Hidden Causes of Obesity

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Excess Weight

- Solution of eating less and exercising more
  - Overly simplistic
  - Lead to mismanagement
- Standard of Care formula

\[ \text{EAT} + \text{EXERCISE} = \text{OBESITY} \]
Weight Homeostasis

• In absence of threat leanness prevails
• In presence of threat excess weight prevails
  *All animals (including humans) wired to resist famine
Hunger Hormones

Ghrelin

NPY

Orexigenic Hormones
Satiety Hormones

- Leptin – decreases appetite by telling brain enough adipose (stored energy)
- Brain becomes RESISTANT
  - Undereating or overeating
  - Threat (stress, illness, or disorder)
- PYY
  - Released empty stomach
  - Constant infusion causes resistance
Weight Homeostasis Formula for Obesity

**Calories IN**
- ++Ghrelin (chronic dieting)
- Leptin resistance
- Psychotropic meds
- Sleep deprivation

**Calories OUT**
- Hypothyroidism
- Liposuction

**Biochemical Lipogenesis**
- Ghrelin
- Metabolic syndrome
- Liposuction
Wired to Survive Famine
Conditions Tipping Weight Homeostasis in Favor of Excess Weight

- Many conditions may increase calories in or decrease calories out regardless of our intentions or actions
  - Undiagnosed/ undertreated hypothyroidism
  - Metabolic syndromes (including PCOS)
  - Chronic dieting
  - Liposuction
  - Sleep deprivation
  - Psychotropic medication use
At the end of the presentation, you should be able to:

1. Describe the effect of the hunger hormone ghrelin on weight control.
2. Explain how the above conditions disrupt homeostasis.
3. Discuss current management strategies for these conditions that promote fitness and health.
Case Study # 1

- Leslie is a 53 yo assistant professor of music at a Fine Arts College. She complains of bloating, muscle/joint pain, increasingly severe fatigue and steady weight gain over the last 5 years. She notices her arms are “crunchy”, or waterlogged and can’t pinch skin like husband. Her formerly slender self (137 lbs at 5’ 8”) has become 184 lbs. She has had her thyroid tested every year but her TSH hovers around 3.7, and antithyroid antibody tests are negative. Her internist recommends Weight Watchers and CURVES to drop the weight and increase her energy. However, more than a 1 ½ hour concert or 30 minutes of exercise causes a fatigue that has her crawling up the stairs to her bed at the end of the day.

*All names are fictional, composite characters, designed to illustrate common health problems.*
What is your first set of differential dxs for Leslie?

- Hypothyroidism
- Autoimmune dz
  - Sjogrens
  - Rheumatoid arthritis
- Perimenopausal excess progesterone
- Chronic fatigue (? Whatever this means)
  - Ebstein-Barr
  - Celiac
  - Hep C
  - Depression
HPI

• Bloating and constipation worse with corn and wheat, but even after cutting them from her diet, she still can wake bone tired, with swelling around her eyes, constipated and bloated despite massive fiber and water.

• Denies eye or mouth dryness, gums healthy, breath good. Joint/muscle pain intermittent and moves to different joints/muscles.

• Negative Ebstein-Barr & Hep C Panel
Remaining Contenders

• Perimenopausal hormones strong contender
  • Increase progesterone increases appetite, bloating
  • Decrease estrogen -> decrease muscle mass, lower metabolism
  • Most likely comorbidity as it can’t explain all symptoms

• Depression always a co-conspirator, not usually associated however with cold intolerance and sluggish, bloated gut or puffy face.
Diagnosis responsible for most sx$s

- Low Thyroid
  - Hashimoto Thyroiditis
  - Non thyroidal Illness
    - Type II hypothyroidism
      - Problems converting T$_3$ to T$_4$
    - Euthyroid Sick
Cardinal Symptoms

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Work-up

- **Labs**
  - Antithyroid antibodies
  - TSH
    - > 2.5 suspicious if symptomatic
  - Free T₄
  - T₃
  - Reverse T₃
    - How much thyroid left over that doesn’t get converted
Pathophysiology Hashimoto’s Thyroiditis

- Autoimmune destruction of thyroid gland
  - Antibody detection +/-
    - Anti-tg (anti-thyroigublin)
    - Anti-TPO (anti-thyroperoxidase)

