Overview of Management of Obesity

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I have nothing to disclose.
Objectives

- Importance of obesity management
- Lifestyle and behavioral strategies for weight loss
- Medical management of weight loss
- Introduction to bariatric surgery
Mortality Risk

Disease Risk

Obesity

- Quality of Life
- Sleep Apnea
- Infertility
- Arthritis
- Gall Stones
- Coronary Heart Disease
- Cancer
- Gout
- High Blood Pressure
- Diabetes
## Causes

### Primary
- Dietary
- Social and behavioral
  - Economic factors
    - Cost of food
    - Gym Membership
  - Two jobs
  - Binge eating
  - Lack of Sleep
  - Psychological factors
    - Stress
    - Low-self esteem
- Sedentary life style
- Pregnancy
- Genetic/Family

### Secondary
- Medications
  - Steroids
  - Anti-psychotics/depressants
  - Progesterone
- Neuroendocrine causes
  - Hypothyroidism
  - Hypothalamic
  - Cushing's syndrome
  - PCOS
  - Hypogonadism
  - GH deficiency
  - Depression
- Genetic
  - Real “genes”
But the 800 lb. Gorilla...
Phases of Obesity Treatment

Phase I
(Weight Loss)
3-6 months

Phase II
(Weight-Loss Maintenance)
Indefinitely

When you stop treatment, the disease comes back!
Surgery

Pharmacotherapy

Lifestyle Modification

Rate of weight loss

Weight stabilization

Dream weight

Initial goal 5-7%

Degree
DON'T FORGET, YOU ARE WHAT YOU EAT.

I NEED TO EAT A SKINNY PERSON.

Dietary therapy...
Dietary Therapy

- Under-reporting of calorie consumption
- Men lose more weight than women
- Metabolic rate declines by 2% per decade (100 kcal/day)
Choice of dietary therapy remains uncertain....

- Total calories vs. macronutrient composition
- Balanced, portion-controlled, low fat diets
- Eliminate alcohol, sugar drinks, and conc. sweets
- Meal replacements/pre-packaged meals
  - Lack of variety
- Fad diets
  - Unsustainable
Spectrum of Dietary Advice

- Eat Less
- Fat or Calorie Counting
- Meal Replacement
- Meal Provision
- Healthy Eating
- Calorie Deficit
- 1:1 or Group Counselling
- VLCD
Any ‘diet’ is better than no diet…

- Predictable initial rate of weight loss
  - 500 kcal/day deficit ~ 1 lb per wk. loss/3-6 m
- Very low-calorie diets: 200-800 kcal/day
  - < 200 kcal/day: starvation diets
  - Lose muscle mass
- Changes in the peripheral hormone signals that regulate appetite
To sustain any diet or diet-induced weight-loss

Exercise therapy…
Exercise Therapy

- Maintaining long-term weight loss
  - A dose-response relationship
- Preserving lean body mass while dieting
Mean weight according to the baseline physical activity (Women’s Health Study)

How much?

JAMA, March 24/31, 2010—Vol 303, No. 12
In the absence of weight loss....
Behavior Therapy....

"Don't step on it... it makes you cry."
Ingestive Behaviour

Homeostatic System

Hunger: Need for Calories

Satiety: Sense of “Fullness”

Hedonic System

Appetite: Need for Foods

Reward: Sense of Pleasure
Behavioral therapy

Assumptions
- Maladaptive eating and exercise patterns
- And these behaviors can be modified by altering
  - Environment
  - Reinforcement contingencies

False Expectations
- Expectations often exceed what is feasible
  - People often predict that they will change more quickly and more easily than is possible
  - People overestimate their abilities in many domains and are unaware that they are inaccurate
  - People often believe that making a change will improve their lives more than can reasonably be expected
ELEMENTS OF BEHAVIORAL STRATEGIES

- Self-monitoring
- Controlling or modifying the stimuli that activate eating
- Slowing down the eating process
- Goal-setting
- Behavioral contracting and reinforcement
- Nutrition education and meal planning
- Modification of physical activity
- Social support
- Cognitive restructuring
- Problem-solving
Pharmacologic therapy....
(adjunct to reduced-calorie diet and exercise)
Efficacy

1 lb. per week

Safety

Numerous side-effects

Durability

Does not cure obesity

Cost

Too expensive
Indications for drug therapy

- BMI > 30 kg/m², who have failed to achieve weight loss goals through diet and exercise alone
- BMI of 27 to 29.9 kg/m² with comorbidities
Currently approved anti-obesity drugs

- Orlistat
- Lorcaserin
- Sympathomimetics: Phentermine, Topiramate
- GLP-1 agonists
- Naltrexone/Bupropion
Drugs that alter fat digestion: Orlistat

• Inhibits pancreatic lipase
  ◦ Fat is not absorbed with > 30% fat in the diet
  ◦ Fecal excretion of fat increased
• Excellent cardiovascular and safety profile
• 60 mg dose as OTC Alli
Weight loss with orlistat

Weight loss (means ± SEM) during four years of treatment with orlistat plus lifestyle changes or placebo plus lifestyle changes in obese patients.

