that exert anticontractile effect in health individuals. Despite sexual dimorphism on PVAT morphology, it is still unknown whether or not there is sex differences in the PVAT modulating vascular function in the setting of obesity. Aldosterone-mineralocorticoid receptor (MR) signaling pathway has been demonstrated to be adipogenic and proinflammatory in classical fat depots and treatment with MR antagonists (A) might reverse vascular dysfunction and remodeling in obese models, especially in female sex. Therefore, we aimed to evaluate the anticontractile effect of PVAT in male and female obese mice and hypothesized that MR signaling would be involved in possible sex differences in PVAT dysfunction in obesity. Male and female C57Bl6/J mice were fed a chow or a high-fat diet (HFD, 60% energy from fat) for 20 weeks. At the last 4 weeks of HFD, female and male mice were treated with the MRA spironolactone (Spi, 100 mg/kg/day). HFD feeding significantly increased body weight and visceral adipose tissue, which was not modified by Spi treatment in both sexes. Resistance mesenteric arteries were isolated with or without PVAT and mounted in a wire myograph to evaluate vascular contractile responses. Lean male and female mice PVAT had an anticontractile effect in the response to phenylephrine that was greater in females than males. The anticontractile effect of PVAT was significantly impaired in obese females but not modified in males. HFD-induced dysfunctional PVAT was prevented by Spi treatment in females. Next, we evaluated the protein expression of aldosterone-synthase CYP11B2, serum and glucocorticoid-regulated kinase 1 (SGK1), and epithelial sodium channel subunits (ENaCs) in isolated mesenteric PVAT of lean and obese male and female mice. There was an increased expression of CYP11B2, SGK1 and ENaCs only in obese female PVAT. Protein expression of adiponectin, a major PVAT-released adipokine was also increased in female mesenteric PVAT. In conclusion, the findings suggest sexual dimorphism in PVAT function in health and in obesity. Although anticontractile role of PVAT was exacerbated in lean female mice, female sex was more susceptible to develop PVAT dysfunction in the setting of obesity which was prevented by MR blockade. HFD-induced PVAT dysfunction in females was associated with increased expression of SGK1 and ENaCs. Therefore, data suggest MR activation as a mechanism mediating sex differences in PVAT dysfunction.

FAPESP, CAPES.

Bone and Mineral Metabolism
BONE AND MINERAL CASE REPORTS II
Bisphosphonate Related Ocular Inflammation
Kavita Seetharaman, MD.
Newton Wellesley Hospital, Newton, MA, USA.

MON-LB67
Bisphosphonate related ocular inflammation
Introduction: Osteoporosis is a major public health problem, increasing in incidence with the growth of the aging population. It affects over 200 million women worldwide and is associated with fragility fractures leading to increased morbidity, mortality and poor quality of life (1). Bisphosphonates are among the most widely used first line forms of treatment for management of osteoporosis. They have a structure like pyrophosphate and inhibit bone resorption by attaching to hydroxyapatite binding sites on the bone in areas with active resorption. While initiating treatment with bisphosphonates, endocrinologists generally discuss side effects including gastrointestinal symptoms related to gastroesophageal reflux disease and gastritis, acute phase reactions related to infusion of the bisphosphonates, musculoskeletal pain, hypocalcemia, osteonecrosis of the jaw, and atypical femur fractures. There are rare but severe side effects causing ocular inflammation related to bisphosphonate use.

- Bisphosphonate Related Ocular Inflammation (BROI).

While these are rare based on few case reports, they are...
significant side effects, which if patients are not aware of or not addressed in timely manner can result in vision loss. We report a clinical scenario of a patient who experienced bisphosphonate-related ocular inflammation.

