The Metabolically Healthy Obese: Should They be Treated?

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What is the Metabolically Healthy Obese?

- Obese
- Normal fasting glucose
- Normal glucose tolerance test (if test is performed)
- Normal lipid profile
- Normal blood pressure
The Metabolically Healthy Obese

• My Task:
  – To present a rationale for treating this group of children and adolescents
  – To touch on major treatment modalities

• Overall Goal:
  – To present a balanced overview of the pros and cons of the subject
Is the Metabolically Healthy Obese Adolescent Truly Healthy?

- Obesity may just be the first sign of the developing metabolic syndrome
- There are other associated and potential problems faced by the “healthy” obese
- Many are already insulin resistant and hyperinsulinemic
Potential Problems for the Healthy Obese Child or Adolescent

• Most obese teenagers become obese adults
• Higher risk of
  – Hypertension
  – Lipid abnormalities
  – Cardiovascular disease
  – Diabetes mellitus
• Lower self-esteem
• Joint problems – i.e. slipped femoral epiphysis
• Obesity may be a sign of an eating disorder or psychological problem
Obesity Associated Conditions

• Obstructive sleep apnea & other sleep disorders
• Exacerbation of asthma - prolonged treatment
• Gastro-esophageal reflux
• Non-alcoholic fatty liver disease
• Increased inflammatory markers
• Increased septal and posterior wall thickness
• Increased glomerular filtration rate
Healthy Obese?

• Is it fair to leave the “healthy” obese adolescent untreated?
• If not, how do we treat?
  – Do we target the obesity or do we target potential complications of obesity?
  – Do we prescribe drugs for “healthy” children?
Treatments for the “Healthy Obese” Adolescent

• Lifestyle intervention
  – Difficult to administer
  – Often disappointing long-term results
  – MAINSTAY OF ANY TREATMENT

• Drugs
  – Weight loss drugs
  – Metformin
  – Limited effectiveness in absence of vigorous adherence to lifestyle changes
Successful Lifestyle Intervention Examples

• School and family based intervention:
  – Cologne, Germany
  – 8 month program
  – Smaller increase in BMI
  – Decrease in systolic blood pressure

• Hospital-based family-centered intervention:
  – Los Angeles, CA
  – 3 month program
  – Weight and BMI increases slowed
  – BMI z-scores lowered
  – Improved emotional well-being
  – Improved risk factors for metabolic syndrome
Orlistat (1)

- The only drug tested in and approved for treatment of obesity in subjects as young as 12 years of age
- Pancreatic and gastric lipase inhibitor
  - Reduces absorption of fats resulting in a caloric deficit
  - Side effects mainly gastrointestinal – usually self limited and mild
Orlistat (2)

- Results in modest weight loss
- Most effective when used in conjunction with lifestyle modification
- Long-term effects unknown but probably minimal since drug is largely unabsorbed
- Relies on weight loss from decreased caloric absorption to secondarily improve or prevent complications of obesity
Metformin (1)

- NOT approved for weight loss
- Weight loss is a side effect of metformin in obese subjects with diabetes
  - Not a consistent side effect
  - Transient even when metformin continued
  - Only works while drug is being taken
- Most studies in non-diabetic obese subjects report little or no weight loss with metformin
Metformin (2)
Experience In Children

• Approved for treatment of type 2 diabetes in children as young as 10 years of age
• Tested in 19 pediatric patients taking psychotropic drugs known to cause weight gain
  – Most lost some weight
  – Not randomized, no controls
• Used at several centers for adolescent girls with Polycystic Ovary Syndrome (PCOS)
PCOS Patients
Is this a Special Subset of Patients?

• Classic PCOS patients are hyperandrogenemic & insulin resistant – i.e., NOT “Healthy Obese”
• Extensive experience with metformin in adult women with PCOS
  – Promotes weight loss
  – Increases fertility
  – Safe
• Several centers have tried metformin for adolescents with PCOS with good results
Identification of Diabetes Prone Healthy Obese Children

- Maternal diabetes during pregnancy
- Family history of diabetes
  - 1st degree relative(s)
  - Especially sibling
- Age
- (PCOS or other elements of the metabolic syndrome)
Other drugs for Obesity / PCOS

• Obesity
  – Glucosidase inhibitors (Acarbose) – limited effectiveness
  – Other – sibutramine (Meridia), phentermine (Ionamin),
    diethylpropion (Tenuate), methamphetamine (Desoxyn) – none for children
  – We need to have others tested in children

• PCOS
  – Birth control pills
  – Do not address underlying problem
Summary – Healthy Obese (1)

- Should be treated
- Obesity is a “Chronic Complex Disease”
  - Dr. V. Hainer
- Lifestyle intervention
  - Diet and exercise
  - Involve family, school and community for best success
- Weigh risks of long-term (lifelong) drugs
  - Not for pre-adolescent children
  - Orlistat - approved from age 12 years
  - Metformin – not approved
Summary – Healthy Obese (2)

• Treatment probably needs to be lifelong
• We need to start educating children from a young age – as young as possible
  – Slow the weight gain
  – Establish a life-long belief in the benefits of physical activity
• An increase in exercise prevents many of the metabolic effects of obesity even if weight loss is minimal or absent
• No treatment regimen has a sustained effect after it is stopped