Absorbs from the Argentinian Society of Osteology and Mineral Metabolism (AAOMM) and Argentinian Society of Osteoporosis (SAO) 2021 Annual Meeting

The Argentinian Society of Osteology and Mineral Metabolism (AAOMM) and the Argentinian Society of Osteoporosis (SAO) are the two national scientific societies dedicated to clinical and basic research into mineralized tissue. Meetings of each society are held annually, attracting a wide audience from throughout Argentina, Latin America, and beyond. During 2021, AAOMM and SAO have made the third Joint Congress of Osteology, which traditionally is balanced between clinical, therapeutic, and basic science. The participation of young scientists and clinicians is actively encouraged. This year, a leader team in musculoskeletal clinical and basic science organized the Annual Meeting. The composition of the Scientific Committee was Dr. Evangelina Giacoia (SAO), Dr. Diana Gonzalez (AAOMM), Dr. María Silvia Larroude (SAO), Dr. Susana Moggia (SAO), Dr. Gabriela Picotto (AAOMM), Dr. María Silvia Larroude (SAO), Dr. Susana Moggia (SAO), Dr. Gabriela Picotto (AAOMM), Dr. María Silvia Larroude (SAO), Dr. Susana Moggia (SAO), Dr. Gabriela Picotto (AAOMM). The composition of the Organizing Committee was Dr. María Lorena Brance (AAOMM), Dr. Graciela Brito (AAOMM), Dr. Vanina Farias (SAO), Dr. María Laura García (SAO), Dr. Paula Rey (AAOMM), Dr. Isabel Torrecilla (SAO), and both current presidents Dr. Lucas R. Brun (AAOMM) and Dr. José Luis Mansur (SAO). The program brought together international leaders such as Dr. Felicia Cosman (USA), Dr. Teresita Bellido (USA), Dr. Gustavo Duque (Australia), Dr. Gerard Karsenty (USA), Dr. Jorge Cannata Andia (España) and Dr. Jorge Malouf Sierra (España).

Analysis of the combined effect of insulin and naringin treatments on the histological and biomechanical properties of bone in a rat model of diabetes mellitus

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Diabetes mellitus (DM) alters the bones increasing the risk of fractures and/or delays the fracture healing. The aim of the present work was to study the histological and biomechanical characteristics of bone in rats with type 1 DM and to evaluate the possible osteoprotective effect of insulin (I) and naringin (NAR), individually or combined. Male Wistar rats were treated for 30 days: 1) controls, 2) DM1, 3) DM1+I, 4) DM1+NAR 80 mg/Kg, 5) DM1+I+NAR. Bone histomorphometry, bone mineral density (BMD), histology and TRAP staining were evaluated in femur. Biomechanical studies were done in cortical bone (3-point bending test) and trabecular bone (compression test). ANOVA and Bonferroni test were used for statistical analysis. Serum OCN levels and BMD were lower in DM1 rats, but treatments with NAR or I+NAR normalized these values. All groups presented lower bone volume as compared
to those from the control group and lower trabecular thickness except that of the I + NAR group. TRAP (+) cells increased in DM1 rats, an effect that decreased with all treatments. DM rats presented lower values of fracture and ultimate loads, which was avoided with I+NAR treatment. Individual and combined exposure to the drugs prevented the decrease in stiffness and absorbed energy induced by DM1. In conclusion, the normalization of serum OCN levels and the decrease in the number of osteoclasts suggest that NAR promotes osteoblastogenesis and inhibits osteoclastogenesis. STZ reduces the resistance to fracture by decreasing the moment of inertia. Only I+NAR restores the resistance to control values. The mechanisms of action of NAR in bone will continue to be studied.

Vascular calcification in chronic kidney disease: a novel risk factor for fractures?