**Clinical History:** 62-year-old female with cerebral palsy presented to the emergency room with 1 day of marked left eye redness and swelling. When the symptoms began, she felt that her eye was itchy. She had mild left eye discomfort. She did not perceive any decreased visual acuity. Patient had her first infusion of bisphosphonate, 4 days prior to the emergency room visit. **On Exam:** She was alert, no apparent distress, left eyelids were swollen, almost completely shut with minimal discoloration, there was underlying severe chemosis and conjunctival redness, pupils equal and round, visual acuity 20/100 OD and 20/100 OS. She was diagnosed with allergic conjunctivitis, and advised to apply Tobradex drops and Diphenhydramine, and to follow-up in eye clinic. Scleritis related to bisphosphonates was also considered as a possible cause of her symptoms. The patient called the endocrinologist about the eye symptoms the following day. The endocrinologist also raised the possibility bisphosphonate related ocular inflammation and advised to be seen in ophthalmology clinic urgently. The endocrinologist also communicated with the ophthalmologist indicating that her eye symptoms could be due to inflammatory response related to bisphosphonates and to consider starting systemic steroids.

The patient was seen in ophthalmology clinic the following day: The ophthalmology exam revealed severe orbital inflammation with conjunctival chemosis OS: Table 1. She was started on Prednisone 80mg a day with tapering by 10mg daily over the next 2 weeks. She was also advised to apply Durezol eye drops twice a day. She was referred to Oculoplastics for further evaluation. **Table 1:** Oculoplastics evaluation next day Table 2: Revealed orbital inflammation with good initial response to steroids and advised to continue prednisone taper.

**Table 2:** On the 2 weeks follow up: Table 3: Resolved orbital inflammation and was advised to stop prednisone

**Table 3:**

**Clinical Discussion:** Bisphosphonates are widely prescribed and effective forms of treatment for osteoporosis in preventing fractures. Ocular side effects are rare but reported over the past 2 decades (2). First time users of bisphosphonates are at a higher risk compared with nonusers (3). There is also an association of bisphosphonate-related ocular inflammation (BROI) with coexisting inflammatory conditions that associated with ocular inflammation, such as rheumatoid arthritis, ankylosing spondylitis, psoriasis, inflammatory bowel disease, systemic lupus erythematosus or sarcoidosis (4,8). Symptoms related to BROI typically occur within 24 to 72 hours of the bisphosphonate exposure but can range between few hours to 3 years. Those who receive systemic bisphosphonates present earlier compared to orally administered bisphosphonates (5,6,7). In prior case reports, patients presented with flu like symptoms, lasting for lasting for 24 to 72h prior to onset of orbital disease (5). The range of ocular inflammation is variable, and can include conjunctivitis, uveitis, scleritis, episcleritis and keratitis. The symptoms can be unilateral or bilateral. Discontinuation of bisphosphonates is necessary for resolution of ocular inflammation (7). The postulated cellular mechanism causing BROI is as follows: Bisphosphonates are secreted into the lacrimal system, and induce an inflammatory response resulting in release of cytokines that results in ocular inflammation: Fig 1: (9).

**Fig 1:** It is unclear as to why BROI is a rare side effect, though related to release of inflammatory reactants, which are also responsible for the more common flu like side effect. The risk of BROI is increased in those with associated inflammatory condition (arthritis or inflammatory bowel disease). It is possible that in individuals susceptible to inflammatory disorders, there is pre-existing infiltration of the lacrimal gland with mononuclear cells which causes a robust local inflammatory response to bisphosphonate treatment in the eye.

Our patient with cerebral palsy and learning disability, was taken to the emergency room within few hours of onset symptoms and signs of ocular inflammation. Though she was diagnosed with severe orbital inflammation, she did not express eye pain, which is commonly seen in scleritis. Through multidisciplinary teamwork between the emergency physician, endocrinologist, ophthalmologist and oculoplastic specialists, she was promptly started on systemic steroids and her symptoms resolved completely with no vision loss.

While considering bisphosphonates as an option for osteoporosis treatment, the endocrinologist should discuss the rare but serious complications of BROI. With use of bisphosphonates in the aging population to treat osteoporosis, specific attention should be given to underlying eye disease, inflammatory conditions, and cognition.

