

Diabetes and Obesity

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The diabetes epidemic

- Prevalence of diabetes worldwide was over 135 million people in 1995
- Projected to be over 300 million by 2025
- Over 80% of type 2 diabetic patients are overweight

Overview of weight loss benefits in T2D

- Modest weight loss is associated with:
 - * decreased endogenous glucose production
 - * increased peripheral insulin-mediated glucose uptake
 - * increased insulin secretion
 - * improved insulin sensitivity

Challenge of weight loss in T2D

- Diabetic patients have greater difficulty achieving/maintaining weight loss than overweight, non-diabetic patients
 - Insulin/sulphonylureas promote weight gain
 - Reduction in glycosuria with treatment and altered regulation of energy balance inhibit weight loss
- Better glycemic control in DCCT associated with a 4.6 kg weight gain!

Epidemiology of T2D in Adolescence

- Incidence per 100,000 youth per year:
1982-0.7 1994-7.2
Higher incidence in some centers
Age: 13.8 + 1.9 years
Gender F>M 1.7:1
Race AA=69%

Pediatric TD2

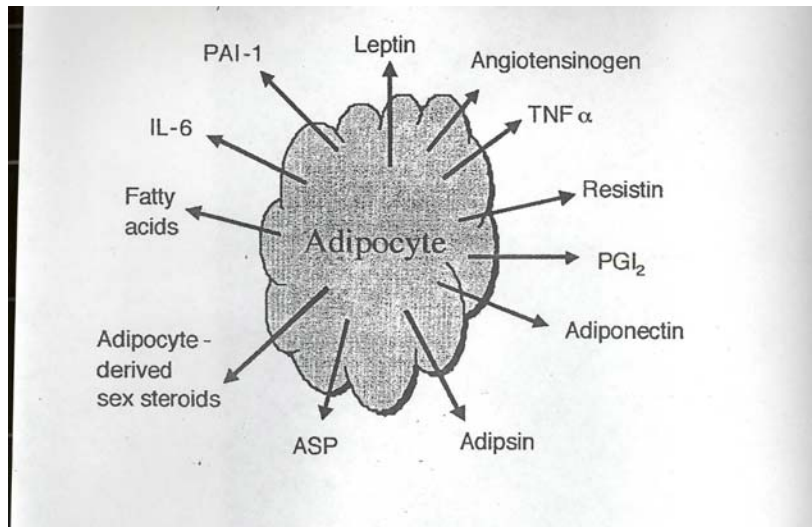
- Mean BMI 37.7 + 9.6 kg/m²
- 38% morbidly obese
- 8% normal weight for age
- Obesity associated conditions 21%
 - Hypertension 17%
 - Sleep Apnea 6%
 - Hypertriglyceridemia 4%

Visceral vs. Subcutaneous fat

- Visceral (abdominal, omental) fat correlates best with the co-morbidities of obesity including insulin resistance and diabetes
- Visceral fat is more metabolically active
- “Cushing’s disease” of the omentum
- The portal-hepatic shunt

A New View of the Adipocyte

- The adipocyte is a metabolically active source of multiple proteins and cytokines that act via autocrine, paracrine and endocrine means
- The adipocyte, gut and brain communicate regarding the body’s state of energy balance and set the “satiety” thermostat



How the adipocyte effects insulin sensitivity

TNF alpha

Levels rise with increasing adiposity

Lowers insulin stimulated glucose uptake in fat and muscle via paracrine effects

Reduces Glut-4 gene expression

Reduces insulin stimulated IR autophosphorylation and IRS-1 phosphorylation

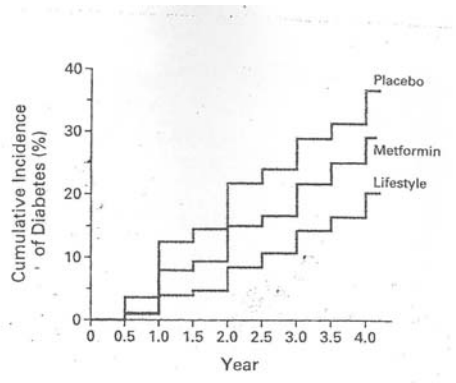
Interferes with pancreatic beta cell insulin secretion

Adiponectin

- An anti-atherogenic and anti-inflammatory Adipokine entrained to the insulin sensitivity state made exclusively in the adipocyte
- Levels reduced in obesity, T2D, in men vs. women, and in CAD; rises with weight loss
- Increases insulin sensitivity by promoting beta oxidation of fatty acids in muscle

Prevention of type II diabetes

- Intentional weight loss associated with a 25% reduction in T2D mortality over 12 years
- Diabetes Prevention Program Research Group study of a large glucose intolerant population:
 - lifestyle vs. placebo: 58% reduction
 - metformin vs. placebo: 31% reduction



Achieving weight loss in T2D: Goals and Strategies

- Seeking to achieve IBW is unrealistic
- Initial goal of 5-10% loss in body weight significantly improves insulin sensitivity, lipid profile and blood pressure
- Goal is “energy restriction”: both low fat and low CHO diets can be effective
- Manipulation of “glycemic index” has little practical value

Helping obese children with T2D or glucose intolerance

- Eating plans which involve parental participation are the most successful
- Self reporting may be helpful
- Reduce liquid calories; stress portion sizes
- Close followup and encouragement are needed

Our approach: the “Add-back” diet!

- Children are given 2.5 grams/kg/ BW at 97% for age as lean meat (usually 15-20 ounces/d); 1 egg=6 ounces protein
- Unlimited Greens (lite dressing), 2 cups green vegetables, 1 “milk” serving, 1 “fruit” serving, diet jello daily.
- Liquids: 8 glasses water, Crystal Lite
- A multi-vitamin and 2 Viactives/d.

Exercise, obesity and T2D

- Obese individuals use higher VO₂ max and achieve higher heart rates during exercise than non-obese... limits exercise tolerance
- Suggest walking at self-selected rate
- Decrease sedentary activities
- Send children outside after school...encourage active inside games like hopskotch, etc.

Diabetes therapies and body weight

- Metformin (biguanide) inhibits hepatic glucose release and promotes mild weight loss.
- Thiazolidinediones (TZDs) increase insulin sensitivity by acting at PPAR gamma. They increase body weight but augment subcutaneous rather than visceral fat

Orlistat and T2D

- Pancreatic lipase inhibitor blocks GI absorption of 30% of fat
- Weight loss is slightly greater in T2D patients on sulphonylureas vs. placebo (6.2 vs 4.3%)
- Two fold greater reduction in waist circ.
- 0.9% drop in HbA1c vs. .4% placebo
- No hypoglycemia

Hanefeld M, Diabetes Obesity and Metabolism, 2000.