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Introduction: progressive renal decline leads to chronic kidney disease-mineral bone disorders (CKD-MBD). Different studies have shown an inverse association with vascular calcification (VC) presence and bone mineral density (BMD), although the mechanisms were not elucidated, it is believed the bone disorder as a main responsible. Until now, this scenario has not been studied in CKD Argentinian population. Objectives: CKD-MBD evaluation in patients stage 5 and 5D before kidney transplantation (KT), by different serum determinations; identifying VC using Kauppila and Adragao scores; determining BMD by bone densitometry; evaluating arterial stiffness through pulse wave velocity (PWV); correlating radiological VC with clinical and serum parameters, BMD, arterial stiffness, and bone fractures; evaluating association between bone fractures and VC degree. Materials and methods: a prospective, observational, and analytical study was conducted. 101 patients hospitalized for living or deceased KT at Private University Hospital of Córdoba were included between June 2019 and December 2020. Results: 28% of patients presented VC. VC was associated with age, dialysis time, donor type, and PWV (p <0.01). Total ALP was the only MBD parameter significantly altered in the VC group (Me= 149.5 IR [62-964] vs 106 [28-449] IU/L; p<0.01). Bone markers and BMD were similar. Logistic regression demonstrated VC increases in 3 times fracture’s chances (OR=3.1; p=0.01; CI=1.2–7.8). Conclusion: positive association was found between VC and fractures in CKD stage 5 – 5D patients. These results indicate the importance of VC evaluation in CKD patients as possible new risk factor for fractures.

What to do after rebound-associated vertebral fractures following denosumab discontinuation?

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Objective: Investigate bone mineral density (BMD) and bone turnover markers (BTM) changes after restarting osteoporosis treatment with denosumab (Dmab), zoledronate or teriparatide, in postmenopausal women who had sustained rebound-associated vertebral fractures (RAVF s) following Dmab discontinuation. Material and Methods: Retrospective observational study. We examined lumbar spine (LS), femoral neck (FN) and total hip (TH) DXA scans (Lunar Prodigy Advance, software 13.6) and assessed C-telopeptide (CTx) (normal value 74-550 pg/mL) and osteocalcin (BGP) (normal value 11-43 ng/mL), at re-initiation treatment (RT) time and 1 year after. Results: We included nine women (mean age 66 years) with RAVFs. Dmab
treatment duration before the RAVFs was 24 months. 78% had received bisphosphonates (BF) before Dmab and 33% had prevalent vertebral fractures. Median number of RAVFS was 2. None of them had received BF after stopping Dmab. After one year of the RT with Dmab (n=4), teriparatide (n=3) and zoledronate (n=2) each of the DXA scan regions were preserved with all regimens, moreover we observed non-significant increase: in LS with teriparatide and in FN with Dmab. However, we found non-significant decreases: on the FN with teriparatide and at the TH with teriparatide and zoledronate. CTx and BGP were significantly decreased with Dmab (p=0.030 and p=0.002, respectively) and did not show a significant change with zoledronate or teriparatide. However, we observed an increasing trend in both BTM with teriparatide. No patient suffered additional vertebral fractures. Conclusions: In these patients with RAVFs after Dmab discontinuation there were no significant changes in DMO with all treatment regimens after 1 year and BTM significantly decreased with Dmab. However larger studies are needed to confirm the tendencies we found.