**References:**

1. IOF statistics: (https://www.iofbonehealth.org/epidemiology).
2. Clark EM, Durup D. Inflammatory eye reactions in patients treated with bisphosphonates and other osteoporosis medications: what are the risks?. Ther Adv Musculoskelet Dis. 2015;7(1):11–16. doi:10.1177/1759720X14566423.
3. Tamman M, Foroughian F, Maberley D. Inflammatory ocular adverse events with the use of oral bisphosphonates: a retrospective cohort study. CMAJ. 2012;184(8):E431–E434. doi:10.1503/cmaj.1117524.
4. French DD, Margo CE. Postmarketing surveillance rates of uveitis and scleritis with bisphosphonates among a national veteran cohort. Retina. 2008 Jun;28(6):889-93. doi: 10.1097/IAE.0b013e31816576ef.
5. Herrero I, Kam Y, Whittaker TJ, Champion M, Ajlan RS. Bisphosphonate-induced orbital inflammation in a patient on chronic immunosuppressive therapy. BMC Ophthalmol. 2019;19(1):51. Published 2019 Feb 14. doi:10.1186/s12886-019-1063-86. Ehsan Rahimy, Simon K. Law. Orbital inflammation after zoledronate infusion: an emerging complication. https://doi.org/10.1016/j.jcjo.2012.09.011 7. Frederick W. Fraunfelder, M.D Bisphosphonates and Ocular Inflammation. NEnglJ Med 2003; 348:1187-1188. DOI: 10.1056/NEJM2003032034812258. Pazianas M, Clark EM, Eiken PA, Brixen K, Abrahamsen B. Inflammatory eye reactions in patients treated with...
biphosphonates and other osteoporosis medications: cohort analysis using a national prescription database. *J Bone Miner Res.* 2013 Mar;28(3):455-63. doi: 10.1002/jbmr.1783.9.Keith Thompson and Michael J. Rogers. New Insights into Old Drugs. BoneKEy-Osteovision. 2006 August;3(8):5-13

### Healthcare Delivery and Education

**EXPANDING CLINICAL CONSIDERATIONS FOR PATIENT TESTING AND CARE**

**Relationship Between Obesity-Induced Metabolic Abnormalities and Nutrient Intake: Sex Differences in Japanese University Students**

Mayumi Yamamoto, MD, PhD, MBA, 1 Mausam Mehta, BS, 2 Akihiro Nishio, MD, PhD, 1 Ryo Horita, PhD, 1 Ricardo Izurieta, MD, Dr.PH, MPH. 3

1Gifu University, Gifu, Japan, 2Morsani College of Medicine, University of South Florida, Tampa, FL, USA, 3College of Public Health, University of South Florida, Tampa, FL, USA.