- Typical loss of 6-10 Kg body weight
- Maintained as long as drug is taken
- Improves BP and diabetes control
- Prevents conversion to overt diabetes
- Improves serum TC, LDL & TG
Orlistat: Adverse effects

Gastrointestinal
  Cramps
  Flatulence
  Fecal Incontinence
  Oily spotting
  Fat-soluble vitamin absorption
Serotonin agonists

- **Selective agonists**
  - Lorcaserin selective to serotonin 2C receptor
  - Reduces appetite

- **Non-selective agonists**
  - Dexfenfluramine & Fenfluramine
  - Also decrease appetite
  - But stimulate receptor 2B –
    - serotonin-associated cardiac valvular disease
BLOOM trial

**Beneficial effects**
- SBP and DBP
- HR
- LDL
- CRP
- Fibrinogen
- Fasting glucose and insulin
Lorcaserin: Adverse effects

- High drop out rates (35-50%)
- Mild – headache, nausea, URI
- No valvular heart disease - but duration is short
- Cannot be used with Cr. Cl < 30 mL/min
- Serotonin syndrome
  - SSRI, SNRI, TCA, MAOI, Bupropion
Sympathomimetic Drugs

- Stimulate release or inhibit reuptake of norepinephrine or serotonin
- Increase satiety
- Approved only for short-term use (12 w)
- Many have been withdrawn
  - Phentermine (most commonly used)
  - Diethylpropion
  - Benzphetamine
  - Phendimetrazine
  - Sibutramine (WD)
  - Phenylpropanolamine (WD)
Both continuous and intermittent therapy with phentermine result in more weight loss than placebo.

Data from Munro, JF, MacCuish, AC, Wilson, EM, Duncan, LJ, BMJ 1968; 1:352.
Adverse effects

- Increase HR, BP
- Insomnia
- Dry mouth
- Constipation
- Nervousness
GLP-1 agonists

- Synthetic analogues of GLP-1 hormone
- Bind to GLP-1 receptor
- Stimulates glucose-dependent insulin release and inhibits glucagon release
- Inhibit gastric emptying & improves satiety
- Injectibles
Liraglutide and Body Weight

Pi-Sunyer X et al. N Engl J Med
2015;373:11-22
Adverse effects

- Nausea & Vomiting
- Serious but less common side-effects
  - Pancreatitis
  - Renal impairment
  - Suicidal thoughts
- In rodents
  - Benign and malignant thyroid C-cell tumors
  - Not recommended for those with personal or family hx of medullary thyroid cancer or MEN2A or 2B
Combination Drugs

- **Phentermine-Topiramate**
  - 8-10% weight loss
  - REMS due to risk during pregnancy
  - Dry mouth, increase in HR, depression/anxiety, kidney stones

- **Bupropion-Naltrexone**
  - 4-5% body weight
  - Smokers
  - Contraindicated with uncontrolled HTN, seizures, eating disorder, bupropion & opioid use
  - Uncertainty about cardiovascular effects
  - Large drop out
  - Nausea, headache, constipation
Surgical therapy
### Candidates for Bariatric Surgery

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>NHLBI Grade</th>
<th>ACC/AHA COR</th>
<th>LOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Appropriate option for patients with a BMI ≥40 or BMI ≥35 with obesity-related comorbid conditions, and who:</td>
<td>A (Strong)</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>a) Are not motivated to lose weight</td>
<td></td>
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<tr>
<td>b) Have not attained sufficient weight loss with behavioral treatment with or without pharmacotherapy</td>
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<tr>
<td>2. No recommendation on bariatric surgery for patients with BMI &lt;35*</td>
<td>N (No Recommendation)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>3. Choice of bariatric surgery procedure affected by patient factors: age, obesity severity, comorbidities, risk of complications, behavioral and psychosocial factors</td>
<td>E (Expert Opinion)</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

*Benefits of bariatric surgery inconclusive for patients with BMI <35
ACC=American College of Cardiology; AHA=American Heart Association; BMI=body mass index; COR=class of recommendation; LOE=level of evidence; NHLBI=National Heart, Lung and Blood Institute; TOS=The Obesity Society

Gastric Bypass

Sleeve Gastrectomy

Source: ASBMS.org
Adjustable Gastric Band

Biliopancreatic Diversion with Duodenal Switch (BPD/DS) Gastric Bypass

Source: ASBMS.org
Bariatric Surgery Reduces Mortality in Swedish Obese Subjects  
(n=2010 vs. 2037)

30% Reduction in All Cause Mortality

Sjostrom L et al. NEJM 2007;357:741-52
Long-Term Mortality After Gastric Bypass Surgery (n=7928 vs. 7925)

- All Cause Mortality: 40%
- Coronary Artery Disease: 56%
- Cancer: 60%
- Diabetes: 92%

Adams TD, et al. NEJM 2004;357:753
Bariatric Surgery
Effect on Cardiovascular Risk
A Systematic Review and Meta-Analysis of 22,090 Patients

- Hypertension: 62%
- Dyslipidemia: 70%
- Diabetes: 77%
- Sleep apnea: 86%

Treatment Success

- Lifestyle (LS) ~ 3-5%
- LS+Pharmacotherapy ~ 5-15%
- LS+Surgery ~ 20-30%

Change in Weight vs. Years