Intake of Cd-containing drinking water and its effect on long bones

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Previous studies conducted by our laboratory using rats given Cd-containing drinking water for six months showed no alterations in bone histomorphometry, though bone marrow adiposity was found to increase. The objective of the present work was to study the effect of chronic Cd intoxication on osteoid synthesis and mineralization dynamics in long bones. Materials and methods: Sixteen male Wistar rats were divided into 2 groups: Cd group received drinking water containing CdCl₂ (25 mg /L) for six months and the control group received water. Prior to euthanasia, the animals were administered an ip dose of tetracyclines. After euthanasia, the femurs were extracted, embedded in methylmethacrylate and sectioned longitudinally. Osteoid measurements included osteoid volume (OV/BV) and osteoid thickness (O.Th). Mineralization dynamics were assessed including: mineralizing surface (MS/BS), mineral apposition rate (MAR) and bone formation rate (BFR/BS). All data were analyzed using Student’s T test (p<0.05). Results: OV/BV (%) (control: 1.92±1.50; Cd: 1.06±0.70) and O.Th(μm) (control: 4.95±1.15; Cd: 4.41±0.84) tended to decrease in the Cd group, though the differences did not reach statistical significance (p>0.05). There were also no significant differences (p>0.05) between control and intoxicated animals in MS/BS (%) (control: 33.01±7.86, Cd: 29.55±7.50), MAR (μm/day) (control: 1.25±0.30, Cd: 1.57±0.36) or BFR/BS (μm/year) (control: 0.42±0.18, Cd: 0.47±0.15). Conclusion: Although the amount of osteoid tended to decrease, chronic Cd exposure did not alter mineralization dynamics under the experimental conditions used here.

Effect of metabolic syndrome (MS) in total and undercarboxylated osteocalcin (OCN) in non-diabetic women

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Bone, fat and pancreas interact to control glucose homeostasis. MS is associated to insulin-resistance and chronic inflammation
that dysregulate energy metabolism; it is also associated to low 25OHD and bone remodeling markers, all negative factors for bone homeostasis. Bone regulates energy metabolism through bone cells activity. Osteoblastic total OCN (tOCN) is decarboxylated by bone resorption to undercarboxylated OCN (ucOCN), regulated by leptin, which promotes β-cell proliferation and insulin production and secretion. We evaluated if MS would exert different effects than nonMS in ucOCN and tOCN in 95 non-diabetic adult women with different BMI. Different letters: statistical significance; *: p<0.05 Ms vs. nonMS. Results (mean±SD): Overweight (OW), type I, II, III obesity (OB) in nonMS and MS, respectively. tOCN (ng/mL): 32.0±14.5\textsuperscript{b}, 22.3±13.1\textsuperscript{b}, 36.5±3.0\textsuperscript{b}, 10.7±4.5\textsuperscript{a}; 28.5±12.5, 24.3±12.1, 21.2±14.9\textsuperscript{*}, 27.3±12.9\textsuperscript{a}. ucOCN (ng/mL): 2.2±1.8\textsuperscript{b}, 2.5±1.7\textsuperscript{ab}, 3.1±2.1\textsuperscript{b}, 4.5±0.3\textsuperscript{a}; 1.0±0.4\textsuperscript{a*}, 3.7±2.4\textsuperscript{b}, 3.6±1.6\textsuperscript{b}, 3.9±1.1\textsuperscript{b}. Insulin (µUI/L): 6.9±2.6, 8.6±3, 9.0±1.6, 7.9±3.6; 11.1±4.6\textsuperscript{a}, 12.5±4.0\textsuperscript{a}, 12.7±4.9\textsuperscript{b}, 13.9±5.6\textsuperscript{a}. Leptin (ng/mL): 10.3±5.5\textsuperscript{a}, 17.9±11.9\textsuperscript{b}, 23.9±6.5\textsuperscript{b}, 38.8±17.6\textsuperscript{b}; 9.9±6.3\textsuperscript{a}, 12.8±2.1\textsuperscript{ab*}, 22.2±10.7\textsuperscript{bc}, 27.5±6.9\textsuperscript{c}. CTX (ng/L): 433±203\textsuperscript{a}, 417±166\textsuperscript{a}, 562±13\textsuperscript{b}, 380±201\textsuperscript{a}; 355±177, 411±172, 360.7±197\textsuperscript{*}, 436±147; 25OHD (ng/mL): 22.9±8.1, 21.4±7.9, 20.0±7.3, 18.2±6.5; 22.4±8.0, 22.2±10.1, 16.4±2.9, 17.5±6.0. Conclusion, bone, fat and pancreas interrelationship in homeostasis glucose control would vary in women having MS. Grants PICT 2018 and PROINCE UNLaM.

