

# FRONTIERS IN BIOMEDICINE

## METABOLIC SYNDROME

### 1.2 Introduction to Metabolic Syndrome

**Metabolic syndrome:** (& other names like Syndrome X, Dysmetabolic syndrome, etc.) a cluster of risk factors for cardiovascular disease and T2D mellitus, which occur together more often than by chance alone

- MetSy is increasingly common in Australia and overseas, with annual incidence thought to be 3%
- ~20-25% of world's adult pop thought to have MetSy
- > 35% of Australian adults have metabolic syndrome

**Risk factors include:**

- ✓ **↑ blood pressure**
  - Blood pressure is the measurement of the pressure of the blood in the artery
  - Heart muscle contracts and pumps blood, and falls when the heart relaxes and refills with blood
  - Blood pressure over 140/90 mmHg is considered high
- ✓ **Dyslipidaemia (↑ triglycerides and ↓ high-density lipoprotein cholesterol/HDL-C)**  
 Reduced HDL cholesterol: the densest form of lipoprotein, involved in the pathway of lipids via reverse cholesterol transport
  - Chylomicrons (lowest density lipoprotein) is delivered through lymph and blood, and remnants go back to liver.
  - As cholesterol and triglycerides go out, lipoproteins get more dense – VLDL, LDL, HDL
  - LDL: "bad" cholesterol that occludes endothelial wall of blood vessels. Monocyte macrophages come to eat LDL, and further occlude endothelium.
  - HDL: brings cholesterol from endothelial wall back to liver.
- ✓ **↑ fasting glucose/hyperglycaemia**
  - Impaired/high fasting glucose is due to insulin resistance, or impaired glucose tolerance.
- ✓ **Central obesity**
  - Measured by large waistline, which varies for different ethnic groups
  - Body mass index (kg/m<sup>2</sup>) isn't the most accurate measure for MetSy.

Dangers of visceral fat

  - assoc with metabolic derangements: Insulin resistance, high triglycerides, inflammation, altered cytokine levels
  - Very near organs, so fat can move into pancreas, causing insulin resistance due to poor insulin signalling
  - Visceral fat cells secrete less leptin and are assoc with higher levels of cortisol
  - Metabolically obese (as opposed to being fat and fit)

**Table 2. Waist circumference thresholds for abdominal obesity<sup>4</sup>**

| Population                   | Recommended threshold in waist circumference for abdominal obesity (high risk) |        |
|------------------------------|--|--------|
|                              | Men  | Women  |
| European/North American      | ≥102 cm  | ≥88 cm |
| Asian                        | ≥90 cm   | ≥80 cm |
| Central and South American   | ≥90 cm   | ≥80 cm |
| Middle Eastern/Mediterranean | ≥94 cm   | ≥80 cm |
| Sub-Saharan African          | ≥94 cm   | ≥80 cm |

**Table 1. Criteria for clinical diagnosis of the MetSy<sup>3</sup>**

| Measure   | Categorical cut point                    |
|---|--|
| Elevated waist circumference  | Population specific (see Table 2)        |
| Elevated triglyceride levels (or drug treatment for elevated triglycerides) | ≥1.7 mmol/L                              |
| Reduced HDL-C (or drug treatment for reduced HDL-C)                         | <1.0 mmol/L in men, <1.3 mmol/L in women |
| Elevated blood pressure (or drug treatment for hypertension)                | ≥130 systolic or ≥85 diastolic           |
| Elevated fasting glucose (or drug treatment for elevated glucose)           | >5.5 mmol/L                              |

**Why is the diagnosis of MetSy important?**

- Identifies patients at ↑ risk of CVD, diabetes and chronic kidney disease
- ↑ chances of risks compared to those without the condition (3x risk of CVD and 5x risk of T2D)
- ↑ risks of mortality (1.6 fold in MetSy patients than without)
- Barriers to diagnosis
- Diagnosis of MetSy needs to be explained in broader context

**Prevention**

- Eat better
- Get active (150 mins of exercise/week)
- Sleep better

### 1.3 MetSy as a social & political sickness

- Incidence: rate at which new cases occur in a population during a specified period.
- Prevalence: proportion of a population that are cases at a point in time. Prevalence is an appropriate measure only in relatively stable conditions, and it is unsuitable for acute disorders.
- Risk Factor: something that increases your chances of getting a disease  
E.g. people  $\geq 50$  years are more likely to develop colon cancer than  $< 50$  = age is (the #1) risk factor for colon cancer

Population Health as Disease Detective:

- Investigating WHERE, WHEN and WHO fell sick helped discover what caused/RISKS of the disease
- Dr John Snow, father of infectious disease epidemiology, mapped cases of cholera in Soho London in 1854 and traced the source back to the water pump in Broad Street.
- Next he demonstrated that people in the same suburb who bought water from different water companies were at risk if the water was collected down river.

