

# 91529 Pathophysiology and Pharmacology 1

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## Week one

### Diabetes and obesity pathophysiology and treatment

#### Diabetes in Australia

- ~ 4.6% of the Australian population
- ~ 5.4% aged 18 years and over, Higher in indigenous Australians
- 10% Type 1 diabetes & 77% Type 2 diabetes
- Diabetes and conditions related to diabetes are among the leading causes of death, illness and disability in Australia

#### Pathophysiology of diabetes

- Type 1 diabetes – Insulin dependent
  - Absolute deficiency of insulin
  - Autoimmune disease
  - Initiated by an environmental factor (infectious or non-infectious agents)
  - In genetically susceptible individuals (Caucasian - 20% higher risk)
  - Weight loss common
- Type 2 diabetes – non-insulin dependent
  - Environmental factors (lifestyle, diet habits, obesity)
  - Excess triglyceride storage blocks insulin signalling pathways
  - Insulin resistance in liver, muscle and fat
  - Defect in insulin secretion

#### Diabetes and insulin lack

- Low, absent of hypoactive insulin level
- BGL remains high after meals
- Hyperglycaemia has 3 effects
  - Increase in osmotic pressure – cellular dehydration – thirst
  - Lose of glucose in urine – glycosuria
  - Glycosuria causes osmotic diuresis – polyuria and electrolyte depletion
- Hyperglycaemia symptoms
  - Polydipsia – excessive thirst
  - Polyuria – excessive urination (nocturia – excessive urination at night)
  - Polyphagia – excessive appetite
  - Frequent yeast infections (women)
- Alternative energy sources needed – weight loss

- Tissue protein is depleted – lethargy
- Fatty acids leave adipose cells
  - Hyperlipidaemia – fatty liver, atherosclerosis, coronary heart disease
  - Fatty acids converted to ketone bodies in liver, causes ketoacidosis and due to acidic nature lowers pH and can cause a coma
  - Quick diagnosis fruity smell, finger tip blood (increased glucose), urine multistix (increased glucose and positive for ketones)

#### Acute complications of diabetes

- Type 1 diabetes – Ketoacidosis
- Type 2 diabetes – hyperosmolar
  - Extreme hyperglycaemia resulting from severe dehydration in the context of impaired thirst mechanisms
- Infections
  - Impaired immune function
  - Impaired wound healing – favourable environment for bacterial, fungal growth

#### Chronic complications of Diabetes Mellitus

- Microvascular complications
  - Retinopathy (Cataract) – chief cause of new cases of blindness
  - Nephropathy – chronic renal failure
  - Sensory neuropathy – pain and numbness in feet, ulcers prone to infections, may lead to amputations
- Macrovascular complications
  - CVD – causes 60-75% of diabetes deaths, accelerated atherosclerosis
  - Peripheral vascular disease – muscle pain/cramps, ulcers, amputations
  - Autonomic neuropathy – impotence, constipation, postural hypotension

#### Diagnostic criteria for Diabetes Mellitus

- HbA1c level > 6.5% OR
- Fasting plasma glucose  $\geq 7\text{mmol/L}$  (no calorie intake >8h) OR
- OGTT (2h post load)  $\geq 11.1\text{mmol/L}$  OR
- Classic symptoms – polydipsia, polyphagia, polyuria, weight loss, lethargy, random plasma glucose  $\geq 11.1\text{mmol/L}$

#### Insulin in Type 1 Diabetes

- Essential for type 1 diabetes, uncontrolled type 2 diabetes for short-term use
- “Human” insulin – recombinant DNA technology – Uses DNA put into bacteria to mass produce insulin in petri dish
- Insulin is a polypeptide, can be digested if taken orally so needs to be injected
- Several formulations
  - Fast/Short acting – neutral (soluble)