**Stress fracture consolidation after the administration of teriparatide in a patient with osteogenesis imperfecta**

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Osteogenesis imperfecta (OI) is a hereditary connective tissue disease caused by genetic mutations of the genes that codify collagen type 1 (COL1A1 and COL1A2) and associated with bone fragility. Teriparatide (TPTD) [Human recombinant PTH 1-34] is an anabolic drug that has become a possible option for the treatment of the OI as well as for delayed fracture healing. Objective: Present a patient with OI type 1 accompanied by a stress fracture due to a severe deformation in the middle third of left femur, which shows evidence of consolidation after a three-months of administration of TPTD. Case presentation: A 58-year-old woman with diagnosis of Type 1 OI and a significant deformation of lateral shaft bowing of the left femur. On presentation, the patient reported pain in her left thigh; after stumbling while walking in the street, which was not relieved with NSAIDs administration. An X-Ray was performed due to pain persistence, showing a stress fracture in the middle third of the left femur. Treatment with 20 µg/day of subcutaneous (s.c) TPTD was initiated. After one month of treatment, the patient showed significant relief of pain, without progression of the fracture by the third month of application. At this point, the treatment was discontinued for economic issues. Due to the pandemic, a radiographic control was obtained after one year of treatment interruption, without showing a trace of fracture. Conclusion: TPTD has shown to be effective to improve stress fracture consolidation caused by femoral bowing deformation in a patient with OI. Further studies are required to confirm this result.
Vitamin D (VD) plays a role in immune response. Recent data shows that low levels of VD could worsen COVID-19 outcomes

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Aim: To establish an association between VD levels among COVID-19 patients with clinical outcomes and inflammatory markers. Methods: Prospective-multicentric-cohort Study. Consecutively recruitment. Patients were grouped according admission status and level of VD [sufficient >30 ng/ml (VDS), insufficient 20-30 ng/ml (VDI), deficient <20 ng/ml (VDD)]. The variables evaluated were age, gender, oxygen mask requirement (O2r), mechanical ventilation (MV), pre-existing comorbidities, inflammatory markers, severity of COVID-19 measured by News Score. Results: 363 patients were recruited (age 53±16), 59% male. 88% from total were hospitalized, whose VD levels were significantly lower than ambulatories (19±11 vs 24.3±14 ng/ml p=0.006). The amount between groups was VDS (15%), VDI (27%), VDD (58%).VD levels correlated negatively with hospitalization days and evolution time (p=0.045-p=0.043). Severity of COVID-19 adjusted by comorbidities was linked to a lower VD status (p<0.001) Also an association with pronation requirement among patients with lower VD levels (p=0.008) was observed. O2r risk was elevated among VDI (OR 2.9 CI95% 1.3-7) and VDD (OR 3 CI95% 1.4-6), multiplying the odds in 2.6 and 3.7 in presence of 1 or more comorbidities with a higher need of ICU in VDD groups (OR 4.8 CI95% 1.2-20). A negative relation between VD levels, basal ferritin and LDH was described (p=0.018 and p=0.045). Conclusion: Among COVID-19 hospitalized VD level was significantly lower than ambulatory patients. There is an association between low VD with a worse course of disease needing more days of hospitalization, thus lengthening the time of sickness. VDI and VDD group had severe forms of COVID-19. VDD presented a higher risk for ICU attention. Further studies are needed to emphasize the importance of adequate levels of VD to improve COVID-19 outcomes.

