Regulation of Metabolism

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Energy

• Constant need in living cells
• Measured in kcal
  – carbohydrates and proteins = 4kcal/g
  – Fats = 9kcal/g
• Most diets are mixed
Metabolic rate

• **Measure MR**
  - Direct = heat
  - Indirect = oxygen consumption

• **Temperature**
  - Influences chemical reactions
  - results in physiological response to change

• **Physical activity** = primary determinant of energy requirements
  - wt loss
  - wt gain
Basal metabolic rate

• Conditions
  - 12 to 14 hours after eating
  - comfortable temperature
  - awake, but resting

• determinants
  - age, sex, surface area, thyroid hormones, genetic components
Anabolic requirements

- **Turnover rate** = rate at which molecule is broken down and resynthesized

<table>
<thead>
<tr>
<th>nutrient</th>
<th>turnover</th>
<th>requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>250g/day</td>
<td>150g/day</td>
</tr>
<tr>
<td>proteins</td>
<td>150g/day</td>
<td>35g/day</td>
</tr>
<tr>
<td>fats</td>
<td>100g/day</td>
<td>negligible</td>
</tr>
</tbody>
</table>

- **Requirements**
  - essential amino acids for proteins and essential fatty acids for fats
  - Water soluble and fat soluble vitamins
  - Minerals and trace elements
Regulation of energy metabolism

• **Two sources**  
  - absorbed nutrients  
  - energy reserves  

• **Preferred energy sources**  
  - depends on available enzymes  
  - brain = blood glucose; skeletal muscle = fatty acid  

• **Eating**  
  - Body fat and endocrine function  
  - large habit component  
  - Partially controlled by hypothalamus  
  - Influenced by neurotransmitters, endorphins, intestinal hormones  

• **Hormonal regulation of metabolism**  
  - absorptive state  
  - postabsorptive state
Energy regulation by islets of Langerhans

- Three cell types produce polypeptide hormones
  - **Beta** (β) cells = insulin
    - Encourages cellular glucose uptake
    - In liver, activates glycogen synthetase
    - Encourages lipid synthesis
    - Stimulates the movement of amino acids into cells
  - **Alpha** (α) cells = glucagon
    - Encourages liberation of reserves
    - Prevents glucose uptake by liver, muscle, adipose
  - **Delta** (δ) cells = somatostatin
    - Not sure
Pancreatic islets = islets of Langerhans
Regulation of insulin and glucagon secretion

- **Effects of glucose and amino acids**
  - **rise in plasma glucose**
    - stimulation of $\beta$ cells
    - inhibits $\alpha$ cells
  - **fall in plasma glucose**
    - decreased insulin
    - increased glucagon
  - **meals high in protein**
    - stimulates insulin
  - **meals high in protein and low in carbohydrate**
    - stimulates glucagon
    - result: increase in blood glucose and increased incorporation of amino acids into tissues
Regulation of insulin and glucagon secretion

- **Effects of autonomic nerves and GIP**
  - **parasympathetic**
    - increased insulin
  - **sympathetic**
    - increased glucagon, inhibits insulin
    - stress hyperglycemia = glucagon + epinephrine
  - **GIP**: stimulates release of insulin before it appears in blood (presence of glucose in intestines)
  - **Goal**: Keep blood glucose between 50mg/100ml and 170mg/100ml
    - higher = glycosilation; lower = brain damage
Absorptive state

• High insulin and low glucagon
• Insulin
  - cellular uptake of glucose
  - uptake & incorporation of amino acids
  - conversion of glucose to glycogen
  - additional glucose to fat
  - incorporation of glucose into adipose tissue
  - suppression of liver glycogen hydrolysis
Postabsorptive state

- Low insulin, high glucagon
  - low insulin encourages movement of amino acids out of the muscles
- cortisol -- stimulates production of enzymes to convert pyruvic acid to glucose
- glucagon
  - stimulates glycogenolysis
  - stimulates gluconeogenesis
  - stimulates lipolysis
  - stimulates ketogenesis
Diabetes mellitus

- **IDDM**: insulin deficiency
  - autoimmune, ketosis (can lead to ketoacidosis)
  - increased blood glucagon secretions
  - 3 p’s = polydypsia, polyuria, polyphagia
- **NIDDM**: insulin resistance and deficiency
  - slow to develop
  - hereditary component
  - overweight
  - usually no ketoacidosis, but serious sequelae
Hyper and hypoglycemia

- **Hyperglycemia** = chronic high blood glucose
  - insufficient secretion of insulin from \( \beta \) cells
  - inability of insulin to stimulate glucose uptake
- **Hypoglycemia**
  - overdose of insulin
  - reactive hypoglycemia = excessive increase in insulin after carbo meal
  - symptoms: tremor, hunger, weakness, blurred vision, impaired mental ability
Metabolic regulation by adrenal hormones

- **Metabolic effects of epinephrine**
  - similar to glucagon
  - conditions for secretion
    - fight or flight
    - low blood glucose
    - fasting

- **Metabolic effects of glucocorticoids**
  - prolonged fasting or exercise = stress
  - Effects
    - lipolysis & ketogenesis, stimulates hepatic enzyme synthesis for gluconeogenesis, promotes release of amino acids from muscle
Metabolic regulation by thyroxin

• **Function**
  - cellular respiration, growth & development in early childhood

• **Cellular respiration**
  - calorigenic effect = increases BMR
  - sets BMR

• **Growth and development**
  - RNA and protein synthesis
  - cretinism

• Hypothyroidism and hyperthyroidism
Metabolic regulation by growth hormone

- Regulation of secretion
  - GHRH
  - increase aa in plasma
  - decrease glucose in plasma

- insulin-like growth factors
  - Mediates action of growth hormone

- Effects on metabolism
  - protein synthesis
  - catabolism

- Effects on body growth
  - hypersecretion & hyposecretion in children and adults
Regulation of calcium and phosphate balance

- PTH, active vitamin D, calcitonin
- bone remodeling
- plasma concentration
- role of $\text{Ca}^{++}$ in body
  - bone formation
  - muscle contraction
  - second messenger
  - membrane permeability
Parathyroid hormone

• **Stimulus:** decrease in plasma $Ca^{++}$
• **Action:**
  - stimulates osteoclasts
  - stimulates $Ca^{++}$ reabsorption by kidneys
  - inhibits reabsorption of $PO_4^{-3}$
  - promotes formation of active vitamin D3
1,25-dihydroxyvitamin D3

- **Action:** raises plasma Ca\(^{++}\)/PO\(_4\)^{-3} by:
  - intestinal absorption
  - resorption
  - renal reabsorption
- **Absence/inadequate secretion**
Calcitonin

- Calcium lowering hormone
- Stimulus
- Action:
  - inhibition of osteoclasts
  - inhibition of reabsorption of $Ca^{++}$ and $PO_4^{-3}$ in the kidneys