Week 11 – Energy Metabolism:

Basal metabolism (BMR):

- Comprises **~2/3's** of daily energy expenditure in an average person (with ~1/3 of energy being expended on physical activity as well as the thermic effect of food)
- Basal metabolism supports basic physiological processes of the body
- Lean body mass is the largest determinant of BMR
- Resting metabolic rate (RMR) is a measure of energy output, and is slightly higher than BMR.

Factors affecting BMR include:

- Height (taller = greater BMR)
- Growth (pregnancy, childhood etc.)
- Fever and stress
- Higher muscle mass
- Smoking & caffeine
- Environmental temperature (heat & cold both raise BMR)
- Ageing (decreases BMR due to a loss of muscle mass)
- Fasting/starvation (decreases BMR)
- Sleep

Glycolysis:

- Converts glucose to **pyruvate**
- Glycolysis is an anaerobic process
- There is a net gain of 2 ATP's from glycolysis (as the steps in purple are repeated twice)

The Fate of Pyruvate:

- Pyruvate (the end product of glycolysis) can be converted to either:
    - **Lactate** (anaerobic process)
    - **Acetyl CoA** (aerobic process)

When is Pyruvate converted to Lactate?

- Pyruvate is converted to lactate when oxygen is limiting (e.g. sprinting), or cells lack sufficient mitochondria
- Lactate is formed when hydrogen is added to pyruvate, which allows the regeneration of NAD^+
- Liver cells recycle muscle lactic acid through the **Cori Cycle**

Citric Acid Cycle (aka the Krebs Cycle):

- Produces 3 NADH, 1 $FADH_2$, plus 2 $CO2_2$ molecules

Electron Transport Chain (ETC):

- **NAD^+ & FAD** carry electrons to the inner mitochondrial membrane – O_2 is the final electron acceptor.
- Hydrogen passes its electrons (that have come from food) onto oxygen. This transfer causes energy to be released, providing energy for the 'pumps' that drive protons into the outer mitochondrial compartment (which produces ATP when the protons/hydrogen ions flow back).

- **The movement of hydrogen ions** (protons) through the channel back into the mitochondrial matrix causes the enzyme ATP synthase to catalyse the conversion of ADP back into ATP.

Reaction	Expenditure	Income
Glycolysis	2 ATP	4 ATP, 2 NADH + H^+
Conversion of pyruvate into Acetyl CoA		2 NADH + H^+
Citric acid cycle/Krebs cycle		6 NADH + H^+, 2 $FADH_2$, 2 GTP

- **Cytochromes** on the inner mitochondrial membrane regulate the transfer of hydrogen electrons with energy transfer for the synthesis of ATP from ADP.

Glucose metabolism balance sheet:

⇒ Approximately **32 ATP** are produced from 1 glucose molecule

⇒ **1 NADH + H^+ = ~2.5 ATP**
⇒ **1 $FADH_2$ = ~1.5 ATP**
⇒ **1 GTP = 1 ATP**

Metabolism of Lipids:

- **Triglycerides** are hydrolysed by hormone-sensitive lipase (HSL) (known as lipolysis), producing fatty acids & glycerol.
- **Glycerol** is converted to glyceraldehyde-3-phosphate to enter glycolysis to either form glucose (gluconeogenesis) or be converted to pyruvate
- **Fatty acids** are converted to acetyl CoA in reactions known as beta-oxidation. Fatty acids cannot be used to synthesise glucose, as acetyl CoA cannot be converted to pyruvate. The process of beta oxidation (the breakdown of fatty acids) involves the cleaving off of 2 carbons units from the fatty acid chain, with this step being repeated until the entire fatty acid has been broken down.

Conversion of Amino Acids to Glucose:

- Amino acids that can be used to make glucose are known as **glucogenic.**
- Amino acids that are converted to acetyl CoA are known as **ketogenic.**

Glucose oxidation after a meal:

- After a mixed meal, only half of the ingested glucose is used for glycogen synthesis (liver & muscle glycogen).
- The remaining glucose is used:
  1. **As an energy source –** insulin activates pyruvate dehydrogenase. Excess glucose results in the almost complete use of glucose as an energy source (*glucose promotes its own oxidation*).
  2. **For conversion to fatty acids or amino acids** – de novo lipogenesis is limited to the liver, and is a minor pathway in humans.

Lipid oxidation after a meal:

- Unlike glucose, lipids do *not* promote their own oxidation after a meal
- This is because:
  - Humans have a virtually unlimited capacity to store lipids

    - There is little requirement to minimize chylomicron concentrations
    - Fat balance is regulated over the longer term
    - Lipids preferentially flow to adipose tissue

Fed vs. Fasted:

- In a **fed state**, insulin is released and glucagon is inhibited. This leads to increased glucose oxidation, increased glycogen synthesis, increased fat synthesis, and increased protein synthesis.
- In a **fasted state**, glucagon is released and insulin is inhibited. This leads to increased gluconeogenesis, glycogenolysis and ketogenesis (production of ketone bodies).