Inflammatory and microtomographic characterization of intramembranous post-tooth extraction bone healing in a rat model of hyposalivation

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Bone healing requires a synchronized inflammatory response for proper tissue repair. Alveolar wound healing is intramembranous and subjected to oral microbial challenge in the oral cavity. Saliva plays a key role in oral wound healing, which is affected by pathological conditions that cause decreased salivary flow. Nevertheless, the role of saliva in alveolar bone repair remains unclear. Aim: To explore inflammatory and histoarchitectural changes in intramembranous alveolar repair following tooth extraction in a model of hyposalxia induced by submandibular and sublingual gland excision (SMx). Methods: Male Wistar rats aged 21 days (n=48) divided into two groups: SMx (SMxG) and Control (CG). Under anesthesia, the rats were subjected to SMx and to bilateral extraction of the 1st upper molar 7 days post-SMx. They were fed a soft diet and euthanized (n=6) on days 3-7-14-30, following FOUBA CICUAL guidelines. Post-tooth extraction socket tissue was obtained for inflammatory mediator level assessment and microtomographic analysis. Data were analyzed by one-way ANOVA. Significance was set at *p<0.05.
Results: Comparison of CG vs. SMxG: TNFα = 3d (126.13±21.35 vs. *191.78±38.78); 7d (2.11±0.49 vs. *5.84±3.15). iNOS= 3d (52.58±10.34 vs. *74.83±13.46); 7d (2.11±0.49 vs. *5.84±3.15). Micro-
CT= BV/TV %: 14d (61.68 vs. *56.68); 30d (63.27 vs. *43.32); 30d (36.73 vs. *45.09). Conclusion: The lack of saliva in SMxG caused inflammatory changes during the first stages of alveolar wound healing, which could lead to the micro-CT findings observed in alveolar bone at the later study time points. UBACYT 2020 174BA.

Hypercalcemic crisis as first manifestation of parathyroid adenoma

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Hypercalcemic crisis (HC) is defined as the presence of serum calcium ≥14 mg/dl with multiple organ disturbances. HC is a life-threatening condition that requires early diagnosis and treatment (hydratation, calcitonin, bisphosphonates and hemodialysis) Parathyroid crisis is a rare complication of PHPT (primary hyperparathyroidism) rising suspicion of malignancy. Proven PHPT requires emergency surgery. A 75-yr-old woman was admitted because of vomiting, dehydration, and syncope. She presented a AV block with asystolia requiring CPR. Clinical chemistry assays revealed extreme hypercalcemia (>20 mg/dl), PTH 2740 pg/ml (VR: 15-65 pg/ml) and creatinine 2.2 mg/dl. Computed tomographic (CT) pulmonary angiography was performed to exclude pulmonary thromboembolism. Neck ultrasound informed multinodular goiter, right nodule (42x34x26 mm) and was negative for parathyroid localization. Tc-99m MIBI scan showed intense focal uptake inferior to the right thyroid lobe. During surgery no pathological parathyroid glands were found and hemithyroidectomy was performed suspecting intrathyroidal parathyroid, but pathology showed thyroid adenomatous hyperplasia. Due to severe persistent hypercalcemia dialysis was performed. CT images were revised. A retroesophageal lesion was observed and removed. Intraoperative decreased from 668 to 131 pg/ml. Pathology confirmed 3295 mg parathyroid adenoma. The patient presented transient hypocalcemia. One year post surgery she remains with normal calcium and PTH levels. Conclusion: severe hypercalcemia is a rare but urgent condition that requires prompt and multidisciplinary management. HC is an uncommon complication of PHPT. It is important to remark the pathological finding of a benign disease, the ectopic localization and dialysis as a tool for management of hypercalcemia.

