addition to novel disease gene discovery. Methods: WES was performed for 13 unrelated patients with congenital hypopituitarism born from consanguineous parents. The variants were filtered assuming autosomal recessive inheritance, rare variants in population databases, in silico analysis predicted as deleterious and pituitary and/or hypothalamic gene expression. To determine whether variants in CDH2 that were predicted to be deleterious were functionally significant, L1 fibroblast lines that have no endogenous CDH2 protein were stably transfected with either human wild type or variant CDH2, the transfected cells were labelled with lipophilic dyes, and cell adhesion properties were assessed.

Results: Homozygous pathogenic or likely pathogenic allelic variants were found in 2 of the 13 patients. First, a female patient with GH, TSH, ACTH and LH/FSH deficiencies presenting ectopic posterior pituitary lobe, non-visualized stalk, and hypoplastic anterior pituitary lobe had two homozygous rare variants predicted as deleterious: PLA2G4A p.Asn703Lys and CDH2 c.865G>A (p.Val289Ile). Only CDH2 is known to be expressed in the pituitary, and Pla2g4a null mice have a pleiotropic phenotype without obvious hypopituitarism. The CDH2 variant is rare and classified as deleterious. Sanger sequencing of CDH2 in four family members of the affected proband revealed that the unaffected parents and two unaffected siblings were heterozygous carriers. The effect of the CDH2 variant on cell aggregation was assessed in cell culture. Large cell aggregates formed in cells transfected with wild type CDH2, but cell aggregates were small or absent in cells that were either non-transfected or transfected with the CDH2 variant. Second, a patient with isolated GHD and no MRI abnormalities was identified with a rare, likely deleterious, homozygous GH1 c.171delT (p. Phe 57Leufs*43) variant. He had a sister who died at the age of 5 and had features of GHD. Conclusion: In a cohort of congenital hypopituitarism from consanguineous parents we had 15% molecular diagnosis using WES. We identified a variant in a known gene, GH1 c.171delT and a variant in a novel gene, CDH2 p.Val289I.

Genetics and Development (including Gene Regulation)
GENETICS AND DEVELOPMENT AND NON-STEROID HORMONE SIGNALING I
Analysis of Clinical Characteristics and Gene Mutation in Four Cases of Gitelman Syndrome
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SUN-LB133
Analysis of Clinical Characteristics and Gene Mutation in four Cases of Gitelman Syndrome
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Abstract: Gitelman syndrome is an autosomal recessive renal tubular disorder characterized by renal salt wasting with secondary hyperreninemia and hyperaldosteronism, chronic hypokalemia with renal K wasting and metabolic alkalosis, and hypomagnesemia, and hypocalcuria. GS was found to be caused by mutations in SLC12A3 encoding the thiazide-sensitive sodium chloride cotransporter (NCC) on the apical membrane of distal convoluted tubule. The prevalence worldwide is estimated at approximately 1:40,000, making it one of the most frequent inherited renal tubular disorders. To date, over 400 mutations scattered throughout SLC12A3 have been identified in GS patients. The majority of patients are compound heterozygous for SLC12A3 mutations, but a significant number of GS patients are found to carry only a single SLC12A3 mutation. The type of the SLC12A3 mutation may be a determinant factor in the severity of GS. The purpose of this

Cardiovascular Endocrinology
VASCULAR DISEASE AND PATHOPHYSIOLOGY
MiRNA-99a and mTOR2 Mediate Enhanced Endothelial Mineralocorticoid Receptor Signaling-Induced Activation of Sodium Channel and Endothelium Stiffness
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SAT-LB97
In diet induced obesity enhanced endothelial cell (EC) mineralocorticoid receptor (MR) (ECMR) and downstream sodium channel (EnNaC) activity increases oxidative stress and inflammation, thereby promoting vascular stiffness and associated impaired endothelial mediated relaxation. For example, consumption of a Western diet (WD) containing excess fat (46%) and fructose (17.5%) for 16 weeks elevated plasma aldosterone levels and increased vascular MR expression in conjunction with increased endothelial and vascular stiffness in female mice. EC specific deletion of either the ECMR or EnNaC significantly attenuated this diet induced endothelial/vascular stiffness. Emerging information suggests that abnormal expression of miR-99a may be involved in these processes. To this point, we recently observed that aldosterone (10^{-7} mol/L) causes a reduction in miR-99a that was prevented by the MR antagonist, spironolactone (10uM) in in vitro ECs. By using RNA sequencing, we also demonstrated that ECMR activation reduced arterial miR-99a expression in diet induced obesity. Since the mammalian target of rapamycin (mTOR2)/SGK1 signaling pathway is involved in aldosterone activation of EnNaC we then explored the effects of miR-99a on mTOR2 expression. Indeed, miR-99a reduced mTOR2. We further observed that inhibition of mTOR2 with PP242 inhibited EnNaC activity as determined by patch clamping of ECs. Collectively these data suggest that consumption of a WD induced ECMR activation and increased EnNaC activity and endothelial stiffness, in part, by reducing the tonic inhibitory effects exerted by miR-99a on mTOR2 mediated EnNaC activation.
study is to analyze clinical characteristics and gene mutation in four cases of GS.