- May present
  - Relapsing Remitting feature
  - Pts can feel intermittently hyPO/ hyPER

- Calories IN  Calories OUT
Poem

I am Hashimotos...
Type II Hypothyroid

- Not recognized by medical science
- GI sensitivities
  - enzymes
  - absorption selenium, other nutrients
- Overall T3
- T4 levels normal
Euthyroid Sick

- Despite normal T4 and T3; resistance at cellular level
- In very sick cardiac patients cells weren’t using thyroid despite levels being okay....new phenomenon.
- Little research on non ICU pt
- Dieting/ starvation may make individual resistant to thyroid at cellular level
Treatment for Hypothyroidism

• In past
  • Treated according to symptoms

• Current practice to treat to TSH
  • Works for some
  • In hypothyroid pts;
    • Want TSH target range .7 – 1.7
Out of the Box Treatment

• Most primary hypothyroidism patients benefit adequately by replacement thyroxine (T4)
• For those still symptomatic on levothyroxine
  • Armour (dessicated thyroid)
  • Combination T4 (levothroid) and T3 (cytomel or triiodothyronine)
  • Dose thyroid early am to boost endogenous cortisol
• Improve gut function, add selenium, when:
  • Low T3
  • High Reverse T3
  • T4 normalish
Case Study # 2

- Chloe is a 19 yo yoga instructor also working as a receptionist in a law office. She comes to the clinic for a second opinion about a recent fasting blood sugar of 103. The MD said it was normal, but Chloe is extremely fit and despite being overweight at 142 pounds at 4’11”, she thinks something else may be wrong.
Differential Diagnoses

- Prediabetes
- Unfavorable metabolic profile d/t overweight
- Polycystic Ovarian Syndrome
- Metabolic syndrome
- Chronic dieting “hibernation syndrome”
HPI

- Chloe is of mixed Irish (mom) / Mexican (dad) descent who was a very skinny child who ate only when hungry until full. Neither mother or father is overweight or prediabetic. No family history of chronic dieting or eating issues. Chloe started menstruating at 11 and the weight gradually crept on. She is very conscientious about food and “eating healthy” she uses an app where she calculates after exercise she’s only eating about 1200 Calories/day. The only time she lost weight was when she went on the HCG diet and ate only 500 Calories daily. She has a slight mustache she bleaches, and she only gets her period 4 or 5 times a year. Otherwise she feels great.
What’s going on with Chloe?

- Polycystic Ovarian Syndrome until proven otherwise
- Metabolic syndrome
Workup

- LH / FSH
- 1 hour PG
- Thyroid panel (T₄, T₃, TSH)
- AM cortisol
- Lipid profile
- Triglycerides
More differential diagnoses

• Hypothyroidism
• Cushings
• Pituitary abnormality
• Childhood/Adolescent metabolic syndrome
Pathophysiology Metabolic Syndrome

- PCOS type of metabolic syndrome
  - Excess androgen secreted by theca cells in ovaries
  - Oligoovulation despite repeated LHI stimulation leads to
    - A string of immature follicles
    - Excessive insulin levels
    - Ultimately insulin resistance

- Primary feature of both
  - Insulin resistance
  - Increasing waist hip ratio
  - Increased visceral adiposity

- 30 – 50% women PCOS get full blown metabolic syndrome
Obesity

Proposed Pathology of Polycystic Ovarian Syndrome

Androstenedione converted to estrone in adipocytes (ie: fat cells)

Estrone stimulates release of luteinizing hormone (LH)

LH stimulates ovaries to produce more androstenedione

Androstenedione travels to adipocytes (ie: fat cells)

Excess androstenedione converted to testosterone, which causes signs and symptoms of PCOS

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Metabolic Syndrome Features

- Must have 3 of 5
1. Insulin resistance
2. Glucose intolerance
3. Hypertriglyceridemia/ hyperlipidemia
4. Hypertension
5. Truncal obesity
Treatment

- Avoid hunger evoking diets
  - While weight loss initially improves insulin sensitivity
  - Chronic dieting
    - Lipogenesis
    - Rebound weight gain
- Medicines to improve
  - Insulin sensitivity
  - Lipid profile
    - Statins
    - Red rice yeast
- Maintain fitness
- Continue eating healthy food
- Tune into hunger and stop when full (intuitive eating app)
Case Study #3

- Lamar is a 33 yo a current high school wrestling coach and former high school wrestler coming into the clinic today for a recheck of his BP. Gaining weight after high school, he went from his low of 159 pounds at 5’8” to 174 pounds after his freshman year. He bit the bullet and went back down to 160 pounds but by the time he left college he had climbed up to 183. Yearly dieting had him yo-yoing till his current weight of 192.
What’s going on with Lamar?