Bilateral sclerosis of long bones due to non-Langerhans histiocytosis (Erdheim-Chester disease)

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Erdheim-Chester Disease (ECD) is a rare non-Langerhans' cell histiocytosis. It is a true systemic disease with almost constant bone involvement (up 96 %) and extrasosseous in 60% of the patients. The most common presenting symptom is bone pain. Extrasosseous involvement is highly variable and nonspecific, enforcing the diagnostic value of skeletal radiologic findings: sclerosis that occurs bilaterally and symmetrically in the diametaphyseal regions of long bones. Although the radiographic changes are considered virtually pathognomonic, definite diagnosis of ECD is established only once CD68(+), CD1a (−) histiocytes are identified within a biopsy specimen. We report a 58-year-old woman with confirmed ECD disease and 10-year follow up whose first symptom was bone pain. Plain radiographs of
long bones (femur, tibia, humerus and radius) showed osteosclerosis. They have asymmetric bilateral diaphyseal involvement with cortical thickening due to endocortical and subperiosteal bone accretion. Periostitis was observed as a wavy contour. Metaphysis were spared. Soon after diagnosis she was treated with IFN-a for 18 months and later with zoledronic (for 9 months, 4 mg monthly), with relief of skeletal symptoms. Follow-up was carried out with plain radiographs, bone scintigraphy and 18F-FDG PET/CT, showing no skeletal progression or extraosseous involvement. Conclusion: Presence of bilateral sclerosis exclusively in long bones should raise suspicion of ECD. The patient reported has some special features a) Exclusively bone involvement at 10 years of follow up b) Bilateral and non-symmetric involvement c) Endosteal and periosteal cortical sclerosis. d) Radiological signs that suggest periostitis d) Absence of metaphyseal involvement, which has been rarely described.

Vascular response to stress: protective action of the bisphosphonate alendronate

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Bisphosphonates are first-line drugs in the treatment of postmenopausal osteoporosis, a period in which the prevalence of cardiovascular diseases in women increases significantly. The aim was to study the effect of alendronate (ALN) on the vascular response to extracellular environmental stress. We focused on alterations in cell growth and migration patterns and the capacity for vascular repair by angiogenesis. Primary cultures of endothelial cells (EC) and vascular smooth muscle cells (VSMC) isolated from murine aorta were used. In order to induce stress conditions, cells were exposed to the pro-inflammatory agent LPS or incubated in a pro-osteogenic medium (OM). Using the MTT assay, we observed that 5 μM ALN totally or partially prevented VSMC proliferation induced by LPS (31% vs control, p<0.02) or OM (108% vs control, p<0.001), respectively. The mechanism of action of this effect involves MAPK, PKC or NOS participation. We also demonstrated that ALN did not modify the basal pattern of VSMC migration (wound healing technique). However, the simultaneous treatment with ALN, reversed the stimulation of cell migration induced by LPS or OM. In addition, ALN increases VEGF synthesis by EC (35.7% vs control, p<0.05) and enhances tube formation (5.34±0.48 vs 7.52±0.5 mm, control vs ALN, p<0.05) in a VEGF dependent manner, since the presence of the VEGF receptor antagonist SU5416 (1 μM), completely suppressed the angiogenic stimulus of ALN. Vascular stress conditions did not affect the proangiogenic action elicited by ALN. In summary, the results presented suggest that, under stress conditions, ALN exhibits a protective action on vascular homeostasis, preserving cell growth and mobility patterns and promoting angiogenesis.

Calcium absorption and bone retention in a model of growing rats: effect of feeding an experimental yogurt-reduced in lactose-containing galactooligosaccharides (GOS).

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GOS are natural prebiotic of maternal milk. They can be enzymatically synthetized in yogurt manufacture from milk lactose obtaining a dairy product reduced
in lactose containing prebiotics and potentially probiotics. It was evaluated if this yogurt containing GOS and reduced in lactose (EY) offered some extra advantages as compared to a regular yogurt (RY) in calcium (Ca) and phosphate (Pi) absorption (Abs) and bone retention during normal growth. Male weaning rats received control diet (C), EY or regular yogurt (RY) during 28 days. Results showed no differences in food consumption and body weight between C and yogurts groups. EY showed the highest increase in fecal lactobacillus colonies, in short chain fatty acids production especially propionate and butyrate, in large intestinal crypt deep, and the lowest caecum pH, CaAbs% increased significantly as follows: EY>RY>C (p<0.05); PiAbs% was higher in EY vs. RY. Femur Ca and Pi content, bone mineral content, density and biomechanical parameters were similar in EY and C but lower in RY (p<0.05). The epiphyseal and hypertrophic cartilage widths were lower in EY and RY than in C (p<0.05) while total cartilage width was similar in EY and C. Conclusion: EY reduced in lactose increased mineral Abs attaining C group bone retention and quality while RY diet consumption did not achieve bone growth and quality of C group. Then EY would be a good strategy to attain an adequate peak bone mass during growth, especially in lactose intolerant subjects. Grant of UBACyT and CONICET.

