Metabolic complications of obesity

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Metabolic Complications of Obesity

Coronary Heart Disease

Insulin resistance (Diabetes)

Atherogenic Dyslipidemia

Nonalcoholic fatty liver disease
Prevalence of Metabolically-normal and Metabolically-abnormal Obesity in US Adults

Men

- Metabolically normal: 29%
- Metabolically abnormal: 71%

Women

- Metabolically normal: 35%
- Metabolically abnormal: 65%

Pathogenesis of Obesity-related Metabolic Dysfunction and NAFLD

- **FFA**: Free Fatty Acids
- **TG**: Triglycerides
- **β-Oxid**: β-Oxidation
- **DNL**: De Novo Lipogenesis
- **VLDL**: Very Low Density Lipoprotein
- **HDL**: High Density Lipoprotein
- **Adipokines**: Fat-derived hormones
- **Visceral fat**
- **Subcutaneous fat**

Glucose production and uptake are influenced by these processes, with FFA and adipokines playing a significant role.
Medical Screening & Body Composition Analyses

- Metabolically Normal
- Metabolically Abnormal

Baseline Testing
- Euglycemic-hyperinsulinemic clamp, VLDL kinetics, Heavy water administration and sigmoidoscopy

Weekly Intervention Visits (8-12 weeks)
- Review high calorie diet, blood tests, body weight, medical evaluation
- Goal: Gain 5 – 7% body weight then maintain for 3 weeks

Post-Weight Gain Testing
- Body composition, analyses, euglycemic-hyperinsulinemic clamp, VLDL kinetics, heavy water administration and sigmoidoscopy

Weight Loss Program (6 months)
Two-stage hyperinsulinemic-euglycemic clamp procedure

- Insulin (mU/m²/min)
  - 7
  - 50

- 20% glucose + [²H₂]glucose infusion
- [¹³C₁₆]palmitate infusion
- [²H₂]glucose infusion

- Time (h): 0-10
- Basal
- Stage 1
- Stage 2

- Blood samples:
  - At time 0
  - At time 5

- Biopsies:
  - At time 0
  - At time 5
Measurement of VLDL Kinetics

$[^2\text{H}_5]\text{glycerol}$

$[^2\text{H}_3]\text{leucine}$

$[^2\text{H}_2]\text{palmitate}$

$[^2\text{H}_3]\text{leucine}$

Blood samples

Weight Gain Intervention

• Estimated total daily energy expenditure + 1,000 additional calories

• Additional calories must come from:
  – McDonald’s
  – Burger King
  – Kentucky Fried Chicken
  – Pizza Hut
  – Taco Bell
Supervised Weight Loss after Weight Gain

- Eliminate 1,000 additional fast food calories
- Decrease daily calorie intake by 30% of estimated total daily energy expenditure
- Structured meal plan
- Increase physical activity
- Cognitive Behavioral Techniques include:
  - Self-monitoring
  - Goal-setting