by levels> 3.8 mg/dL. Hypo and hypermagnesemia cases were considered according to age, gender, year of observation and setting of subjects including outpatients and inpatients. In particular, inpatients were recruited from a total of 25 Hospital Divisions (i.e. Cardiology, Endocrinology, Geriatrics, Hematology, Intensive Care, Internal Medicine, Infectious Disease, Nephrology, Neonatal Intensive Care, Neurology, Neuropsychiatry, Neuroradiology, Oncology, Pulmonology, Pediatrics, Psychiatry, Rheumatology and Surgical Area that included 8 Units). Over the observation period, we recognized 12,696 patients whose Mg levels were checked. Prevalences of hypomagnesemia and hypermagnesemia were 8.43% (n=1071) and 1.78% (n=226) respectively. Hypomagnesemia was encountered more frequently in female [53.3% (n=560)] rather than in male patients [47.7 % (n=511)] ($\chi 2$= 4.03, p<0.045) and was significantly influenced by age: the higher prevalence of hypomagnesemia was found in patients over 65 yr. [59.01% (n=632)], whereas a lower prevalence was detected in the other age groups, specifically in 9.52 % (n=102) of patients aged 0-18 yr. and in 31.46 % (n=337) of patients between 19 and 65 yr. ($\chi 2$= 592.64; p<0.0001). Incidence of hypomagnesemia decreased over time with a borderline significance only in subjects over 65 yr. (r=-0.99; p=0.07). Geriatrics, Oncology and Intensive Care Division showed the highest incidences of hypomagnesemia. The hypermagnesemia prevalence was observed higher in outpatients in comparison with inpatients from any other Hospital Division and the hypermagnesemia incidence did not significantly change over time (r=0.96; p=0.16). Mg disorders, mainly hypomagnesemia, are quite common in clinical practice particularly in older hospitalized patients. Among the other electrolytes' disturbances, Mg disorders, because of life-threatening significances, may be checked and corrected.

Adrenal

ADRENAL CASE REPORTS II

Adrenal Crisis in Early Pregnancy

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SUN-164

Nausea and vomiting are common symptoms in pregnancy, ranging from occasional nausea to fulminant and intractable vomiting. Many underlying metabolic disorders can mimic this, primary adrenal insufficiency (PAI) being one of them. Here, we present a case of adrenal insufficiency early in pregnancy.

A 28 year old lady G1P0 at 8 weeks of gestations, with a past medical history of Grave's Disease, presented to our hospital on 3 occasions over one week with severe intractable nausea and vomiting. On prior visits, she had received intravenous fluids and discharged home. Laboratory work-up was ordered on the third visit and she was found to have severe hyponatremia with level of 111mMol/L. TSH and FT4 levels were both within the reference range. AM cortisol level was low at 2.3mcg/dL. ACTH and renin were both significantly elevated confirming diagnosis of PAI. Intravenous hydrocortisone was commenced immediately with rapid resolution of her symptoms and correction of her hyponatremia. She was followed at the endocrinology clinic, with appropriate up-titration of glucocorticoid and mineralocorticoid doses throughout her pregnancy.

Diagnosis of PAI is usually established prior to pregnancy. Presentation during pregnancy is not common, but it should be considered as a differential diagnosis when symptoms are out of proportion to the gestational status. Normal pregnancy is accompanied by progressive increase in circulating CRH and ACTH, increasing the levels of free cortisol as early as 7 weeks of gestation, rising up to 20-fold by the end of pregnancy. These physiologic changes could explain early presentation of adrenal crisis given insufficient glucocorticoid production. A delay in diagnosis and treatment increases the risk of maternal and fetal morbidity and mortality significantly.

Management of PAI during pregnancy can be challenging as there are no established guidelines and they have mainly been based on observational studies (1). The appropriate selection and dose of the glucocorticoid is important for the treatment of PAI to minimize adverse effects on mother and baby (2). At the time of active labor and delivery, stress doses of glucocorticoids need to be administered to prevent adrenal crisis (3).

In conclusion, early diagnosis and appropriate management of PAI during pregnancy is necessary to sustain a healthy pregnancy.

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Diabetes Mellitus and Glucose Metabolism

LIPIDS, OBESITY AND METABOLIC DISEASE

Increased Fibroblast Growth Factor 21 Protein Expression via in Vivo Delivery of a Liver-Specific Expression Plasmid