**Osteoporosis in men: DXA scans in Mendoza, 2004-2019**

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DXA scans should be performed in all men aged 70 or older and those aged 50 to 69 with fracture risk factors. In Argentina, men account for 28% of hip fractures. We analyzed requests for DXA scans from Greater Mendoza between 2004 and 2019, to find out whether there is a growing awareness of the impact of male osteoporosis. The database of our densitometry service was reviewed. Total number of studies per year was determined and the proportion of female and male patients at or above 50-year-old. Male patients were classified according to the T-score of the lumbar spine and proximal femur as normal, low bone mass or osteoporosis. The evolution of the total DXA studies and those carried out in men was statistically analyzed. A total of 93,659 studies were carried out, of which 4.4% (4166) were men. Of these, 1,333 subjects (32%) were normal, 1,625 (39%) had low bone mass, and 1208 (29%) had osteoporosis. In 71% of the men (2958), at least one risk factor was identified, among them smoking (32%), low-impact fractures (25%), and glucocorticoids (18%). Other factors were present in 9%. About 14% had two or more risk factors. The trend in the total number of studies grew linearly until 2010, and then flattened out as the operational capacity was approached. Studies requested in men increased (p=0.0003 in linear regression). However, the fraction carried out in men did not change significantly, with a range from 2.9% in 2012 to 6.8% in 2014 and an average of 4.4% for 2004-2019. In Greater Mendoza there are about 200,000 people over 50 years of age, of which 43% are men. However, only 4.4% of DXA scans are performed in males. The results suggest that physicians’ attitude regarding osteoporosis in men has not changed in the last 16 years. Further teaching and clarification are clearly required on this issue.

**Spurious hypocalcemia due to interference with leflunomide**

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Calcemia has to be in a narrow range to allow optimal activity of metabolic functions. 50% of calcium circulate as ionized calcium (Ca-i).
Hypocalcemia is defined by an albumin-corrected calcium or Ca-i value below the normal range. This is a case report of falsely decreased Ca-i values due to interference by leflunomide. Case: an 82-year-old woman was hospitalized for bacterial endocarditis and urinary infection. She had rheumatoid arthritis treated with leflunomide 20 mg/day, ergocalciferol 16800 IU/week and calcium citrate 1905 mg/day. Laboratory: Ca-i 0.77 (NR 1-1.35 mmol/l), calcium 9.0 mg/dl (8.5-10.5 mg/dl), phosphatemia 3 mg/dl (2.5-4.5 mg/dl), PTH 55 pg/ml (9-77 pg/ml), Vitamin D 25 ng/ml (>30 ng/ml). She started Intravenous calcium gluconate reposition. Ca-i remained low (0.79 mmol/l), while calcium corrected for albumin was still normal (9.9 mg/dl) so the IV supply was suspended. She persisted with decreased Ca-i (0.86 mmol/l) with normal calcemia (9.1 mg/dl). Given this discordance and the asymptomatic condition without causes of hypocalcemia, an interference was suspected. Ca-i was normal (1.08 mmol/l) measured with another equipment (Diestro), interpreting that it was an analytical interference in the initial measurements (Rapidlab-1265). Discussion: Patients treated with leflunomide may present falsely low Ca-i values depending on the analyzer used. Dissociation between Ca-i and total levels allowed us to suspect the possibility of analytical interference, which was confirmed by measuring Ca-i with other equipment. There are few reports of factitious hypocalcemia due to this mechanism. We consider it is important to report this event to avoid unnecessary diagnostic studies and treatments in patients treated with leflunomide and Ca-i below the reference range.

