Understanding and Treating Obesity

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Format

- Presentation
- Q&A
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Presenter

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Obesity

- Very common
- Growing
- Complex physiology
- Clinically heterogeneous
- Resistant to treatment
- Frustrating
- Global health priority
- Associated with cancer
Obesity by the Numbers

Overweight U.S. adults: 67%
U.S. adults with obesity: 33%
U.S. children with obesity: 17%

Annual U.S. health care expenditures for obesity: $147 billion
U.S. consumer expenditures for weight loss products: $50 billion

Weekly deaths from obesity complications: > 6,000
Disproportional Increase in Severe Obesity

More than 1,000,000 U.S. adults now have a BMI >50

Sturm R. *Health Aff.*, 2004
Complications of Obesity

- Metabolic
- Structural
- Degenerative
- Neoplastic
- Psychological
- Socioeconomic
Obesity Shortens Life Expectancy

Average years of life lost from obesity at age 30

<table>
<thead>
<tr>
<th></th>
<th>BMI = 30</th>
<th>BMI = 40</th>
<th>BMI &gt; 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>White men</td>
<td>1</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>White women</td>
<td>1</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Black men</td>
<td>0</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Black women</td>
<td>0</td>
<td>1</td>
<td>5</td>
</tr>
</tbody>
</table>
Most Common *Undertreated* Complications

- Obstructive sleep apnea
- Fatty liver disease
- Gastroesophageal reflux disease
- Fungal skin infections
- Nutrient *deficiencies*
  - from recurrent dieting and inadequate nutrition during rebound weight gain
Feedback Regulation of Energy Metabolism

- Sensory Organs (GI Tract)
- Leptin
- Adipose tissue
- Liver
- Muscle
- CNS

Environmental sensing
Metabolic needs
Energy stores
Food intake
Nutrient handling
Energy expenditure

Sensory Organs
GI Tract

Leptin

Adipose tissue

CNS

Liver

Muscle
Defending a Body Energy “Set Point”

Energy Intake

Energy Expenditure

(+) Energy Balance

(−) Energy Balance

kcal / 24 hours

Body Mass Index (kg/m²)
Natural Variation and Zones of Opportunity

BMI

Excellent

Poor

Degree of Control

MGH Weight Center
A Biological Basis for Yo-yo Dieting

BMIs:
- Baseline
- Healthy lifestyle
- Weight regain
- Restrictive Dieting
- Rebound weight gain
- Recurrent dieting
- Yo-yo rebound

Degree of Control:
- Excellent
- Poor

MGH Weight Center
Treatment of the Patient with Obesity
Approach to the Patient with Obesity

• **Respect the patient**
  - Avoid pejorative language
    - “Morbid,” “obese,” “recidivism”
  - Understand the challenges faced by the patient
  - The blame game is nonproductive (no one *wants* this problem)
  - Optimize your office environment
    - Physical facilities – chairs, scales, exam tables, gowns, etc.
    - Staff approach and attitudes

• **Work to develop a therapeutic partnership**
  - There is no quick or reliably effective therapy
  - Success often comes after a “trial-and-error” testing of different approaches
  - Start with lifestyle but communicate that there are other approaches to be considered as needed
Approach to the Patient with Obesity

• Demonstrate understanding of the problem
  • Obesity is devastating in ways that go far beyond the medical implications
  • Durable weight loss is extremely difficult (or impossible)
  • Improved lifestyle is achievable but may not lead to weight loss
  • Different people respond to different interventions very differently
  • Take aim at the causes of obesity
    • Food quality (even more than quantity)
    • Physical activity and muscle function
    • Mental health (stress and distress)
  • Focus on important non-weight loss outcomes
    • Quality of life
    • Heath risks (cardiovascular, diabetes, cancer)
Approach to the Patient with Obesity

Identify and treat obesity complications
  • Medical
  • Psychological
  • Socioeconomic

Reduce obesity-based disparities in care
  • Ensure appropriate screening
  • Recognize challenges to diagnosis (physical and technical limitations)
  • Consider effects of obesity on treatment paradigms

Treat the obesity itself
Treatment of Obesity Itself

Treat underlying disorders

- Drugs are common
- Endocrine causes are rare

Stepwise care plan

- Lifestyle modification
  - Healthy diet
  - Regular physical activity
- Medications
- Surgery

Anticipate slow progress
Obesity Treatment Pyramid

- Surgical Treatment
- Pharmacotherapy
- Lifestyle Modification
  - Healthy Diet
  - Physical Activity
Behavioral Therapies

Predictors of Weight Maintenance

- Physical activity
- Problem solving
- Self-monitoring
- Stress management
- Continued contact
Intensive Dietary Intervention

Diabetes Prevention Program

Nathan D et al., NEJM 2002
Diet-induced Weight Loss

Baseline Values Carried Forward Analysis

Change in Weight (%) vs. Time (months)

Low-fat

Low-carb

* *p < 0.05

N.S.

