

OBESITY – A CLINICIAN’S VIEW	2
OBESITY – A SCIENTIST’S VIEW	6
GENETICS OF OBESITY	ERROR! BOOKMARK NOT DEFINED.
NUTRITION	ERROR! BOOKMARK NOT DEFINED.
NEURAL CONTROL OF ENERGY BALANCE	ERROR! BOOKMARK NOT DEFINED.
NUTRITION AS A COMPLEX SYSTEM	ERROR! BOOKMARK NOT DEFINED.
EVOLUTION OF FOOD AND DISEASE	ERROR! BOOKMARK NOT DEFINED.
DEVELOPMENTAL ORIGINS	ERROR! BOOKMARK NOT DEFINED.
POPULATION AND SOCIOECONOMIC ASPECTS OF OBESITY	ERROR! BOOKMARK NOT DEFINED.
PHYSICAL ACTIVITY, EXERCISE AND OBESITY	ERROR! BOOKMARK NOT DEFINED.
GUT MICROBIOME	ERROR! BOOKMARK NOT DEFINED.
PRECISION MEDICINE	ERROR! BOOKMARK NOT DEFINED.

OBESITY – A CLINICIAN’S VIEW

How is Obesity Defined?

- BMI: weight (kg)/height (m²)
- Obesity is caused by excess adipose tissue
- HEALTHY WEIGHT: BMI 18.5-25
- ABOVE HEALTHY WEIGHT: BMI >25
- OVERWEIGHT: BMI >25 and <30
- OBESE: BMI >30
- BMI is not always accurate
 - o An individual with a high muscle mass may have a high BMI even though they are not obese
 - o Similarly, an elderly individual who is frail may have a low BMI even though they are healthy for their age

Obesity in Australia

- 63% of the adult population is obese = 1 in 4 of the population
- Levels of obesity has also increased -> this is a problem because obesity in children tends to continue into adulthood
- Metabolic diseases are harsher in children
- Obesity is more prevalent in men and the older population

Medical Complications of Obesity

- Stroke
- Coronary heart disease
- Dyslipidaemia
- Osteoarthritis
- T2D and hyperinsulinemia
- Hypertension
- Cancer
- Mechanical complications -> hip, knee, ankle replacements from having to carry around excess weight
- Fungal infections in fat folds
- Life expectancy of an obese adult is 2-4 years less than an adult with healthy weight
- BMI >25 = increased risk of diabetes

Treatments for Obesity

Non-Surgical

- o Lifestyle modifications -> diet and exercise
- o Various pharmacotherapies

Bariatric Surgery

- o Laparoscopic adjustable gastric banding
- o Sleeve gastrectomy
- o Roux-en-Y gastric bypass

Endoluminal -> not popular in Aus, expensive

- o Endobarrier
- o Intragastric balloon

- Endoscopic bariatric surgery

Does Lifestyle Modification Work?

- Do not work long term
- Meta-analyses show weight regain in the following 2 years after weight loss from dietary intervention
- However, lifestyle intervention is effective for preventing diabetes
- Diet and exercise do not work for everyone, but with the right support it can be effective

Why is Weight Loss Maintenance so Hard?

- Successful weight loss maintenance = “intentionally losing at least 10% of initial weight and keeping it off for at least 1 year”
- 20.6% of randomly surveyed overweight people reported being successful weight loss maintainers
- **HORMONAL CONTROL:** most peripheral hormones tell us to eat
 - Only one is a satiety hormone
- There are a lot of reasons besides hunger why we eat -> social, boredom, comfort
- Some medications increase appetite
- **ADAPTATIONS TO WEIGHT LOSS**
 - 10 weeks after weight loss, the hunger hormone (ghrelin) increases and the satiety hormones (peptide YY, amylin and CCK) decreases
 - Even after 61 weeks, ghrelin was still increased, and the satiety hormones were decreased
 - Once an individual has gained weight, when they lose it their energy expenditure will be lower for the rest of their life
 - They will have to eat less to maintain their weight because their body no longer needs as much fuel to function
 - Excess food/fuel will cause weight gain
- Our bodies do not want to lose weight -> evolutionary adaptation to survive famine

Pharmacotherapies?