Osteopathia striata with cranial sclerosis and renal carcinoma

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Osteopathia striata with cranial sclerosis (OSCE) is a rare skeletal dysplasia (incidence <1/10000) caused by WTX gene mutation on the X chromosome (AMER1), a WNT signaling repressor. The clinical presentation is highly variable. Typical manifestations are longitudinal striations in the metaphysis of long bones, craniofacial sclerosis, macrocephaly, cleft palate and hearing loss. As aberrant activation of WNT signaling promotes tumorigenesis, AMER1 is considered a tumor suppressor gene. The association of this entity with Wilms tumor and other neoplasms has been reported in the literature. We present a patient with OSCE and clear cell renal carcinoma. Case: a 76-year-old woman was hospitalized with paraparesia and dysphonia. Medical history: OSCE, total thyroidectomy for benign nodular pathology, cataracts, heart failure, atrial fibrillation, hearing loss and diabetes. She had no known family history of OSCE. Bone alkaline phosphatase was increased 20 μg/L (3-14.5). Rx: generalized osteosclerosis with linear striae. MRI: dorsal fracture (D4), expansive lesion that involves the vertebral body and pedicles with medullary compression. CT: osteolytic lesions, pathological vertebral fracture, neoformative image in the left kidney and expansive perilaryngeal lesion. Dorsal decompression was performed. The pathological anatomy reported bone metastases of clear cell renal cell carcinoma and the cervical lesion showed carcinoma infiltration. Conclusion: OSCE is a rare disease and association with neoplasms particularly Wilms tumor has been described. Our patient has OSCE and a clear cell renal carcinoma. There are no reports in the literature of this association. More studies are required to elucidate the pathogenesis and establish screening recommendations in patients with this pathology.
Intermediate osteopetrosis: a case report

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Osteopetrosis (OPT) is a heterogeneous group of rare bone diseases characterized by reduced osteoclastic resorption and high bone mass. It is classified as autosomal recessive infantile (malignant), autosomal dominant adult (benign) and intermediate OPT, a third group, typically with short stature, cranial nerve defects and recurrent fractures. Clinical case: a 20-year-old woman with diagnosis of OPT in childhood and more than 30 low-impact trauma fractures for 2 years of age. She has strabismus and nystagmus. She has no history of kidney stones, jaw osteomyelitis or corticosteroid therapy. Her parents are of european origin, healthy and not consanguineous. She has other relatives with osteosclerosis. Physical examination: normal weight, short stature, bilateral nystagmus and absence of facial dysmorphism. Laboratory: hemogram, calcium, phosphatemia, creatinine and acid base status within normal ranges; vitamin D 9 ng/dl (30-50), PTH 39 pg/ml (9-77), βCTX 0.26 ng/ml (0.092-573), osteocalcin 7.4 ng/ml (11-46) and CPK 522 IU/L (30-145). Rx: generalized increase in bone density, widened femoral metaphysis adopting Erlenmeyer flask morphology and vertebral platform sclerosis. DXA: Z-score +13.4 in lumbar spine and +11.8 in total hip. She presented a low trauma proximal femur fracture in 2017. She evolved with pseudoarthrosis and periprosthetic fractures, requiring multiple interventions. She was treated with vitamin D, magnesium citrate and calcitriol. Calcemia and calciuria remained within the normal range. Fracture consolidation was achieved, she had no further fractures and currently walks unaided. We present a clinical case of intermediate OTP and recurrent fractures treated with calcitriol. Other options as interferon gamma 1b and bone marrow transplantation have been described in this entity.