UNDERSTANDING OBESITY

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Objectives
A. To examine the diagnosis of obesity.
B. To explore etiologies for the growing prevalence of obesity.
C. To review co-morbidities associated with obesity.
D. To introduce an approach to medical management of obesity.

Recommended Reading
- Korner J, Leibel RL. To Eat or Not to Eat – How the Gut Talks to the Brain. N Eng J Med. 2003;349:926-928. (on reserve in library)

A. Introduction
1. Statistics
   - 100 million Americans or 3/5 of adults are overweight
   - about 1 out of 5 children are overweight
   - Cost of obesity to society -$100 billion dollars / year
   - Obesity is 2nd only to cigarette smoking in morbidity & mortality
   - contributes to 300,000 premature deaths annually

2. CDC Trends in the US
   - Obesity Trends Among U.S. Adults: 1985
   - Obesity Trends Among U.S. Adults: 1990
   - Obesity Trends Among U.S. Adults: 1995
   - Obesity Trends Among U.S. Adults: 2000

B. Diagnosis
1. Definition / Criteria
   a. BMI-body mass index-weight(kg) / height^2(m^2)
      weight(lbs)/ height^2(in^2) x 704.5 (normal 18.5 to 25)
   Overweight or obese
      - multi-factorial: mixture of genetic & environmental
      - Overweight: BMI 25-30
– Obese: BMI >= 30
– Extreme Obesity: BMI > 40
– males ideal BMI: 20-22; females ideal: 19-21

b. Percent Body Fat
   females- nrl: 20-30%; borderline: 30-33%; obese:>33%
   males- nrl: 12-20%; borderline: 25-27%; obese:>27%

2. Body Composition
   • 1) Lean Body Mass- 15% to 20%
   • 2) Body Fat- 20% to 25%
   • 3) Body water- 50% to 60%
   • 4) Mineral mass- approximately 5%

3. Body Fat
   • 50% of fat is in subcutaneous form
   • Females have more fat tissue
     females- nrl: 20-30%; borderline: 30-33%; obese:>33%
     males- nrl: 12-20%; borderline: 25-27%; obese:>27%
   • Men have more lean body mass
   • For survival
     – men need 3% body fat
     – women need 12% fat
   • Ovulation & Pregnancy require 20% body fat

4. Other Parameters to Assess Weight
   • Ideal body wt: outdated
   • Waist circumference: increases m&m
     – males >102cm (40 in.); Females >88cm (35 in.)
   • Waist/Hip ratio: inaccurate
     – if >.95 in males: increases m&m
     – if >.80 in females: increases m&m
   • Triceps/abdominal/thigh fold
   • Devices used to measure body composition : Underwater weighing/ Bod Pod/ DEXA

C. Mechanisms
1. Hunger and satiety centers affecting appetite
   – hypothalamus
   – paraventricular nucleus
   – nucleus accumbens
2. Neurotransmitters
   – serotonin & dopamine
   – galanin
   – neuropeptide y
   – norepinephrine
   – Ghrelin
3. Theories
   • Genetic connection
   • Environmental/Social connection
   • Psychological connection
   • Physiological connection
4. Genetics
   • OB gene - leptin protein
   • Twin Studies
   • Metabolic “set point”
     – Massa studies
   • Genetic variances
     – i.e. : hyperplasia / hypertrophy ratio
       a. Single Gene Obesity Syndromes
          (rare human mutations)
          (1) Leptin (adipose tissue)
             • Influences appetite, insulin/glucose, reproduction
             ⇒ Leptin or leptin receptor deficiency
          (2) Melanocortin (brain)
             • Influences appetite, adrenals, pigmentation
             ⇒ POMC, PC1, or MC4R deficiency
   b. Polygenic Obesity Syndromes
     • > 40 syndromes of genetic abnormalities within chromosome regions described.
     • ⇒ appetite, growth, sexual development, mentation, various somatic abnormalities.
       Examples: Prader-Willi, Bardet-Biedl, Alstrom, Albright hereditary, Osteodystrophy
5. Set-point theory

