THE SKINNY ON OBESITY

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And an associate of both Jones & Burr…but it’s OK…we’ve all got our cross to bear!

PS I really was a nice boy before I met them!
• Definition, diagnosis

• Epidemiology of overweight & obesity

• Clinical consequences of overweight & obesity
  • Pathophysiologic relationships
    • Diabetes, HTN, dyslipidemia, CAD, OSA, sexual dysfunction, etc.

• Endocrinology of obesity

• Treatment
  • Diets? Don’t make me laugh
  • Lifestyle, medication, vagal nerve block, bariatric surgery
• Humanity in the hunter-gatherer stage of human & social evolution did not suffer from obesity (or type 2 diabetes)

• Obesity on a societal scale is a product of the Industrial Revolution
  • The human genome changes very slowly over experiential periods of time, and differs very little now from what it was at the start of the Industrial Revolution (what’s that…a couple dozen generations at most)
  • The Industrial Revolution led to plentiful availability of food
    • Since the beginning of the Industrial Revolution, food began to be processed, concentrating calories and removing nutrients and fiber: *The whiter the bread, the sooner you’re dead*
  • The Industrial Revolution led to labor-saving devices, leisure time
    • Evolution of the settee spud…*the couch potato*
  • More recently, the curse of fast food (A *curse*? I mean the F-bomb to the 10th power). *F*st *f*od is a f***ing10 killer.
  • For those lower on the socioeconomic strata, unhealthy food is *cheaper* than healthy food
In the fast food world, marketing is everything!

“Our challenge is to convince the public that heart attacks and diabetes are sexy”
YOU COULDN’T PUT SODIUM AZIDE IN THE WATER SUPPLY, BUT YOU CAN SELL THIS POISON TO ANYONE
OBESITY: IT’S OFFICIAL

• In June 2013, the American Medical Association, exercising the pinnacle of diagnostic acumen, officially defined obesity as a disease

• I can’t tell if that’s helped advance research in the field or patient care one iota.
THE GROSSLY SIMPLISTIC (AND LARGELY UNHELPFUL) VIEW TO MANAGING OBESITY

- Establish negative energy balance
  - Fewer calories *in*
  - *More* calories expended
DEFINE OBESITY

• Body Mass Index (BMI) in kg/m²
  • <18.5 = underweight
  • 18.5-24.9 = normal weight
  • 25.0-29.9 = overweight
  • 30.0-39.9 = obese
  • >39.9 = severe obesity

• Waist circumference (most helpful in discriminating within the overweight BMI category)
  • Women: >35 inches (88 cm)
  • Men: > 40 inches (102 cm)

• (Jones’ criteria) If you run into the wall and your tummy gets there before your nose…
BMI V. DEATH: J-SHAPED CURVE
IT DOESN’T HAVE TO BE ONE OR THE OTHER…
OBESITY EPIDEMIC: IT’S GETTIN’ WORSE, FOLKS...
DATA SHOWN FOR BMI > 30 VERSUS TIME

Data shown for BMI > 30 kg/m²
Within subsets of patients with overweight and/or obesity

- Deranged endocrine and immune responses
  - Sick fat disease (SFD) (adiposopathy)
    - Elevated blood glucose
    - Elevated blood pressure
    - Dyslipidemia
    - Other metabolic diseases
- Abnormal and pathologic physical forces
  - Fat mass disease (FMD)
    - Stress on weight bearing joints
    - Immobility
    - Tissue compression (e.g., sleep apnea, gastrointestinal reflux, high blood pressure, etc)
OBESITY COMORBIDITIES: CONSEQUENCES OF “SICK FAT” AND/OR FAT MASS

- Type 2 diabetes
- Hypertension
- Dyslipidemia (high triglyceride, low HDL, small, dense LDL, high VLDL)
- Nonalcoholic fatty liver disease (NAFLD, NASH)
- Atherosclerotic disease (MI, stroke, PAD)
- Obstructive sleep apnea
- Arthritis and arthralgia
- Impaired fertility
- Cancers
- Cholelithiasis & cholecystitis
<table>
<thead>
<tr>
<th>Hormone (good, bad, ugly)</th>
<th>Ghrelin (-)</th>
<th>Leptin (+)</th>
<th>Adiponectin (+)</th>
<th>Neuropeptide Y (NPY) (-)</th>
<th>Endocannabinoids (-)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tissue Source</strong></td>
<td>Neuroendocrine cells in the GI tract</td>
<td>Adipose tissue</td>
<td>Adipose tissue</td>
<td>Neuroendocrine cells in the gut and hypothalamus</td>
<td>Pot-heads, many tissues</td>
</tr>
<tr>
<td><strong>Target Tissue</strong></td>
<td>Gut, beta cell, throughout the CNS</td>
<td>Hypothalamus</td>
<td>I still don’t know, but I’m goin’ with hypothalamus</td>
<td>Hypothalamus, elsewhere in CNS</td>
<td>CNS, gonads, immune cells</td>
</tr>
<tr>
<td><strong>Role in Physiology &amp; Fun Facts</strong></td>
<td>The “hunger hormone”; stimulates appetite. High in Prader-Willi Syndrome; low in regular obesity; high in anorexia; low after RYGB; blocking receptor treats obesity in animals.</td>
<td>The “satiety hormone”, antagonizes ghrelin in hypothalamus. Levels increased in obesity (leptin resistance).</td>
<td>Decreased in obesity &amp; type 2 diabetes; increases energy expenditure</td>
<td>Potent appetite stimulant.</td>
<td>A family of signaling lipid derivatives with appetite stimulant (among many) properties.</td>
</tr>
</tbody>
</table>
• That poor li’l ol’ thyroid gets blamed for everything!
  • BUT…it is very seldom related to your patients’ obesity
    • I’m stating the obvious…you already know that!

