Ch 2, part 1: Cell Respiration & Cell Metabolism

Objectives:
1. Understand what molecules our cells metabolize for energy.
   - Carbohydrates (first!)
   - Lipids (next)
   - Amino acids (routine & emergency)
   - Lactic acid (routine & emergency)
2. Understand the basics of cell respiration.
3. Become familiar with anaerobic & aerobic cell respiration

1. Types of Cell Metabolism

   i) Carbohydrate metabolism – making or breaking down carbohydrates (ex. Glucose and glycogen).

   ii) Lipid metabolism – making or breaking down lipids (ex. Ketones, fatty acids, triglycerides)

   iii) Protein metabolism (amino acids) – making or breaking down protein.

   iv) Lactic acid metabolism – making or breaking down lactic acid.
Glucose metabolism:

Glycolysis = use of glucose for making ATP during cell respiration.

Glycogen metabolism:

Glycogenesis = making of glycogen from glucose molecules. “genesis” = to create

Glycogenolysis = breaking down glycogen into glucose. “lysis” = to break apart

(Ques: what do you remember from Ch 1 about this process?
What pancreatic hormone can stimulate this in the liver?

Lipid metabolism:

Lipogenesis = making lipids (from extra glucose) such as ketones, fatty acids, & triglycerides, to store energy in fat cells and the liver.

Lipolysis = breaking down lipids, like triglycerides, into fatty acids & ketones to use for energy.

Glycogenesis = creation of glycogen from glucose molecules

(enzyme in liver & skeletal muscle) → glycogen synthase

Glucose + glucose → Glycogen

Glycogenolysis = breakdown of glycogen into glucose

(enzyme in liver & skeletal muscle) → glycogen phosphorylase

(enzyme in liver only!) → glucose 6-phosphatase

Glycogen → glucose 6-phosphate → free glucose
2. Basics of Cell Respiration – use of glucose in cell respiration: 
*Pg 27 – 29 Wiki text*

**Glycolysis**

= 1st step in use of glucose for cell respiration

- Occurs in cell cytoplasm

- Conversion of 1 glucose molecule into:
  - > 2 pyruvate
  - > 2 NADH2
  - > 2 ATP

Pyruvate then can go one of 2 ways
  - depends on if O2 is present or not
Pyruvate from glycolysis then can go one of 2 ways - depends on if $O^2$ is present or not

**Glycolysis**

- **Anaerobic respiration**
- **No oxygen**

**Fermentation**

- **Products**
  - $2 \text{ ATP}$
  - Lactic acid (lactate)

---

**Ischemia, Serum Lactate, and Heart Attack**


“Ischemia” = loss of blood supply

**Loss of blood flow to heart:**
- without arterial blood & O2 heart resorts to anaerobic respiration. Loss of blood & O2 to heart can cause ...

“angina pectoris” = pain associated with loss of O2 supply to heart.
- Prelude to “myocardial infarction” (heart attack)

- Normal serum lactate = 1- 0.5 mmol/L
- **Hyperlactatemia** (high serum lactate) = $> 4 \text{mmol/L}$

*Serum Lactate as a Marker of Acute Myocardial Infarction*
Aerobic respiration

3 Steps of aerobic respiration (AFTER GLYCOLYSIS):
1. Pyruvate processing (pyruvate conversion)
   2 pyruvate enter → 2 Acetyl CoA, 2 NADH, 2 CO₂

2. Kreb’s cycle (citric acid cycle)
   2 Acetyl CoA enter → 2 ATP, 6 NADH₂, 2 FADH₂, 4 CO₂

3. Electron transport chain (ETC)
   2 NADH₂, 6 NADH₂, 2 FADH₂ enter → 30 – 32 ATP, 10 NAD⁺, 2 FAD⁺, 12 H₂O
Electron Transport Chain within the cell mitochondria – ATP production!
Click HERE to see GIF online

Question:
Why do we need oxygen???

= As final electron acceptor in ETC in production of ATP!

Click HERE for blank flow diagram.
Click HERE for key.
When aerobic respiration goes wrong!

Read online Clinical App: cyanide

Where Cell Respiration Occurs
Review

• Our cells can metabolize carbohydrates, lipids, protein, and lactic acid
• Carbohydrate metabolism includes:
  ➢ Glucose metabolism for ATP (glycolysis during cell respiration)
  ➢ Glycogen metabolism
    - Making glycogen (glycogenesis), requires enzyme glycogen synthase
    - Breaking down glycogen (glycogenolysis), requires enzyme glycogen phosphorylase in skeletal muscle & liver, and glucose 6 phosphatase in liver.
• Glycolysis is conversion of glucose into 2 ATP, 2 NADH2, and 2 pyruvate
• Pyruvate can either go through aerobic respiration or anaerobic respiration
• In aerobic respiration, pyruvate goes thru pyruvate conversion to make 2 Acetyl CoA, 2 NADH2, 2 COS
• 2 Acetyl CoA enters Krebs cycle to make 6 NADH2, 2 FADH2, 4 CO2
• H ions enter electron transport chain to make ~ 30 – 32 ATP, 6 NADH+, 2 NADH+, and 12 H2O.
• Altogether aerobic respiration of 1 glucose yields 32 – 34 ATP

Metabolism of carbohydrates, lactic acid, lipids, & amino acids.

**Gluconeogenesis** = creation of glucose from non-carbohydrate sources. (include making glucose from lactic acid, lipids, amino acids)

**What conditions occur to make following happen in body?**

- **Lactic acid metabolism occurs when**
  when body lacks carbohydrates, and causes cells to break down lipids for energy.

