of cryptorchidism; (ii) the presence of a completely definable genetic cause for the disease; (iii) the presence of a complete CHH form. No significant association was found with the cumulative dose of hCG administered in 24 months. The statistical analyses regarding SA could not find the same associations. Multiple regression analyses investigating the eunuchoid habitus and a measure of the difference of subject’s final height from his target (deltaSDSth), showed a significant association with: (i) age at the beginning of the induction; (ii) the duration of growth during induction; (iii) and (for deltaSDSth) bone age before the induction. Duration of growth during induction resulted to be associated with previous testosterone priming and with partial CHH. In summary, our study confirms cryptorchidism and complete genetic forms of CHH as negative predictors of testicular response probably because they usually affect early phases of life with a complete GnRH deficiency. We also found that the eunuchoid habitus and deltaSDSth are associated not only with delayed treatment, but also with the duration of stature growth during the induction, apparently related to earlier androgenization.

Neuroendocrinology and Pituitary
ADVANCES IN NEUROENDOCRINOLOGY

PROKR2 Neurons of the Amygdalohippocampal Area in Reproductive Function

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SUN-253
Kallmann Syndrome (KS) is characterized by infertility and anosmia due to deficiency in gonadotropin releasing hormone (GnRH) neuronal migration and olfactory bulb dysgenesis. Genetic studies have revealed that KS is caused by loss-of-function mutations in several genes including the prokineticin receptor 2 (PROKR2) gene (Abreu et al., 2008, Hardelin & Dode 2008). Mice with global deletion of Prokr2 replicate the phenotype of KS patients (Ng et al., 2005, Matsumoto et al., 2006). Whereas the role of PROKR2 during development is defined, little is known about PROKR2 neurons in adult reproduction. PROKR2 mRNA are highly expressed in reproductive control sites of the adult mouse brain (Cheng et al., 2006). Previous studies in our lab found PROKR2 mRNA and Prokr2-Cre GFP+ cells highly expressed in the amygdalohippocampal area (AHi, also called posterior nucleus of the amygdala) in a sexually-dimorphic pattern. Male mice have higher PROKR2 expression in the AHi compared to female mice (Mohsen et al., 2017). The amygdala is an important site of socio-sexual inputs and reproductive neuroendocrine responses in rodents and primates, including humans. We hypothesize Prokr2-Cre neurons in the AHi have a role in both male and female reproductive function. Using genetic tracing techniques, we mapped AHi Prokr2-Cre neuronal projections in both male and female mice and found dense innervation to reproductive control sites such as the medial preoptic area and the ventral premammillary nucleus in a sexually dimorphic pattern. A soiled bedding exposure test in sexually experienced male mice showed that an estimated 45% of cFos + cells in the AHi express Prokr2-Cre GFP. Dense sex steroid receptors expression was observed in AHi Prokr2-Cre GFP neurons of both male and female mice. Our preliminary data suggests AHi Prokr2-Cre neurons have a reproductive function in male and potentially also in female mice. Future studies will focus on selective activation and inhibition of these neurons using chemogenetic technology to determine putative inputs to brain sites that control the hypothalamo-pituitary-gonadal axis. We expect our studies will contribute to the understanding of the role of PROKR2 neurons in adult reproduction and reproductive deficits associated with PROKR2 mutations.

Neuroendocrinology and Pituitary
CASE REPORTS IN UNUSUAL PATHOLOGIES IN THE PITUITARY II

Pleotropic Clinical Presentation in Two Brazilians Patients with Confirmed IgG4-Related Hypophysitis

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MON-264
Background: Hypophysitis is a rare condition characterized by inflammation of the pituitary gland, usually resulting in hypopituitarism and pituitary enlargement with mass effect symptoms. IgG4-related hypophysitis can occur alone or as part of a multiorgan disease. Treatment with glucocorticoids is effective in 97% of the cases in reducing pituitary mass.

Clinical cases: Case #1. A 56-yrs man with previous diagnosis of Mikulicz syndrome was referred to our service with fatigue and erectile dysfunction. Laboratory evaluation revealed hypogonadotropic hypogonadism, hyperprolactinemia (PRL=108 ng/mL) and central hypothyroidism. Sellar MRI depicted a pituitary mass with pituitary stalk thickening and a homogeneous uptake of gadolinium. During clinical follow-up, he also presented retroperitoneal fibrosis and IgG4-related disease was confirmed by serum IgG4 elevation and a pathological review of the previous salivary gland biopsy. Prednisone 80 mg/d treatment was initiated, with recovery of the thyrotrophic axis, reduction of PRL levels and significant reduction of the pituitary lesion. Due to maintenance of inflammatory activity and worsening of renal function, azathioprine therapy was associated, with subsequent inclusion of rituximab. Case #2. A 16-yrs boy was referred to our service presenting severe headache, bilateral visual deficit, right eyelid ptosis, hyposmia, polyuria and polydipsia. Cranial MRI depicted an extensive skull base mass involving pituitary gland, optic nerves, cavernous sinuses, olfactory bulb and clivus. Hormonal evaluation confirmed normoprolactinemia, hypogonadotropic hypogonadism and diabetes insipidus. Biopsy of the lesion revealed meningeal inflammation with IgG4 elevation and a pathological review of the previous biopsy revealed meningeal inflammation with IgG4 elevation and a pathological review of the previous biopsy. Inclusion of rituximab led to reduction and gonadotropic axis recovery occurred after...
40 days of prednisone 60mg/d. After the drug withdrawal, methotrexate was introduced. However, after three years, headache and hypoaemia recurred. A new MRI revealed increase of lesion and mycophenolate and rituximab were iniciated, with clinical improvement without recurrences over time.