• Check thyroid function in everyone, but it’s been estimated that untreated hypothyroidism will increase body weight by up to 10-15% above ideal body weight. So if you have a 300 pounder, please don’t look to the thyroid for the explanation.

• And yet, 93.7% of obese patients know it’s their thyroid!!! As stated above, that poor li’l ol’ gland gets blamed for everything!

• As Dr.’s Burr and Jones will also tell you, we, as endocrine specialists, would easily miss half the patients with thyroid dysfunction if we relied solely on history and physical exam. So check ‘em, but their TSH of 18 ain’t the cause of their BMI of 43!
RENTAL CHAIRS...SORT OF LIKE WHAT YOU’D DO TO A RENTAL CAR
OBESITY: FUNDAMENTALS OF TREATMENT

- Nutrition
  - Reduce caloric intake
    - Diet details don’t matter – *all* that matters is adherence
    - Eat healthy food – this *does* matter
- Regular exercise *for life*
- Behavioral therapy (*psycho-babble*)
- Weight loss pharmacotherapy
  - BMI > 27 with obesity comorbidities
  - BMI > 30 without obesity comorbidities
- Bariatric surgery
  - BMI > 40
- Vagal nerve block
- *Beware of the snake oil!*
PHARMACOTHERAPY FOR OBESITY

- Guidelines:
  - BMI > 27 with obesity comorbidities
  - BMI > 30 without obesity comorbidities

- FDA-approved obesity drugs for chronic treatment
  - Qsymia (phentermine & topiramate): stimulant and anticonvulsant
  - Belviq (lorcaserin): serotonin 2C receptor agonist
  - Contrave (naltrexone & bupropion): nrcotic antagonist and antidepressant
  - Saxenda (liraglutide high dose): GLP-1 receptor agonist
  - Xenical, Alii (orlistat – fun party drug)
  - Phentermine: stimulant (not for chronic therapy)
    - Duration of treatment, a few weeks
    - Amphetamine: DEA CII stimulant (really not for chronic therapy)

- Obese & type 2 diabetic, FDA-approved
  - GLP-1 receptor agonists
    - Exenatide, liraglutide (low dose), dulaglutide, albiglutide
  - SGLT-2 inhibitors
    - Canagliflozin, dapagliflozin, empagliflozin
AND THEN THERE’S “DR.” OZ

I USE THE TERM “DR.” VERY LOOSELY HERE
PAY NO ATTENTION TO THE MAN BEHIND THE CURTAIN

• Garcinia cambogia
  • The latest snake oil for weight loss
    • David Hannum (but attributed to PT Barnum): *there’s a sucker born every minute*. These are the people who buy Garcinia cambogia.
  • Dr. Oz endorsed (so you know it’s bullshit)
    • Recall the old med school joke: psychiatrists know nothing and do nothing; internists know everything and do nothing; surgeons know nothing and do everything; pathologists know everything and do everything, but it’s too late.
    • Dr. Oz is a surgeon, and he’s telling you about metabolic stuff…yeah…right!
      • Why work when you can play a doctor on TV?!
      • When your patients have metabolic issues, do you refer them to a surgeon?
  • The one, true, unambiguous, indisputable benefit of garcinia cambogia: financial security for snake oil salespeople; they’re are laughing all the way to the bank! And so is “Dr.” Oz.
OBESITY PHARMACOTHERAPY
CONSIDERING QSYMIA, BELVIQ, CONTRAVE, AND SAXENDA

• No head to head studies, and variations in populations studied, make drug effectiveness ranking purely speculative and subject to marketing rather than objective claims.

• Disclaimer: I am not considering phentermine and amphetamine, which are not approved for chronic therapy, and frankly have risks that probably outweigh benefits

• Generally, can expect 5-10% weight loss in a year; of course there can be significantly greater losses in some patients
  • Consider non-responders; d/c after 3 months
  • Ergo, these weight loss drugs do not compete with bariatric surgery for degree of weight that can be lost
OBESITY THERAPY VIA VAGAL NERVE BLOCK
THE NEWEST KID ON THE BLOCK

- Enteromedics VBLOC Maestro System
  - Two electrodes are surgically (laparoscopically) implanted at the vagal nerve trunk near the gastroesophageal junction; the pulse generator is implanted under the skin like a pacemaker.
    - Outpatient surgery, if all goes according to plan
    - Pulse generator battery recharged noninvasively

- Nerve impulses delivered intermittently (programmable) block afferent and efferent vagal nerve traffic between viscera and brain.
  - MOA not known, but bottom line: satiety signal dominates hunger signal

- FDA approved in January 2015
  - BMI > 40, or BMI > 35 with obesity comorbidities
  - Available later 2015 at Bariatric Centers in US

- Median weight loss 20% of excess body weight

- Experience is limited so far, but it may become a player in the obesity field
BARIATRIC SURGERY
ALTERATION OF GI FUNCTION BY SURGICAL MODIFICATION OF GI ANATOMY

• Roux-en-Y Gastric Bypass (RYGB):
  • Results in 65-80% loss of excess body weight
  • Malabsorption

• Sleeve gastrectomy: removal of much of stomach along greater curvature.
  • Results in 50+% loss of excess body weight
  • No malabsorption

• Biliopancreatic Diversion with Duodenal Switch (BPD-DS)
  • Results in 75-80% loss of excess body weight
  • Malabsorption

• Improvement in obesity comorbidities
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WE’VE BEEN SOLD A BILL OF GOODS