Using Physiologic, Genetic, and Epigenetic Information to Provide Care to Clients Who are Obese

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* Precision Initiative
* Announced in 2015
* Goal: prevention and treatment strategies that take individual variability into account
* Employs genetics & biological databases to identify methods for individualized practice
* Needs: Prevention and treatment of obesity & obesity-related disorders
* Obesity
* Complex process involving multiple interactions among behavioral, environmental, immunologic, genetic & epigenetic factors
* High association with many chronic disease states
* Complex diseases with genetic and environmental factors that contribute to chronic low-grade inflammatory response
* Adipose Tissue Formation
* White fat – stores energy in the form of triglycerides and is the major source for the chronic inflammatory state
  + Subcutaneous - beneath skin
  + Visceral - abdominal cavity & mediastinum
* Brown fat – primarily in infants & small amounts in adults
  + Ability to dissipate energy through thermogenesis
* Beige or Brite fat – interspersed in white fat
  + Cold induced to generate heat
  + Exercise induced to generate heat and reduce chronic inflammatory response that leads to comorbidities
* During Periods of Overnutrition
* Beige or Brite fat decreases thermogenic activity, becomes resistant to insulin and activates “obesity-generated” inflammation.
* Treg cells (T regulatory cells) regulate the host metabolism – slow it down to conserve energy – the body “thinks” it needs to save the extra calories
* Interleukin 33 (regulatory cytokine) produced by the Treg cells decreases
  + Study on rats (Han et al) – gave interleukin 33 to rats which led to reduced inflammatory markers and reversal of insulin resistance
* Eating
* Complex physiological, psychological, social & genetic factors regulate
* Taste and taste sensitivity under genetic control
  + Sensitive to bitter taste – avoid specific foods, especially dark leafy green vegetables, herbs, & some spices
  + High genetic preference for sweet and high fat foods
    - Linked to height variations among children
  + Unami – savory flavor in tomatoes, soy sauce, and food additive (MSG)
    - Some prefer, some avoid
* Genes Directly Related to Obesity
* Leptin – ob/ob mutant mouse
  + Mouse weight directly related to leptin
  + Humans easily become leptin resistant (inflammatory response)
* APOE gene family
  + Functions in lipid metabolism and deposition of fatty tissue
  + APOE3 form is associated with more efficient use of dietary energy, increased fat storage, higher BMI & body weight in children
  + APOE4 carriers increased fatty acid mobilization & utilization as a fuel – function of this allele decreases with age
* Genes cont
* BDNF & POMC – **rare** early onset severe obesity related to a number of genetic disorders including Prader-Willi, Fragile X, ACTH insufficiency, etc.
* OLM4 & HOXB5 – early onset severe obesity genes
  + Linked to gut development & gut flora
* FTO – defects in this gene are associated with the most widespread causes for obesity
  + Controls brain in hypothalamic nuclei areas where energy balance and feeding patterns are regulated
  + A & T alleles respond to food and satiety differently
    - AA – high obesity risk, TT – low obesity risk, AT – moderate obesity risk
    - AA also respond to external clues differently
* Epigenetics
* Study of heritable changes in gene expression
  + Active or “turned on” genes versus Inactive or “turned off” genes
  + Adding of methyl groups (CH3) in areas of promoters with high concentration of C-P-G (cytosine – phosphate – guanine)
  + Changes occur under environmental influences
  + Methylation or lack of during pregnancy influences development of infant gene regulation (which genes are on or off in developing infant)
  + Results in major changes in gene function with years of environmental influences
    - Diet, smoking, exercise, stress, illness, etc.
* Diet
* Sugar & artificial sweeteners
  + 32 genetic variants associated with high intake of sugar sweetened foods & beverages
  + Example – aspartame in combination with MSG promoted fat accumulation and increased pre-diabetic symptoms
  + Stevia has been found to reduce & eliminate insulin resistance in mice (early results)
* Over 4,000 food additives are found in American diet. Must be proven to be harmful to be removed
  + Use of artificial colors increased 5-fold from 1950 to 2010
  + Zebrafish are now being used to test chemicals and response related to obesity
* Exercise
* Human differences in responsiveness recognized more than 30 years ago
* Differences – exercise capacity, skeletal muscle oxidative potential, adipose tissue lipid mobilization
* KIF5B gene – kinesin family of genes
  + Inhibited – diminishes biogenesis & numbers of mitochondria
  + Overexpression – enhanced mitochondrial biogenesis (increased mitochondrial mass)
* CREB1 – regulates heart rate & mitochondrial function
* Several genes related to formation and maintenance of muscle tone
* Recommendations
* Not simply calories in, calories out
* Dietary intake of “real” and/or fresh foods
  + Avoidance of added sugars and food additives
* Ongoing, regular routine exercise
* Balance of GI tract flora
* Education of clients on reading and understanding of food labels
* Genetic testing
  + Early onset obesity
  + Strong family history
* Development of individualized diets to meet the needs of specific clients
  + No longer “one size fits all” types of diets
* Genetic Risk (Belsky, etal 2012) – 38 year longitudinal study on 1,037 individuals
* Genetic Testing recommended for all with family history of early onset obesity
  + Polygenic risk can be mediated by rapid growth or significantly increased physical activity
* Parental BMI is a weak indicator of childhood risk – may have stronger epigenetic consequences
* FTO gene is the strongest genetic indicator at this time
* Children – often put on weight just before growth spurts
* Rebound period – early adult/late teen years
  + Rapid increases in BMI at this stage strong indicator of adult obesity
* Education of Clients
* <http://health.gov/DietaryGuidelines/>
* Minimum of 3 gram Fiber per 100 calories
* Added Sugars less than 10% of total
* Saturated Fats less than 10% of total
* Sodium less than 2,300 mg daily
* Physical Activity
* Children & Adolescents 60 minutes or more daily
  + Aerobic, Muscle-strengthening, Bone-strengthening
* Active Adults
  + 150 minutes per week – 75 vigorous
  + Move towards 300 for very healthy individuals
* Active Older Adults
  + 150 minutes per week – 75 vigorous
    - Aerobic & Muscle-Strengthening
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