**Methods:** Four patients with closely resembling Gitelman syndrome was selected.

**Results:** Six SLC12A3 gene mutations were found in these four patients. There were one SLC12A3 homozygous mutation in case 1 and case 3, and two SLC12A3 heterozygous mutations in case 2 and case 4, respectively. This six gene mutations include missense mutations, frameshift mutations, and nonsense mutations. Four patients were diagnosed with Gitelman syndrome. Case 4 is the most severe with high hypokalemia, accompanied by ventricular arrhythmias, which may be related to the presence of two SLC12A3 gene mutations in the patient.

**Conclusions:** Four patients in this study were diagnosed with Gitelman syndrome based on their clinical characteristics and genetic testing results. For patients with hyperreninemia and hyperaldosteronism, chronic hypokalemia with renal K wasting and metabolic alkalosis, and hypomagnesemia, and hypocalciuria need to exclude Gitelman syndrome.

Key words: Gitelman Syndrome, Mutations, SLC12A3 gene

Cardiovascular Endocrinology

**Hypertriglyceridemia; Inflammation and Muscle Metabolism in Obesity and Weight Loss I**

*An Unusual Case of Acute Myocardial Infarction Revealing Underlying Polycythemia Secondary to Exogenous Bioidentical Testosterone Therapy*

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**SAT-LB94**

**BACKGROUND:** Many patients seeking testosterone therapy are turning to compound pharmacies for customized bioidentical testosterone replacement. These pharmacies market “bioidentical” hormone therapies as more effective and superior to traditional FDA-approved synthetic therapies. Bioidentical formulations are available as injections, creams, and subcutaneous pellet implants. Exogenous testosterone replacement is associated with polycythemia complicated by increased blood pressure, blood viscosity, and platelet aggregation (1). The ensuing hypercoagulable and prothrombotic changes predispose individuals to adverse cardiac events, including myocardial infarction.

**CLINICAL CASE:** A 66-year-old male with hypertension, type 2 diabetes, and hyperlipidemia presented with chest pain and dizziness. Initial EKG was unremarkable but troponin levels were elevated and the patient was admitted to telemetry. Lexiscan indicated anterior territory ischemia and coronary angiography revealed 95% stenosis of the left anterior descending artery (LAD). He underwent percutaneous coronary intervention (PCI) with stenting of the LAD. During the patient’s workup, he was noted to have elevated hemoglobin (20) and hematocrit (60) levels and was treated with 1g hydroxyurea as phlebotomy was unavailable. JAK2 mutation and EPO level screenings were ordered and unremarkable. The patient was noted to have multiple subcutaneous testosterone pellets in his buttocks which he stated were implanted three weeks prior. Serum total testosterone was elevated at 1226 ng/dL. Hematology was consulted and the patient continued daily 1g hydroxyurea. After discharge, the patient continued outpatient follow up with hematology and received plasmapheresis for management of polycythemia.

**CONCLUSION:** Considering polycythemia can arise secondary to exogenous testosterone use and is a known risk factor for cardiovascular events, it is likely this patient’s myocardial infarction was complicated by his use of exogenous bioidentical testosterone. Compound pharmacies providing bioidentical testosterone are not required to report adverse events, provide black box warnings, or show evidence-based safety and efficacy profiles for their products. The increasing availability and use of non-FDA-approved testosterone therapies warrants increased physician vigilance, particularly for patients with existing cardiac conditions or predisposition to hypercoagulable and prothrombotic states. The lack of regulation and research in the realm of compound pharmacy hormone products calls for further studies and reforms to protect patients from the risk of developing detrimental complications.

**REFERENCE:** (1) Xu, L., Freeman, G., Cowling, B. et al. Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. *BMC Med* 11, 108 (2013).

**Diabetes Mellitus and Glucose Metabolism**

**Diabetes Complications I**

*A Case of Metformin Associated Lactic Acidosis and the Importance of Medication Reconciliation in End-Stage Renal Disease*

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**SAT-LB128**

**Background:** Metformin is commonly used in the treatment of diabetes mellitus due to its low cost, ease of administration and titration, and favorable side effect profile as it does not cause weight gain and rarely causes overt hypoglycemia. An important yet rare side effect of metformin use is metformin associated lactic acidosis (MALA) which can be seen in patients with significant renal impairment and is associated with high mortality.

**Clinical Case:** We present a 54-year-old man with hypertension, type 2 diabetes mellitus, and recently diagnosed end-stage renal disease (ESRD) on hemodialysis who presented with shortness of breath and syncope and found to have an elevated lactate to 40.5 mmol/L (reference range: 0.5-2 mmol/L). Notably, the patient was admitted at an outside hospital two and a half weeks prior for a new diagnosis of ESRD and initiated on hemodialysis three times a week. At the time of discharge from his prior hospitalization,