Foster et al., NEJM 2003
## Medications Approved for Obesity

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism of Action</th>
<th>Potential Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sibutramine - CIV</td>
<td>Adrenergic, Serotonergic, Dopaminergic</td>
<td>Hypertension, tachycardia (avoid use with SSRIs)</td>
</tr>
<tr>
<td>(Meridia™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orlistat - CIV</td>
<td>Lipase Inhibitor</td>
<td>Steatorrhea, incontinence</td>
</tr>
<tr>
<td>(Xenical™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phentermine - CIV</td>
<td>Adrenergic</td>
<td>Tachycardia, hypertension</td>
</tr>
<tr>
<td>(Adipex™, Ionamin™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diethylpropion - CIV</td>
<td>Adrenergic</td>
<td>Tachycardia, HTN, anxiety</td>
</tr>
<tr>
<td>(Tenuate™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzphetamine - CIII</td>
<td>Adrenergic</td>
<td>Tachycardia, HTN, anxiety</td>
</tr>
<tr>
<td>(Didrex™)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phendimetrazine - CIII</td>
<td>Adrenergic</td>
<td>Tachycardia, HTN, anxiety</td>
</tr>
<tr>
<td>(Bontril™, Prelu-2™)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Orlistat Induces Weight Loss

Torgenson et al., Diabetes Care 2004
Weight Maintenance on Sibutramine

Randomization at 6 months *in those with ≥ 5% initial weight loss*

James *et al.*, *Lancet* 2000
# Weight Loss from Other Medications

## Strategy: Aim for Double Benefits when Possible

<table>
<thead>
<tr>
<th>Medication</th>
<th>Indicated Uses</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>Depression</td>
<td>Avoid in bipolar disease</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Seizures, Migraines, Mood disorders</td>
<td>May produce neurological side effects</td>
</tr>
<tr>
<td>Zonisamide</td>
<td>Seizures, Mood disorders</td>
<td>Few studies</td>
</tr>
<tr>
<td>Metformin</td>
<td>Type 2 diabetes, PCOS</td>
<td>Rare liver toxicity</td>
</tr>
<tr>
<td>Exenatide</td>
<td>Type 2 diabetes</td>
<td>Injectable</td>
</tr>
<tr>
<td>Pramlintide</td>
<td>Type 2 diabetes</td>
<td>Injectable</td>
</tr>
</tbody>
</table>
Topiramate Induces Weight Loss

Van der Merwe T et al., 12th European Congress on Obesity 2003
Pramlintide Induces Weight Loss

Aronne L et al., JCEM 2007
Medication-induced Weight Gain

Medications likely account for 5-10% of obesity in the U.S.
# Treatment of Medication-induced Obesity

**Strategy:** Replace Weight Gain Promoting Medications

<table>
<thead>
<tr>
<th>Category</th>
<th>Common Weight Gain Promoting Medications</th>
<th>Potential Alternatives that Promote Less Weight Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRIs</td>
<td>Celexa™, Lexapro™, Paxil™</td>
<td>Prozac™, Zoloft™, Bupropion</td>
</tr>
<tr>
<td>Mood stabilizers</td>
<td>Olanzapine (Zyprexa™), Clozapine (Clozaril™), Risperidone</td>
<td>Topiramate, Zonisamide, Geodon™</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Valproate</td>
<td>Phenytoin, Topiramate</td>
</tr>
<tr>
<td>Insulinotropic agents</td>
<td>Insulin, Sulfonylureas, Thiazolidinediones</td>
<td>Pramlintide, Exenatide</td>
</tr>
<tr>
<td>Steroids</td>
<td>Corticosteroids</td>
<td>Immunosuppressants, TNFα blockers</td>
</tr>
</tbody>
</table>
Behavior Therapy Augments Sibutramine