- Medications for obesity have a bad reputation/history due to adverse side effects

Orlistat

- **NORMAL:** dietary fat -> hydrolysed by gastric and pancreatic lipases -> free FAs and triglycerides -> absorbed
- **ORLISTAT:** dietary fat -> inactive gastric and pancreatic lipases -> unable to hydrolyse dietary fat -> decreased fat absorption -> increased fat excretion
- Intestinal lipase inhibitor
- Fat passed out in stool -> oily, fatty stool
- Does not result in great weight loss
 - Initial weight loss
 - Plateau
 - Regain
- Weak medication given 3 times a day orally
- Perceived as a safer option due to peripheral action
- Unpleasant gastrointestinal side effects

- Rare cases of severe liver injury
- Potential risk of kidney injury, pancreatitis and renal stones

Phentermine

- Increased noradrenaline in hypothalamus -> anxiety, insomnia
- Used in combination with migraine and seizure medication
- Oral medication given once a day
- Good weight loss results
- Recommended short-term use -> 12 weeks
- Cardiovascular side-effects -> hypertension and tachycardia
- CNS side effects -> insomnia, restlessness, alters sexual behaviour, hormonal secretion and mood

Liraglutide

- GLP-1 receptor agonist
 - o Glucagon-like peptide 1 has the ability to decrease blood glucose via insulin secretion
- Works on the pancreas to produce more insulin
- Results in slower release of nutrients
- 10% weight loss seen after one year
- Subcutaneous injection given once a day
- Unpleasant gastrointestinal side effects -> nausea, vomiting, constipation, and diarrhoea
- Long-term safety data is lacking

Bariatric Surgery

- Most effective treatment with the best long-term results

LAGB – Laparoscopic Adjustable Gastric Banding

- Expensive
- Introduces a foreign body -> infection prone
- A reversible treatment for an irreversible illness -> can lead to yo-yoing
- Band does not affect hormones
- Slips, erosions, oesophageal dilation, inadequate weight loss

Gastric Bypass

- Smaller stomach -> restrictive
- Endocrine changes
- Greater metabolic benefits
- DUMPING: a lot of food being dumped into the small intestine at once -> high glucose -> high insulin release -> sweaty, shaky symptoms
- Vitamin deficiency, ulcers, weight regain, stricture, obstruction, no endoscopic access to stomach or duodenum

Sleeve Gastrectomy

- Irreversible
- Keyhole operation
- Smaller stomach
- Less manipulation of intestines
- Good weight loss
- Less remission of diabetes and metabolic diseases

- Bariatric interventions provide meaningful weight loss; however weight regain is still possible
- Can lead to numerous nutritional deficiencies

Endoluminal Therapies

Endoluminal Sleeve

- A barrier that lines the majority of the small intestine
- Food bypasses the duodenum and proximal jejunum
- Isolation of duodenal mucosa from nutrient contact
- Bile isolated from nutrients
- No expedited delivery of nutrients to distal gut

Intragastric Balloon

- Balloon inflated in stomach -> smaller stomach

OBESITY – A SCIENTIST’S VIEW

- Obesity is a risk factor for number of diseases
- One of the top health risks in Australia
- Obesity is on the rise, but it is not increasing at a uniform rate in all places -> people/different groups of people have very different genes, eating habits etc.
- Although no one is the same, doctors and medicine treat everyone the same

Genes

- SNPs in the human genome differs in different people once every hundred base pairs
- BMI is 65% inheritable
- Obesity can be genetically programmed
 - o In sibling mice, one was given a leptin mutation (Ob/Ob mutation) -> cannot make leptin, overweight
 - o It was thought that leptin was an appetite suppressor
 - o In humans with the same Ob/Ob mutation, when administered with recombinant leptin it resulted in weight loss
 - o This mutation is rare -> mostly in Pakistani families with inbreeding 0> homozygous mutation
- The lifespan of humans used to be very short -> many died of starvation, wild animal attacks or infectious diseases
- Genes co-evolved with this -> genes that allowed us to survive starvation were retained and those that made us susceptible to starvation were lost
- Groups from different places evolved on specific diets -> e.g. Romans = CHO, Eskimos = fish
 - o Is there a different ideal diet for people who evolved from these different areas?

Environment

- Western diet = high fat and sucrose
- On a western diet, mice became prediabetic, overweight with a fatty liver
- Deterioration in bone function
- Increased plaque in arteries
- Increased anxiety and decreased short-term memory
- When worms, mice and flies are fed 24% less calories than normal, they live up to 30% longer
- Genetic diversity makes a large difference -> a high fat diet is good for some and bad for others
- Some mice showed increased lifespans in response to calorie restriction and others showed decreased lifespans

Diet

- CONCEPT: one day we could use food/diet as a drug
 - o If we knew what the healthiest diet was for each individual, would it be as, if not more, beneficial to health as a drug?
 - o But what is the right food?