- Rebound weight gain after chronic dieting
- Hypothyroidism
- Metabolic syndrome
HPI

• Denies cardinal symptoms hypothyroid
• Feels well and still works out at the gym one hour a day 5-6 times per week. He claims he eats less than he used to at 150 pounds and is very frustrated with his weight
Probable Diagnosis

- Metabolic syndrome ruled out
  - Lipid and thyroid panel come back normal
  - A1C 5.7
- Suspect starve/splurge mentality
- Dieting effects of lowered metabolism
Treatment

• While “life style” touted as primary treatment
  • “losing weight” for will power champion Lamar
    • Increases ghrelin
      • Lowers thyroid
      • Increases fat cells
      • Decreases sympathetic nervous system expenditure
  • Rebound weight gain
    • Decrease leptin sensitivity
Treatment Continued

• Life style treatment for Lamar
  • Focus on
    • Healthy foods
    • Staying fit
  • Eat intuitively (get intuitive eating App)
    • Shun diets (starving)
    • Shun bingeing (splurging)
Case Study # 4

- Sal is a 26 yo Afganistan veteran army medic and recent grad from an ADN program with 2 children 2 and 4, and has started working nights in the local VA hospital. He is here for his annual exam. He is complaining of fatigue, sleepiness, and bummed about his weight. In the normal weight range throughout his life, he has gone from 184 lbs at 5’11” to 226 lbs in the last year. He loves his job but it’s hard to juggle family and career and still take care of himself.
What is your differential dx for Sal?

1. Hypothyroid
2. Fatigue Contenders
3. Emotional eating
4. Sleep deprivation/ stress/ PTSD
HPI

• Gets home from night shift at 8:00 am, says good bye to wife, takes 4 year old to preschool, watches 2 year old, takes nap with her from 12 – 1:30, picks up preschooler and watches kids until his wife gets home at 5:45. He takes a nap from 6 – 9:30 and leaves for work at 10:15.

• He admits his eating is erratic and he craves carbs.

• Denies dry skin, constipation, and cold intolerance. A further investigation into “fatigue” reveals it is actually daytime sleepiness. His wife says he’s snoring more, though he doesn’t remember waking more than twice a night.
Diagnosis

- Sleep Deprivation
- + Cal IN – Cal OUT
  - Increased ghrelin and cortisol
    - Stress hormone sends threat messages CNS
      - Increases hunger hormones
      - Decreases leptin sensitivity
  - Hunger hormones like ghrelin known to:
    - Decrease thyroid function
    - Decrease sympathetic nervous system energy expenditure
    - Promote lipogenesis
Treatment

- Best remedy = sleep!
  - Uninterrupted to include stage 4 and REM
  - At home sleep study for sleep apnea
  - If positive treatment may include
    - Dental appliances
    - C pap
    - Clinical trials
    - Surgery
  - Naps can be helpful
Case Study # 5

- Ines is 36 yo mother of 3 who co-runs a statistical consulting company in Campinas, Brazil and Los Angeles. After an emergency C section for her last child, she decided 3 years ago to get scar revision/ liposuction “to smooth things out”. At 5’2” and 120 pounds most of her life, she is finding it very hard to stay slim and finds her weight has crept up to 142 pounds. Her bra size has also seemed to disproportionately increase from 34 B to 36 DD. She also notices she has extra fat pads under her arms and on her back.
What’s going on with Ines?