**MON-LB310**

Background: Preventive measures and interventions for obesity in young adults are urgently needed. However, evidence-based guidelines for interventional programs in this generation have not been established worldwide because of limited access to data on this group. To establish effective methods of obesity prevention in young adults, we analyzed the relationship between nutrient intake and obesity-related metabolic factors in each body mass index (BMI) group among Japanese university students. Methods: A cross-sectional analysis was performed using annual health checkup data, which is conducted mandatory for all students according to the School Health and Safety Act in Japan, from Gifu University’s incoming class of 2017. Nutrient intake information was obtained from the brief-type self-administered diet history questionnaire (BDHQ), which has been adjusted and validated for the Japanese population. Inclusion criteria were aged 18-30 years and completed the self-administered diet history questionnaire (BDHQ), which has been adjusted and validated for the Japanese population. Inclusion criteria were aged 18-30 years and completed the all examination items including BDHQ. From a total of 1277 students’ data, 1202 satisfied and were included in the analyses (participation rate: 94.1%). Nutrition and metabolic data were compared among BMI groups (lean, <18.5 kg/m²; normal, 18.5-24.9 kg/m²; obese, ≥25.0 kg/m²), according to criteria of the Japan Society for the Study of Obesity (2002) using one-way analysis of variance with post-hoc Tukey honestly significant difference analysis in SPSS software version24 (IBM Corporation, Armonk, New York). Results: The percentage of obesity was 8.1% in men and 1.4% in women, showing a significant difference. Among men, BMI groups were significantly different in the intake of 11 nutrients which were protein, fat, saturated fat, cholesterol, omega 3 and 6 fatty acids and micronutrients K, Mg, P, Fe, and Zn, significantly high in nine metabolic parameters, which were blood glucose, hemoglobin A1c, uric acid (UA), aspartate aminotransferase (AST), alanine aminotransferase (ALT), systolic and diastolic blood pressure (BP), low-density lipoprotein (LDL) cholesterol, triglycerides (TG) and significant low in high-density lipoprotein (HDL) cholesterol among obese group. Among women, BMI groups were not significantly different in nutrient intake, significantly high in five metabolic parameters, which were UA, ALT, systolic BP, LDL, and TG, and significant low in HDL among obese group. Conclusion: This study suggested that the effect of obesity on metabolic abnormalities in Japanese university students may be more remarkable in men than in women. This sex difference might be partially explained by the significant increase in protein and fat intake in obese men. For women, other factors may contribute to obesity and metabolic abnormalities. Education for appropriate volumes of nutrient intake could be effective in male university students.

### Thyroid

**THYROID CANCER CASE REPORTS I**

**Coexisting Malignant Struma Ovarii and Cervical Follicular Variant Papillary Thyroid Carcinoma**

Jubran Afzal Khan Rind, MBBS, Zeb Ijaz Saeed, MD.

1Indiana University, Indianapolis, IN, USA, 2IU Health Physicians, Indianapolis, IN, USA.

**SUN-LB81**

A 44-year-old woman presented with left lower quadrant abdominal pain for 2 months. Further evaluation revealed a left adnexal mass and she underwent a TAH-BSO. A 12 cm mass arising from the left ovary was resected which on microscopy appeared to be papillary thyroid carcinoma follicular variant arising from a mature teratoma (struma ovarii). A thyroid ultrasound showed two subcentimeter right thyroid nodules without any concerning lymphadenopathy. A total thyroidectomy was then performed to allow her to receive adjuvant RAI. The cervical thyroid pathology showed a 0.6 cm follicular variant papillary thyroid carcinoma with negative margins without angioinvasion, lymphatic invasion or extrathyroidal extension. Thyroid hormone suppression with levothyroxine was started. Preoperatively, thyroglobulin was 1381 ng/ml (nl range 1.3-31.8 ng/ml). After TAH-BSO and thyroidectomy, thyroglobulin was undetectable and so was the anti-thyroglobulin antibody. With an undetectable thyroglobulin level, it was decided not to pursue adjuvant RAI and continue TSH suppression with levothyroxine. Simultaneous existence of malignant struma ovarii and cervical papillary thyroid cancer is rare and has a favorable prognosis compared to metastasis to the ovaries from primary cervical thyroid papillary carcinoma. Due to the rarity of this condition, management is not clear or well supported by evidence. Various approaches are suggested by different authors, including thyroidectomy after resection of malignant struma ovarii to facilitate adjuvant RAI, only performing surgical resection of the ovarian tumor in the absence of high risk features or performing thyroidectomy and RAI only in metastatic or recurrent disease. References:1.Aaron Leong, Philip J. R. Roche, Miltiadis Palouras, Louise Rochon, Mark Trifiro, Michael Tamila, Coexistence of Malignant Struma Ovarii and Cervical Papillary Thyroid Carcinoma, The Journal of Clinical Endocrinology & Metabolism, Volume 98, Issue 12, 1 December 2013, Pages 4599-46052.Synchronous malignant struma ovarii and papillary thyroid carcinoma Pablo Fernández Catalina, Antonia Rego Ines, Mónica Lorenzo Solar, Paula Sánchez Sobrino DOI: 10.1016/j.endo.2016.08.006