   “Set-point” theory holds that typical weight-loss / weight regain pattern is explained by
   homeostatic metabolic feed-back system:
   Weight loss →
   ↓ RMR →
   + energy balance → return to preset weight
a. Effects of energy restriction vs. weight reduction on RMR

- Energy restriction → transient ↓ RMR, which is greater than expected for ↓ in body size.
- Upon return to energy balance, RMR is appropriate for new body size.

b. Does ↓ RMR explain the weight regain tendency of obesity-prone persons?

Specifically …

✔️ Is RMR ↓ in weight-reduced subjects? NO
✔️ Is RMR ↓ in weight-reduced vs. never-obese subjects? NO
✔️ Does ↓ RMR predict weight gain? NO

In course of evolution, feed-back systems undoubtedly developed to regulate weight (e.g., hypothalamic control of food intake). However, such regulatory systems …

- Do not appear to be operating through modulation of RMR, and
  Must be overwhelmed by lifestyle factors (e.g., ↓ PA) conducive to + energy balance.

c. Set Point Theory- Key Points

✔️ Metabolic factors (e.g., RMR) did not distinguish women who were successful vs. unsuccessful at weight control.

✔️ Lifestyle dependent factors (e.g., PA) did distinguish women who were successful vs. unsuccessful at weight control.

Not all studies agree

Some investigators have reported ↓ RMR, during and after weight loss, supporting the set-point theory.

D. Multifactorial Etiology

1. Environmental / Social

- Childhood- parents’ role
- Socioeconomic status
- Cultural perspectives
  – learned patterns
- Behavioral influences
  – Pavlov and operant conditioning

2. Environmental / Social

Our genes permit us to become obese,
but … the environment determines if we become obese.


3. Psychological
- Depression/unhappiness
- Distortion of body image
- Scheduled eating times vs. eating when hungry
- Childhood assoc. w/ food and maternal love

4. Physiological
- Gestational/early infancy
  - brown fat
- Ages 5- 7 yold
  - hyperplasia vs hypertrophy
- Gynecoid vs Android
  - android connected w/ more m&m
- Circadian Rhythm

E. Complications of Obesity
1. Neuroendocrine Disorders Associated with Obesity
- Hypothyroidism
- Cushing’s syndrome
- Castration, ovarian failure
- Polycystic ovary syndrome
  -- ↑ insulin, ↑ LH, ↑ androgens
  -- cystic ovaries, ↓ menses, masculinization, hirsutism
- Insulinoma
- Hypothalamic lesions

2. Major co-morbidities of obesity
- Hypertension
- Diabetes mellitus
- Coronary heart disease
- Gallbladder disease
- Sleep Apnea
- Osteoarthritis
- Certain cancers

3. BMI and/or abdominal adiposity are associated with cancer of …
• Endometrium *
• Breast (postmenopausal women) *
• Colon (men & women)
• Prostate
• Cervical and Ovarian
• Gallbladder (men & women)
• Renal cancer- not Clear Cell

*Possible mechanism: ↑adiposity →
↑ androstenedione being converted
to estrone in adipocytes

F. Assessment of Obese individual

• Calculation of BMR/BEE: Basal Metabolic Rate or Basal Energy Expenditure
  – sum of all internal characteristics at rest
  – direct measurement of BMR
  – factors affecting BMR

• Calculation of Total Energy Expenditure
 1. BMR/BEE- Basal Metabolic Rate or Basal Energy Expenditure
  • Women- .9kcal/kg/hr
  • Men- 1.0kcal/kg/hr
  • Calculate for 24 hr period
  – .9or1.0 x wt x 24hrs
  • Harris Benedict Equation- (wt, ht, and age)
  – men: 66.47 + 13.75 w + 5.00h - 6.76a
  – women: 655.1 + 9.56w + 1.85h - 4.68a