- **Lipogenesis occurs when**
  you have excess glucose to use. Adipose and liver cells convert glucose into lipids.

- **Lipolysis occurs**
  when body lacks carbohydrates, and causes cells to break down lipids for energy.

- **Amino acid metabolism occurs**
  when consume protein, or with heavy skeletal muscle use, or during starvation.
**Lactic acid (lactate) metabolism = “The Cori cycle”**

= lactic acid (from skeletal muscle activity & anaerobic respiration) can cause “metabolic acidosis” and drive blood pH ↓.

**Liver “recycles” lactic acid in blood into:**

- **Free glucose** (to be returned to blood stream)
  - (due to enzyme only in liver – glucose 6 phosphatase)
- ** Stored glycogen** (for future need)
- Reverses metabolic acidosis

**Lipid Metabolism:**

“**Lipogenesis**” = conversion of excess glucose into ketones, fatty acids, and white fat (triglycerides) stored in adipose & liver. **Stimulus = “insulin”**

“**Lipolysis**” = conversion of white fat (triglycerides) or ketones into molecules that can be used to make ATP, glucose, and glycogen. **Stimulus = “cortisol”**
Lipid Metabolism:

“Lipogenesis” = conversion of excess glucose into white fat (triglycerides) in adipose & liver. Stimulus = “insulin”

1. Extra blood **Glucose** enters glycolysis to produce **pyruvate**

2. **Pyruvate** goes thru conversion into **Acetyl CoA**

3. **Acetyl CoA** used by liver to make:
   a) **cholesterol** – used to make cell membranes, to make steroid hormones, and to make bile.
   b) **ketones** – can be used to make ATP (energy) when no carbohydrates available.
   c) **fatty acids** – get converted into triglycerides (or white fate)
      - Metabolized for energy (ATP) if no carbs in lipolysis.

Lipid Metabolism:

“Lipolysis” = conversion of white fat (triglycerides) into molecules that can be used for energy (ATP).

A) Triglycerides turned into **ketones** by liver (process = ketogenesis)
   Ketones metabolized for energy (ATP) if no carbs (process called ketosis)

B) Triglycerides turned into fatty acids, if needed, can be converted **back** into Acetyl CoA & enter kreb’s cycle to make ATP & H’s

   OR Acetyl CoA can be converted back into **pyruvate**, and then changed into:
   - glucose (gluconeogenesis)
   - glucose can be stored as glycogen (glycogenesis)
Lipid Metabolism, contin...

**Ketogenesis** = making ketones

**Ketosis** = *use of ketones for energy (lacking carbs)*
Click [HERE](#) for clinical app on ketosis.

**Ketoacidosis** = drop in blood pH from ketosis (BAD!)

**Metabolic acidosis** = metabolizing molecules that drop blood pH.

Click [HERE](#) for blank flow diagram. Click [HERE](#) for key.
Amino acid metabolism

- Amino acids = building blocks of protein
- Essential a.a. = that which we need to consume in diet because body doesn’t make
- Nonessential a.a. = ones our body can make.
- Excess a.a. converted by liver into pyruvate or other acids. These can be used:
  - 1) in Kreb’s cycle for ATP (when pyruvate goes thru conversion to make Acetylene CoA)
  - 2) converted to fat (lipogenesis) or glucose (gluconeogenesis)

Un-used a.a. (excess or what body absolutely cannot use)
> liver converts a.a. into Urea and is excreted by kidneys as ammonia.

- blood panels include BUN (blood urea nitrogen) to determine kidney function.
- Normal BUN = 10 – 20 mg/dl. Higher BUN called “azotemia” and can indicate excess a.a. metabolism and /or kidney failure.

Click HERE for blank flow diagram. Click HERE for key.
Ques: Metabolism of what molecules can lead to metabolic acidosis?

Answer: 
> Amino acids 
> Fatty acids 
> Ketones (ketoacidosis) 
> Lactic acid 

Disorder in amino acid metabolism:

**Phenylketonuria (PKU) — Read online Clinical App:**
Genetic condition of mutation in gene for enzyme Phenylalanine hydrolase (PAH).

[Need PAH to metabolize amino acid “phenylalanine”. Without PAH phenylalanine builds up in body and is converted to “phenylketone”, which is excreted in urine.]

Phenylketone is toxic, causes seizures.

**Treatment:**
Restrict phenylalanine in diet. (nutrition labels have a warning)
Review

- Metabolism of lactic acid, lipids, and protein
- Lactic acid metabolism occurs all the time due to skeletal muscle activity
  - Lactic acid in blood causes metabolic acidosis.
  - Liver recycles lactic acid into glucose & glycogen thru the Cori cycle. (Gluconeogenesis)
- Lipid metabolism includes making lipids (lipogenesis) and breaking them down (lipolysis)
  - Lipogenesis involves converting excess glucose into pyruvate (thru glycolysis), and then into Acetyl CoA (thru pyruvate conversion)
    - Acetyl CoA used by liver to make: cholesterol, ketones, & fatty acids.
    - fatty acids converted to triglycerides (white fat) for storage
  - Lipolysis is simply going backwards biochemically from triglycerides to fatty acids & ketones, which can be metabolized for energy OR converted to glucose (gluconeogenesis)
- Amino acids can be converted by liver to urea for excretion by kidneys as ammonia,
  - Liver can also convert excess a.a. into pyruvate and then to glucose (gluconeogenesis)
  - If kidneys not functioning, urea build up in the blood causing azotemia.
  - PKU = genetic problem metabolizing a.a. phenylalanine. Must avoid phenylalanine in diet because body cannot process it and turns it into toxic phenylketones.