Wadden T et al., NEJM 2005
# Efficacy of Current Therapies

<table>
<thead>
<tr>
<th>Weight Loss (% of patients)</th>
<th>6-month</th>
<th>5-year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehensive, behavior-based (diet and exercise)</td>
<td>60-75</td>
<td>1-5</td>
</tr>
<tr>
<td>Medications (sibutramine, orlistat, phentermine)</td>
<td>70-90</td>
<td>1-5</td>
</tr>
<tr>
<td>Surgery (gastric bypass, gastroplasty)</td>
<td>80-90</td>
<td>50-70</td>
</tr>
</tbody>
</table>
Weight Loss Surgery

Roux-en-Y Gastric Bypass

Adjustable Gastric Banding
Effectiveness of Obesity Treatments

Swedish Obesity Subjects
Diabetes Prevention Program

- Lifestyle & Medications
- Gastric Banding
- Gastric Bypass

Percent Total Weight Loss

Time After Surgery (years)
## Outcomes of Gastric Bypass

<table>
<thead>
<tr>
<th>Disorder</th>
<th>% Improved</th>
<th>% Resolved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>100</td>
<td>82</td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
<td>96</td>
<td>72</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>96</td>
<td>63</td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>96</td>
<td>41</td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>93</td>
<td>74</td>
</tr>
<tr>
<td>Hypertension</td>
<td>88</td>
<td>70</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>88</td>
<td>41</td>
</tr>
<tr>
<td>Gout</td>
<td>86</td>
<td>72</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>86</td>
<td>57</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>83</td>
<td>44</td>
</tr>
<tr>
<td>Asthma</td>
<td>82</td>
<td>13</td>
</tr>
<tr>
<td>Depression</td>
<td>55</td>
<td>8</td>
</tr>
</tbody>
</table>
## Complications of Gastric Bypass

<table>
<thead>
<tr>
<th>Complication</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for re-operation</td>
<td>5 %</td>
</tr>
<tr>
<td>Major wound infections</td>
<td>2 %</td>
</tr>
<tr>
<td>Anastomotic ulcer/obstruction</td>
<td>5 %</td>
</tr>
<tr>
<td>Persistent dumping syndrome</td>
<td>3 %</td>
</tr>
<tr>
<td>Micronutrient deficiency</td>
<td>22 %</td>
</tr>
<tr>
<td>Steatohepatitis</td>
<td>3 %</td>
</tr>
<tr>
<td>Symptomatic gallstones</td>
<td>2 %</td>
</tr>
<tr>
<td>Venous thrombosis</td>
<td>2 %</td>
</tr>
<tr>
<td>Anastomotic leak</td>
<td>0.7 %</td>
</tr>
<tr>
<td>Overall major morbidity</td>
<td>10 %</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>0.3 %</td>
</tr>
</tbody>
</table>
Surgery Decreases Long-term Mortality

Adams et al., NEJM 2007

- 15850 gastric bypass patients and matched controls (Utah)
- 7.1 year mean follow-up
- Gastric bypass group exhibited overall 40% reduction in mortality
- Specific-cause mortality after gastric bypass
  - 56% reduction from CAD
  - 92% reduction from type 2 diabetes
  - 60% reduction from cancer
  - 58% increase for accidents or suicide
Indications for Weight Loss Surgery

1. BMI > 35 in association with major medical complications of obesity
   OR
   BMI > 40
   (more stringent BMI criteria for adolescents)

2. Failure of other approaches to long-term weight loss
Contraindications to Surgery

- End-stage lung disease
- Unstable cardiovascular disease
- Multiorgan failure
- Gastric varices
- Uncontrolled psychiatric disorder
- Ongoing substance abuse
- Age > 75 or < 15 years
- Noncompliant patient
Practical Guidance

• Embrace modest weight loss
  • Focus on what is achievable – and sustainable
  • Understand biological limits
  • Be clear about what treatment can and cannot do

• Understand that one size does not fit all

• Cherish non-weight outcomes
  • Recognize all successes of therapy

• Go slow, gain the patient’s confidence, and try different approaches (“Pac-Man”)

• Focus more on what you can offer more than how the patient behaves
Practical Guidance

• Be realistic
• Be optimistic
• Be encouraging
• Be there
Understanding and Treating Obesity

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September 14, 2010
Upcoming Webinars, Programs, Services

October

• Employee Engagement
  • 10/7 at 12:15pm

• Health Literacy & Patient Education in PC
  • 10/14 at 12:15pm

• Program and Course Information

www.massgeneral.org/stoecklecenter/pec/course_catalog
Wrap-Up

• Today’s session - available online.
• Evaluations

Thank you for your participation!