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SAT-652

Fibroblast growth factor 21 (FGF21) is an important liver-secreted hormone that activates thermogenesis in white and brown fat deposits. In various models of obesity, FGF21 administration consistently facilitates weight loss and improved metabolic function. Several FGF21 variants,

which have been engineered to improve protein stability and solubility in solutions containing preservatives, are currently in human clinical trials. In addition, in vivo FGF21 gene therapy using viral vector is being explored as an alternative therapeutic approach. In this study, we present a simpler method of in vivo FGF21 gene therapy, in which liver-specific delivery of an unpackaged plasmid construct expressing an HA-tagged FGF21 protein increases de novo hepatic FGF21 production and secretion in mice. Our data show that FGF21 protein expression can be successfully restored into the livers of FGF21 conditional knockout mice for at least two weeks after a single tail vein injection with the expression plasmid, and that the HA-tagged protein is secreted and readily detectable in serum. In wild-type C57BL6/J mice, in vivo plasmid delivery significantly increased hepatic FGF21 protein 2.3-fold after two weeks, and was associated with reduced body mass and a 14% reduction in fasting serum glucose. In addition, elevated hepatic FGF21 levels correlated with a 27% decrease in the ratio of fat to body mass, visibly smaller subcutaneous and visceral white fat adipocytes, and a 3.3-fold increase in uncoupling protein 1-dependent mitochondrial respiration in the white fat. Together, these data suggest that in vivo plasmid delivery may potentially be an effective strategy for promoting hepatic FGF21 expression in models of obesity. We are currently testing this hypothesis with experiments in high-fat diet-challenged mice.

Neuroendocrinology and Pituitary

PITUITARY TUMORS: TRIALS AND STUDIES

Post-Operative Day One Morning Cortisol Value as a Biomarker to Predict the Recurrence of Cushing Disease

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OR23-03

Tumor removal by transsphenoidal surgery (TSS) is the first line treatment for Cushing disease (CD). However, recurrence is relatively common. A one week post-operative (post-op) nadir cortisol has been used as a biomarker to predict recurrence[1]. We identified 299 CD patients from our longitudinal multidisciplinary clinic or our institutional RPDR search tool who met biochemical diagnostic criteria[1] and had undergone TSS between May 2008 and May 2018, to evaluate post-op cortisol levels as biomarkers to predict long-term remission and to characterize clinical features of Cushing syndrome. Predictors of recurrence were identified with logistic regression, using recurrence as the dependent variable, and a Kaplan-Meier survival curve analysis was performed to compare long-term remission after TSS among the 202 patients who reached initial remission and had at least 1 year of follow-up. The post-op day 1 morning (AM) cortisol had significant association with CD recurrence (OR=1.025, 95%CI:1.002-1.048, p=0.032). The time to recurrence was significantly longer in patients with post-op day 1 AM cortisol <5 μg/dL. In contrast, one week post-op nadir cortisol (OR=1.081, 95%CI: 0.989-1.181, p=0.086), urinary free cortisol (OR=1.032,95%CI: 0.994-1.07, p=0.098), or late night salivary cortisol (OR=1.383, 95%CI:0.841-2.274, p=0.201) had no significant correlation with recurrence. There were no significant differences in time to recurrence for post-op day 2 AM cortisol <5 μg/dL. Among patients who developed post-op adrenal insufficiency, recurrence was significantly lower if glucocorticoid replacement continued for more than one year. In addition, tumor proliferative index (MIB-1) had a significant correlation with recurrence (OR=1.287, 95%CI:1.106-1.498, p=0.001). The most common symptoms and signs of initial presentation of CD were weight gain (91.6%), central obesity (79.6%), menstrual disorders (77.9%), round face (65.9%), hypertension (63.2%), mood disorders (60.2%), dorsocervical fat deposition (59.9%), supraclavicular fat deposition (59.9%), osteoporosis (58.9%), fatigue (58.2%), bruising (55.9%) and facial hirsutism (54.2%). Most of the best discriminating CD features did not have high sensitivity, such as purple striae (31.4%), facial plethora (33.4%) and proximal muscle weakness (30.8%). Our data show that post-op day one morning cortisol level above 5 μg/dL had significant association with recurrence. In contrast, the one week post-op nadir cortisol level had no significant value to predict recurrence. Our data also suggest that nonspecific symptoms and signs of CD are more common than stereotypical signs. **Reference:** Nieman LK, et al. Treatment of Cushing's Syndrome: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2015; 100:2807-2831

Thyroid

BENIGN THYROID DISEASE AND HEALTH DISPARITIES IN THYROID I

Pharmacokinetics (PK) and Exposure-Response Relationship of Teprotumumab, an Insulin-Like Growth Factor-1 Receptor (IGF-1R) Blocking Antibody, in Active Thyroid Eye Disease (TED)

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SAT-432

Introduction: Teprotumumab treatment resulted in statistically and clinically meaningful improvements across multiple facets of active TED and was generally well-tolerated in Phase 2 and 3 trials.[1,2] An initial intravenous infusion of 10 mg/kg followed by 20 mg/kg every 3 weeks was selected based on in vitro activity and clinical PK profile, to maintain pharmacologically active exposures and >90% saturation of IGF-1R over dosing intervals and to achieve efficacy at a well-tolerated dose for this vision-threatening disease.

Methods: Population PK analysis were performed on data from a Phase 1 oncology study (n=60)[3] and Phase 2 and 3 trials in active TED (N=83)[2,3] and covariate effect