Week 1 Obesity and Inflammation

What is the definition of overweight/obesity?

BMI cut offs

- Underweight: <18.5kgm
- Healthy weight: 18.5-24.9kgm
- Overweight: 25-29.9kgm
- Obesity Class I: 30-34.9kgm
- Obesity Class II: 35-39.9kgm
- Obesity Class III: >40kgm

Other considerations: body fat mass, distribution of fat mass

Internal contributors to obesity:

Genetics

- FTO gene: twins with FTO gene put on different conditions (overfeeding vs negative energy balance), still high correlation between each on how they gain or lose weight.

Metabolic and Physical Conditions

Metabolic and Physiological dysregulation

- Disordered eating: bulimia, binge eating, food addiction.
- Dementia and Alzheimer's: forget whether they have eaten so eat again.
- Appetite dysregulation
- Hypothyroidism: low level of thyroid hormone
- Age related changes in metabolism: thermogenesis
- Physical disabilities: don't have the ability to exercise
- Microbiota: bacteria in intestine

External contributors to obesity:

Built environment (low energy expenditure)

- Sedentary lifestyle due to occupation and built environment (eg whether the facilities a person lives in promotes exercise such as cycling lanes, stairs.

Food environment (high energy intake)

- Foods: flavour, variety, portion size, energy density, food forms eg liquid drinks vs solid form
- Feeding behaviours: eating frequency, food culture
- Food costs and food marketing
- Food convenience: 24hr food outlets, vending machine

Components of metabolic syndrome

The clustering of cardio-metabolic risk factors including:

- Central/abdominal obesity
- Hypertension
- Hyperglycaemia (high glucose levels)
- Dyslipidaemia (high triglyceride/lipid levels)
- Low HDL cholesterol

Higher risk of MetS for Asian males compared to European as fat accumulates close to the organs.

Cut offs for MetS:

Inflammatory cytokines:

Inflammation is a protective mechanism: cell is eliminating toxin, repair of cells etc; but over a long period of time the inflammation becomes chronic and that is problematic.

Common features:

- Promote inflammation
- Promote thrombosis (eg blood clotting)
- Stimulate insulin resistance
- Increase blood pressure

Adipokine

- Bioactive mediators secreted from the adipose tissues that can modulate metabolism, physiology and cell signalling pathways (eg adiponectin, leptin, RBP-4 and resistin)
- Tell the brain and other organs when enough or need for energy/lipids.
    - Leptin
        - Hypertensive

- Major long term satiety signal
- Subcutaneous rather than visceral fat is the major producer
  - o Resistin
    - Insulin resistance
    - Decreases anti-inflammatory effect
    - Decreases insulin sensitivity
  - o Angiotensinogen
    - Hypertension
    - Adipocytes are the major source after the liver
    - Expressed more in visceral adipocytes than in subcutaneous

Cytokine

- Low molecular weight proteins that are secreted by one cell for the purpose of altering either its own functions (autocrine effect) or those of adjacent cells (paracrine effect)
- Released by other tissues, not just adipose.
- Pro-inflammatory cytokines released from adipose tissue:
  - o IL-6
    - Insulin resistance and dyslipidaemia
    - Increases vascular inflammation
    - Decreases insulin signalling
    - Major regulator of hepatic CRP
  - o CRP
    - Prothrombotic and inflammation
    - Increases vascular inflammation
    - Correlates with metabolic syndrome and diabetes
  - o IL-1B
  - o TNF-a.
    - Prothrombotic and inflammation
    - Increases vascular inflammation
    - Decreases insulin sensitivity and insulin signalling
  - o NF-kB

- Controls transcription of DNA, cytokine production and cell survival
- Response to stress, cytokines, free radicals, heavy metals, oxidised LDL

Adipocytokine

- A collective term for both adipokines and cytokines released by adipose tissue

Summary:

- Adipokines tend to have systemic effects (whole body), while the effects of cytokines tend to be more local at the cells themselves or neighbouring cells. Cytokines released by the adipose tissue are known as Adipocytokines and their effects are largely on adipose tissue, but cytokines are also released by other types of tissues and cells such as macrophages in the body so the effects of cytokines (eg pro-inflammatory cytokines), is not limited to adipose tissue only and inflammation can therefore occur in other organs such as muscle and liver.

<u>Adipose tissue</u>

Subcutaneous: under skin

Visceral/ectopic fat: surrounds organs.

- Related to MetS
- Measured through:
    o The topography of adipocytes is important
    o CT and MRI scans
    o Waist adiposity acts as a proxy to predict visceral fat.
    o Cheapest/easiest measurement: waist circumference as there is a good correlation between WC and MetS.

Hypertrophy

- Increase in size of cells
- Usually occurs in adulthood
- More associated with inflammation: hypertrophic obesity is associated with infiltration of macrophages into adipose tissue

Hyperplasia

- Increased number of adipocytes
- Usually occurs in children

White vs Brown adipose tissue

- White = BAD
    o fat storage, endocrine organ, different locations have different implications, secrete cytokines
    o we can stimulate white into brown
- Brown = GOOD
    o Site for lipid oxidation to produce heat (mitochondria) to keep body warm and therefore we want more brown than white.