2. Total Energy Output
• TEE (kcal) = BEE + AEE + TEF

• Energy level to derive AEE (activity EE)
  – sedentary: 20%
  – very light: 30%
  – moderate: 40%
  – heavy: 50%

3. TEF- overhead cost of food metabolism
  – approx. 10% of total daily calories (kcal)

4. Components of Energy Expenditure
Example

- 26 y.o., 220 lb female, 160 cm, sedentary activity, and consumes 2500 kcal/day
  - \[ \text{BEE} = 0.9 \text{kcal/kg} \times (220 \text{ lb} / 2.2 \text{ lb/kg}) \times 24 \text{hrs} \]
  - \( \text{BEE} = 2160 \)
  - \( \text{H-B equation: 1785 kcal(approx. 1800)} \)
  - \[ \text{TEE} = \text{BEE} + (.20 \times \text{BEE}) + (.10 \times 2500 \text{kcal}) \]
  - \( \text{TEE} = 1800 + 360 + 250 \)
  - \( \text{TEE} = 2410 \text{ or approx. 2400} \)

5. Measurement of Total Daily Energy Expenditure

- Direct Calorimetry
  - directly measures amount of heat given off by body
  - uses airtight calorimetric chamber - water
  - have to assess for at least 24 hours
  - very expensive - not currently used

- Indirect Calorimetry
  - estimates heat given off by body by measuring oxygen consumption and CO2 production
  - uses metabolic chamber or a mask, hood, or mouthpiece - gases are collected and analyzed
  - measures O2, CO2, and also nitrogen excretion if possible
  - determining RQ (respiratory quotient) - ratio between CO2:O2
  - \( 1 \text{ liter O2 consumed} = 4.81 \text{kcal} \)

G. Management

- Diet
- Exercise
- Acceptable wt loss
- Counseling & Behavior Modification
- Medications
- Surgery

1. Diet

- Fad diets do not work
  - 80 - 90% of followers regain the lost weight
- Ketogenic Diets- “Atkins Diet”
- Step-wise planning
— 1) decrease calorie intake
— 2) decrease fat intake
— 3) very low calorie diets
   • strict doctor supervision

a. Basic Facts about Dieting
   • Popular or Fad Diets
     • short lived - based on marketing gimmick
     • athletes are susceptible
     • justified typically by scientific claim that is speculation or unproven
     • endorsed by famous individuals/athletes
   • How to recognize a fad diet
     • claims to be new, modern, improved, or recently discovered
     • claims rapid loss of weight or fat
     • claims weight loss success with little of no exercise
     • includes special foods, special combinations, bad foods, magic foods, miracle foods that burn fat
     • includes a rigid menu that must be followed daily
     • includes supplements, meal, foods, that claim to cure disease or ailments

b. Atkin
   • Atkins first published his “Diet Revolution” in 1972, Americans were just coming to terms with the proposition that fat—particularly the saturated fat of meat and dairy products—was the primary nutritional evil in the American diet.
   • Claims:
     — Induces significant wt loss
     — Reduces incidence of Diabetes Type 2
     — Actually decreases Triglycerides, LDL
     — Increases HDL

(1). Four Steps of Atkins Diet
   • Phase 1: Induction
     Restrict carbohydrate consumption to 20 grams each day, obtaining carbohydrate primarily from salad and other non-starchy vegetables.
   • Phase 2: Ongoing Weight Loss (OWL)
     Add carbohydrate, in the form of nutrient-dense and fiber-rich foods, by increasing to 25 grams daily the first week, 30 grams daily the next week and so on until weight loss stops. Then subtract 5 grams of carbohydrate from your daily intake so that you continue sustained, moderate weight loss.
   • Phase 3: Pre-Maintenance
     Make the transition from weight loss to weight maintenance by increasing the daily carbohydrate intake in 10-gram increments each week so long as very gradual weight loss is maintained.
   • Phase 4: Lifetime Maintenance
     Select from a wide variety of foods while controlling carbohydrate intake to
ensure weight maintenance and a sense of well-being. This lifestyle is the foundation for a lifetime of better health.