**Conclusion:** Although a rare disease, IgG4-related disease should be included in the differential diagnosis amongst pituitary masses, with or without other affected organs. Immunosuppression with corticosteroids is the first treatment choice and other alternatives must be used in case of persistence of disease activity or relapse. These are very few Brazilian patients reported with IgG4 related disease. We described two cases with IgG4-related hypophysitis: one young patient, without involvement of other organs and another of middle age with systemic involvement, reinforcing the pleotropic clinical picture. Both required rituximab therapy due to disease progression.

**Adrenal**

**ADRENAL - HYPERTENSION**

**A Single-Center Experience of Patients with Metastatic Pheochromocytoma/Paraganglioma Treated with 177Lu-DOTATATE**

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**MON-196**

The prevalence of metastatic pheochromocytoma/paraganglioma (PPGL) is reported to be 3% to 36% of all the cases. The five-year overall survival rate of such patients ranges from 40 to 77%. The management of metastatic PPGL is challenging taking into account the fact that the optimal strategies for clinical care beyond surgical resection are not guided yet. Peptide receptor radionuclide therapy (PRRT) using somatostatin analogues is effective in other neuroendocrine tumours, can be indicated in patients with positive scans for the respective radiopharmaceuticals. We report preliminary data of the prospective study aimed to assess the safety and efficacy outcomes of 177Lu-DOTATATE for 6 patients with histologically confirmed PPGLs with metastatic progression after the complete PPGL surgery. The mean age of our cohort was 53 years (range 14–73); an equal number of male and female patients was included. Two of them had germline mutations in RET and SDHB genes, respectively. Radiological response utilized RECIST 1.1 criteria; toxicity was graded according to common terminology criteria for adverse events version 4. PRRT scheme varied between three and four cycles. Partial response (PR) was achieved in one and stable disease (SD) in four patients. One patient had treatment refractory with disease progression and dramatic increase of chromogranin A concentration (+268%). Biochemical response (>50% decrease) of chromogranin A was found in 1/6 patients and of catecholamines in 2/6 patients. No hematological or kidney toxicity grade 3–4 was registered.

Median overall survival and median progression-free survival rate will be reported after the end of the study. To date, about 250 PPGL patients have been treated with PRRT. PRRT using 177Lu-DOTA-SSAs has shown promise for treatment of PPGLs with improvement of clinical symptoms and/or disease control in the setting of retrospective small case reports or case series. However, more well-designed prospective studies are required to confirm these findings.

**Cardiovascular Endocrinology**

**PATHOPHYSIOLOGY OF CARDIOMETABOLIC DISEASE**

**The Associations Between p,p’-DDE Levels and Serum Levels of Lipoproteins and Their Subclasses in an Elderly Population Determined by Lipidomics Analysis**

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**SUN-571**

Low biodegradability and high lipophilicity of p,p’-dichlorodiphenyldichloroethylene (DDE), a metabolite of the insecticide DDT, leads to transport with lipids and accumulation in adipose tissue. This persistence allows for DDE to effect adipose tissue and lipid metabolism. A few small human studies have shown an association between DDE and blood lipids, although with some inconsistent conclusions. The aim of this study was to investigate the association between DDE exposure and altered levels of circulating lipids in a large human cohort. To evaluate the associations between DDE and human lipid profiles, plasma was collected from a subset of elderly Swedes in the Prospective Investigation of the Vasculature of Uppsala Seniors (PIVUS) cohort who were free from lipid lowering medication (n = 571). DDE concentrations in plasma were measured using high-throughput solid phase extraction and gas chromatography-high resolution mass spectrometry. Lipidomic analysis of plasma was performed with nuclear magnetic resonance spectroscopy. Linear models of lipids and DDE were statistically adjusted for sex and body mass index. Detectable levels of DDE were found in the plasma samples of all subjects. With elevated DDE levels, the comprehensive lipoprotein profile showed an elevation in total concentration of all diameters of very low density lipoprotein (VLDL) (p<0.001), low density lipoprotein (LDL) (p<0.008), intermediate density lipoprotein (IDL) (p<0.02), and in small high density lipoprotein (HDL) (p<0.05). Triglycerides and DDE were associated to varying degrees in lipoproteins (IDL > VLDL > LDL > HDL) and within total serum (p<0.005). DDE levels were positively associated with cholesterol and cholesterol ester levels only in VLDL and LDL (p<0.05) and with apolipoprotein B (p<0.0009). The positive associations observed between each lipoprotein class and elevated DDE support previous data suggesting that DDE interacts with lipoproteins within plasma. We speculate that both physio-chemical and biological mechanisms may explain why DDE does not uniformly associate with lipids across lipoproteins.