Obesity trends among US adults:

- 1985-1990:  $\uparrow$  states have 10-14% obesity
- 1991-1996:  $\uparrow$  states have 15-19% obesity - Decline of industry/manufacturing, loss of jobs. Manufacturing became more automated too.
- 1997-2000:  $\uparrow$  states have  $\geq 20\%$  obesity
- 2001-2004:  $\uparrow$  states have  $\geq 25\%$  obesity
- 2005-2010:  $\uparrow$  states have  $\geq 30\%$  obesity
- Highest prevalence amongst black non-hispanics, then Hispanics, then white non-hispanics.

**More adults are obese in more unequal rich countries**

- Japan and Korea have least obesity.  
Japan: narrow diff between rich and poor = low income inequality
- Aus, Mexico, US more obese.  
USA: most income inequality, and fattest. Obesity in developed countries is a disease of poverty/inequality amidst affluence

#### Epigenetics and deep history

Centuries of marginal diet & famine for:

- Irish, urban British
- most Europeans except for Dutch
- Russians
- Chinese
- South Asia,
- Africans from the west of Africa, Slaves in US, Brazil etc
- Mother's eggs are formed during grandmother's pregnancy, so influences us.
- In US, those whose grandmothers had been in Ireland during famine, had higher death rate (per 1000 population according to mother's birthplace) than German and Italian migrants.
- Irish have much higher organic heart disease

But epigenetics is an insufficient explanation – have to also look at the total social & economic environment. At the same time as obesity has increased, so has income inequality.

#### Changes in activity levels

- New evidence that becoming over-weight causes kids to do less, not other way around
- Many people who are over-weight still work all day on their feet, lift weights, use their upper arms.
- People perhaps walk less, but the decline in walking happened earlier.

#### Food

- Early 1970s: high food prices & falling farm incomes threatened the re-election of Richard Nixon
- Earl 'Rusty' Butz, US Secretary for Agriculture brokered free trade deal with Malaysia to export cheap, subsidised corn in return for Palm Oil.
- US corn growers urged to plant corn from corner to corner. Subsidies destroyed Mexican corn farmers' exports → desperate illegal immigration to US.
- Sugar cane growers (Cuba & Aus) lost markets to high-fructose corn syrup/HFCS55
- Fast food industry able to cut costs of production of sweet drinks (Coca cola, Pepsi), french fries & popcorn → much more affordable fast food over real food. Now cheaper in US to buy a McDonald's meal than a pear.

Corn Syrup: used in USA since 1975

- 7x sweeter than Cane Sugar, so when Coca Cola and Pepsi changed from 50/50 HFCS/cane sugar to 100% HFCS, costs fell 20% → lower prices and bigger portions
- protected frozen food against freezer burn, & kept long-life products tastier

- In baking products (biscuits, buns, bread) → cheaper, tastier and 'browned in the oven'
- Result: 80% of supermarket products contain HFCS55 or SUGAR
- Huge ↑ prepared foods, processed foods, frozen meals: cheaper, tastier, easier
- Aus uses cane sugar, but still sugar is added for all these other properties

#### Problem with Fructose

- It bypasses the usual complex breakdown processes in the body, going straight to the liver = 'metabolic shunting'
- Not seen to be a problem at first, but now some argue that it quickly produces insulin resistance
- One orange normally has its fructose dispersed with fibre.
- A glass of fruit juice = 6 oranges, no fibre to break down the sugar and concentrated Fructose
  - Fructose in large undiluted quantities = dangerous
  - Children now receive most of their 'fruit nutrition' as juice

#### Palm Oil on those French Fries

- Palm Oil imported in deal on free trade
- Mid 1970s: new technologies made it a viable commercial fat: for frying french fries, margarine, bread, pies
- As dense and saturated as beef lard, more saturated than pig lard
- But, cheap, 'good in the mouth' and above all STABLE → products did not biodegrade on the shelf and lasted longer
- Neither do they biodegrade in the body
- Saturated fat → ↑BP, cholesterol; body fat

#### **Economic Results**

- ✧ Food prices fell dramatically and consumers had cheap, tasty, sweet and fatty food that they did not have to prepare themselves.
- ✧ In USA animal feed prices fell dramatically as cattle, pigs and chickens were moved to feed on mass produced subsidised corn
- ✧ In USA, high calories in animals not evolved to eat corn → hypergrowth (chickens matured weeks earlier, cattle grew so much flesh their legs cannot hold them up.)
- ✧ High profits from food → monopolies controlling all food production from farm to supermarket → mass industrialised food production highly profitable → factory farming or food lots
- ✧ Food production → automated, centralised, using unregulated labour (which causes lots of food poison deaths in USA due to release of diseases like Salmonella)

#### Changes in human diet & human shape

- The changes to our food in industrialised economies in the last 40 years have been greater than since the rise of agriculture.

#### **The MetSy epidemic has come from:**

- profound change in the food provided for us by industry, and which we find cheap, convenient and satisfying AND
- sudden affluence in populations genetically selected for scarcity.