of intestinal epithelium attachment of a group of STEC strains; however, the virulence repertoire of STEC strains lacking LEE, has not been fully characterized. The incidence of LEE-negative STEC strains has increased in several countries, highlighting the relevance of their study. In order to gain insights into the basis for the emergence of LEE-negative STEC strains, we performed a large-scale genomic analysis of 367 strains isolated worldwide from humans, animals, food and the environment. We identified uncharacterized genomic islands, including two PAIs and one Integrative Conjugative Element. Additionally, the Locus of Adhesion and Autoaggregation (LAA) was the most prevalent PAI among LEE-negative strains and we found that it contributes to colonization of the mice intestine. Our comprehensive and rigorous comparative genomic and phylogenetic analyses suggest that the accumulative acquisition of PAIs has played an important, but currently unappreciated role, in the evolution of virulence in these strains. This study provides new knowledge on the pathogenicity of LEE-negative STEC strains and identifies molecular markers for their epidemiological surveillance.

OFICINA DE APOYO A LA INVESTIGACIÓN CLÍNICA - OAIC

J ULTRASOUND MED. 2019 AUG;38(8):1995-2004. DOI: 10.1002/JUM.14888.

ULTRASOUND CHARACTERISTICS OF THE HAIR FOLLICLES AND TRACTS, SEBACEOUS GLANDS, MONTGOMERY GLANDS, APOCRINE GLANDS, AND ARRECTOR PILI MUSCLES.

Wortsman X, Carreño L, Ferreira-Wortsman C, Poniachik R, Pizarro K, Morales C, Calderon P, Castro A.

OBJECTIVES: To explore the capability of very high-frequency ultrasound (US; 50-71 MHz) to detect the normal morphologic characteristics of the hair follicles and tracts, sebaceous glands, Montgomery glands, apocrine glands, and arrector pili muscles. **METHODS:** A retrospective study, approved by the Institutional Review Board, evaluated the normal US morphologic characteristics of the hair and adnexal structures in a database of very high-frequency US images extracted from the perilesional or contralateral healthy skin of 1117 consecutive patients who underwent US examinations for localized lesions of the skin and 10 healthy individuals from December 2017 to June 2018. These images were matched with their counterparts from the database of normal histologic images according to the corporal region. The Cohen concordance test and regional mean diameters of the hair follicles and adnexal structures were analyzed. **RESULTS:** The normal hair follicles and tracts, sebaceous glands, Montgomery glands, apocrine glands, and arrector pili muscles were observed on US images and matched their histological counterparts in all the corporal regions. There was significant US concordance ($\kappa=0.82$; $P=.0001$) among observers. Regional mean diameters (millimeters) of the hair follicles, sebaceous glands, and apocrine glands are provided. **CONCLUSIONS:** The hair follicles and tracts, sebaceous glands, Montgomery glands, apocrine glands, and arrector pili muscles are detectable with very high-frequency US, including some regional and anatomic variants. Knowledge of their normal US appearances is a requisite for detecting subclinical changes, understanding the physiopathologic characteristics, and supporting the early diagnosis and management of common dermatologic diseases.