Clinical Chemistry

January 2018 Audio Summary

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**ON THE COVER** The supersize burger. This image evokes one of two questions: Doesn't that look good? or How many calories are in that thing? The fact that we respond more to the former at an alarming rate is the reason why there is an obesity crisis around the world. Yet, while it is accepted that excessive caloric intake is a relevant factor, the causes of obesity and best strategies to reverse trends in the prevalence of the disease are topics of much debate. Thus, it is timely to devote this special issue of *Clinical Chemistry* to the problem of obesity and current research to inform strategies for addressing the problem. In addition of issues of relevance to laboratory medicine, the articles in this issue provide an overview of the challenges that obesity presents to the broader scientific community.

**Dairy Consumption and Body Mass Index Among Adults: Mendelian Randomization Analysis of 184,802 Individuals from 25 Studies**
By the Mendelian Randomization of Dairy Consumption Working Group

Associations between dairy intake and body mass index have been inconsistently observed in epidemiological studies, and whether a causal relationship exists remains ill defined. This study applied Mendelian randomization analysis to analyze associations between dairy intake and body mass index, using a dairy intake associated genetic polymorphism upstream of the lactase gene as an instrumental variable. Mendelian randomization analysis showed that the genetically determined higher dairy intake was significantly associated with higher body mass index. These findings provide strong evidence to support a causal effect of higher dairy intake on increased body mass index among adults.

**Genetic Evidence That Carbohydrate-Stimulated Insulin Secretion Leads to Obesity**
By Christina M. Astley et al.

This paper uses a genetic approach to test the fundamental precept of the carbohydrate-insulin model of obesity, that a high glycemic load diet, by increasing insulin secretion, promotes weight gain. The study authors used a method termed "Mendelian randomization," in which genetic predictors of an exposure of interest are used to estimate the causal effect between that exposure and an outcome. After selecting genetic variants to isolate and estimate the effect of insulin secretion on body weight, they found evidence of a causal role for early insulin secretion in obesity. Their findings suggest a role for "precision medicine" in dietary interventions.

**Weight History and Subclinical Myocardial Damage**
By Chiadi E. Ndumele et al.

This study evaluated the association between weight history and subclinical myocardial damage, as indexed by increased concentrations of high sensitivity cardiac troponin-T. Within each current weight category, prior excess weight was associated with increased high sensitivity cardiac troponin-T, with the strongest associations seen for those with past and current obesity. Duration of obesity and cumulative weight (expressed in excess body mass index years), were both significantly associated with increased high sensitivity cardiac troponin-T. These findings indicate chronic toxic effects of adiposity on the myocardium, and underscore the need for weight maintenance strategies targeting the entire lifespan.

**Adipose Tissue LPL Methylation is Associated with Triglyceride Concentrations in the Metabolic Syndrome**
By Daniel Castellano-Castillo et al.

This study considered the possible role of DNA methylation in the metabolic syndrome. Both epigenetics and metabolic syndrome have been related to lifestyle. DNA methylation at the lipoprotein-lipase promoter in visceral adipose tissue was investigated by the performance of a fat challenge test, since lipoprotein lipase is a major key in metabolic processing of triglycerides. Individuals with metabolic syndrome were found to have higher lipoprotein-lipase methylation, a worse metabolic profile, and slower metabolic processing of triglycerides as lipoprotein lipase methylation increased. These results suggest the use of epigenetics-based treatments and specifically lipoprotein lipase methylation as a possible target for the improvement of hypertriglyceridemia and metabolic disorders.

**Remnant Cholesterol and Myocardial Infarction in Normal Weight, Overweight, and Obese Individuals from the Copenhagen General Population Study**
By Anette Varbo et al.

In this prospective cohort study of over 100,000 individuals from the Copenhagen General Population Study, the authors found an association between higher body mass index and higher calculated remnant cholesterol concentrations. Moreover, they found that stepwise higher concentrations of calculated remnant cholesterol were associated with stepwise higher risk of myocardial infarction in a similar pattern for normal weight, overweight, and obese individuals. These results indicate that high remnant cholesterol is linked to high body mass index, and that remnant cholesterol is a risk factor for myocardial infarction independent of overweight and obesity.

**Adiposity and Genetic Factors in Relation to Triglycerides and Triglyceride-Rich Lipoproteins in the Women's Genome Health Study**
By Shafqat Ahmad et al.

Previous results from Scandinavian cohorts have shown that obesity accentuates the effects of common genetic-susceptibility variants on increased triglyceride concentrations. Whether such interactions are present in the US population, and further, are selective for particular triglyceride-rich lipoprotein sub-fractions is unknown. This study replicated the prior Scandinavian results using data from the Women's Genome Health Study and conducted a meta-analysis of these results with those from three Scandinavian cohorts. Obese individuals demonstrated a differential association with aggregated triglyceride-associated genetic-risk, and these effects were accentuated in the large triglyceride-rich lipoprotein sub-fraction. These results suggest that obese individuals may be more susceptible to aggregated genetic risk associated with common triglyceride raising alleles with the effects accentuated in the large triglyceride-rich lipoprotein sub-fraction.