for each analyte and internal standard, and triplicate injections are used to minimize instrument instability. The within- and between-day imprecision for the CDC RMP are 2.2–3.9% and 1.8–2.6%, respectively. By comparisons with the RMPs at Ghent University in Belgium, Radboud University Medical Center in the Netherlands, and the Reference Material Institute for Clinical Chemistry Standards in Japan, the CDC RMP reported a bias within +2.5% of the mean for all labs. Factors affecting measurement accuracy were investigated, to maximize recovery for optimum performance of the method. FT4 was detectable in all samples, and thus, suitable for analysis of hypo-, eu-, and hyperthyroid patients. A comparison among hypo-, eu-, and hyperthyroid patients of a commercially available immunoassay and the CDC RMP indicated a mean bias of -37.7%. The CDC CSP has also evaluated the RMP for accurate measurement of FT4 in pregnant individuals. This candidate reference method for FT4 in serum demonstrates good accuracy and precision, and can be used as a viable base for accuracy to which routine methods for FT4 can be compared. 1. Van Houcke, S.K., et. al. *Clin. Chem. Lab. Med.* 2011, 49, 1275–1281.

Adipose Tissue, Appetite, and Obesity

RARE CAUSES AND CONDITIONS OF OBESITY: PRADER WILLI SYNDROME, LIPODYSTROPHY

Variants in Known Monogenic Causal Genes of Hypertriglyceridemia Are Not Major Contributors for Hypertriglyceridemia in Lipodystrophy Due to a LMNA Mutation

Masako Ueda, MD[1], Adam D. McIntyre, MSc[2], Alan T. Remaley, MD, PhD[3], Robert A. Hegele, MD, FACP, FRCPC[4], Daniel J. Rader, MD[1].

[1]University of Pennsylvania, Philadelphia, PA, USA, [2]Robarts Research Institute, Schulich School of Medicine and Dentistry, Western University, London, ON, Canada, [3]National Institutes of Health, Bethesda, MD, USA, [4]Robarts Research Institute, London, ON, Canada.

SUN-593

Background: Lipodystrophy is a heterogeneous disorder of adiposity, and one common lipid manifestation is hypertriglyceridemia (HTG). The *LMNA* gene, which encodes for nuclear envelope proteins, is a known causal gene for heritable lipodystrophy. At present, underlying mechanisms for each clinical manifestation of lipodystrophy due to a *LMNA* mutation are unknown.

Hypothesis: A likely explanation for HTG in lipodystrophy is the paucity of adipose tissue where excess triglycerides (TGs) are normally stored, thus it may not be due to a specific defect in lipoprotein metabolism. Consequently, rare variants in HTG-associated genes would not be expected to be major contributors for HTG in lipodystrophy with *LMNA* mutations.

Method: A proband and her father with a clinical diagnosis of lipodystrophy were recruited into an IRB-approved study investigating molecular etiologies of dyslipidemia at the University of Pennsylvania. Next-generation sequencing (NGS) with the LipidSeq panel, targeting causal genes for lipodystrophy, and monogenic HTG was performed, and confirmed by Sanger sequencing. Also, unweighted TG-polygenic scores by summing the number of TG-raising alleles from 14 single nucleotide polymorphisms (SNPs) associated with TG levels were assessed.

Results: The proband and her father were diagnosed with lipodystrophy of two different subtypes, generalized in the daughter and partial in the father. The proband reported a gradual loss of subcutaneous fat starting around age 10. A highest reported TG in the proband was19,000 mg/dL with eruptive xanthomas, whereas TG in the father was never >500 mg/dL. Their BMI's and DEXA body fat% were 12.9 kg/m^2 and 7% in the proband, and 25.7 kg/m^2 and 25% in the father, corresponding to their fat storage capacities. The molecular analyses revealed only a lipodystrophy causal mutation in *LMNA*, c.29C>T, T10I with no other significant findings in18 other lipodystrophy-related genes. No deletion or duplication was identified by a targeted array CGH of *LMNA*.

As predicted, no rare monogenic variants in HTG-causal genes (*LPL*, *GPIHBP1*, *APOA5*, *APOC2*, *LMF1*, *GPD1*) were identified in either subject. However, TG-polygenic scores were 17/28 (95th %ile) in the proband, and 13/28 (50th %ile) in the father, the same trend as the level of HTG levels seen in them. Apolipoprotein E genotypes were noncontributory, (3/3) in the proband, and (3/4) in the father.

Conclusion:

Our findings support that the pathophysiology of HTG in lipodystrophy is likely to be due to lack of TG-storage space (adipose tissues), and is unlikely due to a defect in lipoprotein metabolism seen in patients with rare monogenic HTG-variants. Although the HTG-polygenic score was higher in the proband, and the accumulative effects of the at-risk alleles may be contributor to the HTG phenotype, it is unlikely to be the leading cause of severe HTG seen in the proband.

Adrenal

ADRENAL CASE REPORTS II

Case Report: Mifepristone Taper in an Individual with Equivocal Cushing's Syndrome Screening Tests

Christopher Martin, MD[1], David Perez-Molinar, BS[2], Tyler C. Drake, M.D.[3].

[1]Allina, Edina, MN, USA, [2]University of Minnesota, Minneapolis, MN, USA, [3]Minneapolis VA Health Care System, Minneapolis, MN, USA.

SUN-186

We present a 75-year-old male evaluated by the inpatient endocrine service during an admission for hemorrhagic stroke. Approximately 1 year prior to this admission he was started on mifepristone therapy for presumed Cushing's Syndrome. Initial Cushing's work-up was equivocal: 1 mg dexamethasone suppression cortisol level of 1.9 and midnight salivary cortisol 167 ng/dl. Random ACTH measurement was not obtained as part of this initial evaluation. Review of prior imaging studies did not demonstrate obvious culprit pituitary nor adrenal lesions. Mifepristone induced hyperaldosteronism, thyroid dysfunction and adrenal insufficiency were demonstrated presumably secondary to cortisol receptor antagonist induced up-regulation of adrenocorticotropic hormone and cortisol. We describe our experience stopping mifepristone and performing re-evaluation.