- If Ines was a ground squirrel
  - Compensatory fat regain after lipectomy
Pathogenesis of Fat Regain in Humans after Liposuction

- Adipose tissue is metabolically active
- Sudden loss in animals causes
  - Compensatory gain
  - Non lipectomized areas
Epidemiology Post Lipectomy Humans

- Studies on patients post lipectomy (liposuction)
  - Immediately post lipectomy (< 18 months)
    - Weight loss/ no weight gain
    - Seldom improvement in metabolic profile
  - Long term
    - Poorer metabolic profile
    - Weight gain
    - Fat regrowth in non lipectomized areas
Treatment

• Continue to eat intuitively
• Healthy foods
  • Lower fat prevents fat regrowth
• Focus on fitness
  • Exercise decreases visceral adiposity
  • Improves metabolic profile
  • Prevents fat regrowth
Case Study # 6

Jessica is a 48 year old grounds keeper at a local university. While she had never really thought about PMS, she now dreads the end of every month. Feeling hopeless, anxious, and very low spirited at this time, she is finally referred to a psychiatrist who tells her he thinks she has PMDD (premenstrual dysphoric disorder). He starts her on the lowest dose of Zoloft in February.

In August Jessica comes to you for annual check up weighing 23 pounds more than she did last year when she weighed 146 pounds at 5’ 5”.

Jessica’s Chief Complaint is sudden weight gain.
What is going on with Jessica

1. Psychotropic medication side effect
2. Hypothyroid
3. Emotional eating
4. Perimenopausal changes
   1. Increasing hunger
   2. Decreasing lean mass
HPI

- Steady weight over her life until recently
- Gaining about 5 lbs / month since March
- Denies dry skin, constipation, fatigue
- Hungrier, but no emotional eating
Diagnosis

• SSRI side effect weight gain:
  • Zoloft
  • Praxil
  • Prozac
  • Lexapro

• Pathophysiology suggested weight gain due to increased appetite
• Impact on formula -> increase appetite
Treatment

* Discontinue Zoloft
* Treat PMDD hormonally
  * estrogen dominant OCP
  * Lupron depot ---but BEWARE
* Evaluate for luteal cysts
* Increase amount of moving and walking to stabilize hormones
* Switch antidepressant medication
  * Prozac
  * Wellbutrin
* Qsymia -again BEWARE
Qsymia

• Topiramate / phentermine
  • Topiramate anticonvulsant - SE weight loss
  • Phentermine sympathomimetic anorectic (part of Phenphen)
• Currently approved for weight loss 2012
• Many side effects/ adverse effects
• Tompomax may have less side effects
  • Mechanism of action
  • Side effects
Follow UP

- Jessica switched to Wellbutrin
  - Adequate relief depressive sx
  - Anxiety treated with psychotherapy

- Added Qsymia (topiramate/phentermine)
  - 16 mg
  - Dosing regimen:
    1. 7.5 mg/46 mg daily
    2. 12 weeks IF weight loss NOT > 3% BW
    3. Increase to 7.5 mg/46 mg
    4. May escalate 11.25 mg/69 mg daily for 14 days
    5. followed by dosing Qsymia 15 mg/92 mg daily up to Qsymia 15 mg/92 mg after an additional 12 weeks of treatment
    6. Discontinue if NO >5% BW on 15 mg/92 daily
Follow Up Visit

- Six months later Jessica down 18 pounds
  - Complains of paresthesia and abdominal bloating
- Discontinue Qsymia
- Add psychotherapy
Summary

It is true that a sedentary lifestyle, large portion sizes, and calorically dense “fast food” are risk factors for excess weight.

Not the whole story

A number of health conditions:
- hypothyroidism
- metabolic syndrome
- chronic dieting
- liposuction
- sleep deprivation and stress
- Psychotropic medications

Work to increase calories-in, and decrease calories-out
• Because the human body is wired to survive famine
• If a threat is perceived
  • even if in error homeostatic cues unleash hunger hormones which:
    • Slow the resting metabolic rate
    • Decrease thyroid production
    • Increase appetite
Weight Homeostasis Formula for Obesity

**Calories IN**
- ++Ghrelin (chronic dieting)
- Leptin resistance
- Psychotropic meds
- Sleep deprivation

**Calories OUT**
- Hypothyroidism
- Liposuction

**Biochemical Lipogenesis**
- Ghrelin
- Metabolic syndrome
- Liposuction
Conclusion

- Current recommendations make it very hard to get or stay lean.
- The extreme measures patients take to shed pounds can actually make things worse.
- Nurse practitioners are very likely seeing these patients in their practice, and need the knowledge about weight homeostasis to adequately diagnose and manage.
Bibliography


• Is vitamin D deficiency an independent risk factor for obesity and abdominal obesity in women? Endokrynologia Polska [0423-104X] Tamer, Gonca yr:2012 vol:63 iss:3 pg:196 -201