♦ Evidence

• Evidence is not confirmed

• Athletes need more carbohydrates
  – one slice of white bread has 10-15 g carbs

• Wt loss: attributed to diuresis in first few weeks

• Most of wt loss may be attributed to a lower energy intake

• decreased appetite may also contribute to wt loss

c. Starvation Diets (fasting)

• used as quick method to lose weight - very rapid

• provide less than 200 kcal/day

• problems that can occur
  – major protein losses - muscle and organ
  – fluid & electrolyte losses - dehydration & hypotension
  – malnutrition often develops - bone loss possible
  – refeeding needs to be done slowly
  – long term success is poor
  – RMR is blunted - increase likelihood to gain wt.
  – severity depends on length of time following.

d. Very Low Calorie Diets (VLCD)

• provide 200-800 kcal/day

• in existence since 1930’s - not popular until 1970’s

• 1977-78 58 deaths reported in obese individuals that had been on this diet

• protein sparing modified fast (PSMF)
  – increased protein (1.5g/kg), low kcal (200-400), improved nitrogen balance, with rapid weight loss

• ketogenic diet - no carbohydrate

• non-ketogenic - some carbohydrate

**Major side effects**

– Hair loss

– Postural hypotension

– Negative protein balance

– Negative calcium balance

– Gallstones

  New gallstones can form within 4 weeks

  Incidence rates = 15 to 25 - fold higher

  than in general obese population
e. Low Calorie Diets
   • provide 800-1200 kcal/day
   • comprised of regular foods, or specially formulated
   • enough carbohydrate to avoid ketosis
   • involves MVI supplement
   • commercial programs
   • Weight Loss 1-3#/week
   • relatively safe
   • too low energy intake for men, active persons, some women - designed for obese individuals
f. Moderate Energy Restriction Diets
   • increasingly common to recommend with the addition of physical activity
   • energy content of at least 1200 kcal/d
   • based on current intake for weight maintenance
   • weight loss less rapid
   • FFM and RMR are not compromised
   • healthy dietary practices stressed
   • assists in long term weight maintenance
g. Energy Density and Food Intake
   a. CONCEPT:  *Time-calorie displacement*
      “Unlimited intake of low energy-dense foods will prolong eating time, increase satiety, and reduce energy intake compared to intake of high energy-dense foods.”
      Duncan KH et al.  Am J Clin Nutr 1983
      Time-calorie displacement approach to weight control
      Effect of fat vs. water content on energy density

      Cumulative *energy intake* in 18 women given ad lib access to meals of LOW, MEDIUM, and HIGH energy density
      Energy Density and Food Intake
      Effect on calorie consumption
      Subjects consumed similar amounts of food but \( \geq 400 \text{ kcal/d} \) more calories on high vs low energy-dense meals, despite comparable feelings of fullness.
      **IMPLICATION of Time-calorie displacement**
      Energy intake is determined by *weight* of food consumed, NOT fat or calorie content.

      Bell et al.  AJCN 67:412, 1998

2. Acceptable Weight Loss
   • Ideally should lose 1 to 2 lbs / week
   • Reduce total calorie intake by 500kcal per day for one pound wt loss in one week
      — Count kcal/day minus 500 kcal (1 lb wt loss/wk)
3. Exercise

- Anerobic vs Aerobic exercise
  - anerobic- mainly wt bearing exercises
  - aerobic- mainly cardiovascular exercises
- Previously: aerobic better than anerobic for wt loss- due to greater efficiency
- Now: Anerobic better than Aerobic
  - increases lean mass thus increases energy req.
  - However in HTN, causes increase in BP

4. Counseling

- Reshaping psychological viewpoints via professional help

- Team effort
  - psychiatrists/psychologists
  - nutritionist
  - exercise physiologist/ fitness trainers

5. Behavior Modification

- Three deadly sins:
  - genetics
  - destructive diet
  - sedentary lifestyle
- Cognitive/behavior methods - modify diet
  - spacing the food - time interval
- Lifestyle changes

6. Medications

a. Long term FDA approved weight loss drugs

  - Sibutramine (Meridia): centrally acting
    - action: inhibits uptake of serotonin and norepinephrine
    - promotes satiety and thus decreased food intake

  - Orlistat (Xenical):
    - action: inhibits gastric and pancreatic lipases blocking hydrolysis of trigly. into fatty acids

b. Phen-Fen and Ephedra controversies

  - cardiac side effects (valular dysfunctions, MI)

c. OTC weight control aids

7. Surgery
• Still not a cure & reserved for severely obese
  – Roux-en-Y Gastric Bypass, Lap banding, Pancreatic-Biliary Diversion
• relapse occurs after body adapts to surgical change
  – “Liposuction”- purely cosmetic- 5-10 % fat removal : wt gain re-occurs
  a. Bariatric Surgery
    (Roux-en-y gastric by-pass)
  • Most patients lose 50-100 % of excess weight.
  • Wt loss plateaus at 12 - 24 months.
  • Weight regain occurs (~ ½ of patients regain 50% of lost weight at 5 years).

(1) Bariatric Surgery- Vitamin Deficiencies

• Vitamin B12 deficiency- Intrinsic Factor cannot bind
• Iron and Folate deficiencies- ph
• B vitamin def.- B1, B2, B6 (neuropathies)
• Malabsorption leads to fat -soluble vitamin deficiencies
• Vit. A, D, E, K

(2) Ghrelin

• Ghrelin (pronounced grell-in), a hormone produced in the stomach
  and taken up by adipose tissue and effects the satiety center of brain.
• Discovered in 1999, it causes the hunger pangs that strike before
  meals.
• Obese people don't have unusually high ghrelin levels - until they start
  losing weight. As fat disappears, ghrelin soars, triggering intense
  hunger and helps explain why it's so hard to stick with a diet.
• Dramatically reduced in Post- Gastic Bypass patients
• (NEJM- 2002)

Summary

• No magic bullets in treatment of obesity
• Understand factors behind weight gain
• Management- using patients idiosyncrasies
• Quest for new alternatives including weight management medications
• natural anorexigenic agents
• continuous drug rx- long term management
• Last resort- Bariatric surgery
SAMPLE EXAM QUESTIONS
True or False

Genetics
In the general population, relative to diet and physical activity, genetic factors represent the primary cause of obesity.

Endocrine disorders
Among patients with severe degrees of obesity, endocrine disorders (eg, hypothyroidism) are most likely to exist.

Metabolism
An obese person has a RMR (as total # calories burned/day) that is generally higher than that of a lean person of the same age and gender.

Set-point theory
Previously obese, weight-reduced persons have a RMR that is normal relative to their new body size; hence, low RMR does not predispose them to regain the weight.

Diet
Gallstones represent the major adverse health outcome of rapid weight loss diets (eg, average loss of > 3 lb/wk).

Diet
Satiety (feeling of fullness) is primarily determined by the fat content of the foods we eat.

Multiple Choice Questions
1. What is body mass index?
   a. Body mass relative to the reference standard for height.
   b. Weight in pounds divided by height in inches squared.
   c. Weight in kg divided by height in meters squared.
   d. Measured by skin-folds.
2. Approximately what percent of adult Americans are now classified as obese?
   a. 15%
   b. 22%
   c. 33%
   d. 50%
3. Which of the following is not known to be associated with obesity?
   a. Testicular cancer
   b. Sleep apnea
   c. Osteoarthritis
   d. Breast cancer
4. The best predictor of long term success in maintenance of body weight following weight reduction is _____.
   a. Regular physical activity / exercise
   b. Reported adherence to a low fat diet

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c. Participation in a group support program
d. The amount of initial weight loss

Answers: 1-c, 2-b, 3-a, 4-a

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