Ch 2, part 1: Cell Respiration & Cell Metabolism

Powerpoint updated Aug 20, 2022

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**
4. **Become familiar with metabolism of lipids, carbohydrates, and amino acids.**

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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, trigylcerides)

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

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

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What conditions occur to make following happen in body?

- Lactic acid metabolism occurs when
  using skeletal muscles
- Lipogenesis occurs when
  consume food, mobilize glucose, extra glucose in blood. Glucose in cells (liver & fat cells) converted fat.
- Lipolysis occurs
  when you run out of glucose & glycogen, cells use lipids for energy
- Amino acid metabolism occurs
  consume & metabolize protein, or you ran out of carbs, and lipids for energy.

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Glucose metabolism:

Glycolysis = use or metabolism of glucose to make energy (ATP)

Glycogen metabolism:

Glycogenesis = making glycogen from glucose.

Glycogenolysis = breaking down glycogen into glucose (Liver can do this in response to Glucagon

(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, primarily, glucose (in liver & fat cells)

Lipolysis = breaking down lipids for energy

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Glycogenesis = creation of glycogen from glucose molecules

(enzyme in liver & skeletal muscle)

synthesis = make

enzyme

Glycogen Synthase

Glucose + glucose → **Glycogen**

Glycogenolysis = breakdown of glycogen into glucose

Stimulus = glucagon

(enzyme in liver & skeletal muscle)

phosphorylate = break down

(enzyme in liver only!

enzyme

Glycogen phosphorylase

Glucose 6 phosphatase

glycogen → **glucose 6-phosphate** → **free glucose**

ATP

blood

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Glycogen metabolism

Click **HERE** for blank flow diagram. Click **HERE** for key.

If insulin is present the liver takes up blood glucose and can undergo glycogenesis.

Glucose + Glucose ⇒ Glycogen

What enzyme is needed for this to happen?

_____

If glucagon is present, the liver can breakdown glycogen into free glucose (glycogenolysis)

Glycogen ⇒ Glucose 6 phosphate ⇒ free glucose

What enzyme is needed for this to happen?

_____

What enzyme does the liver have (but not skeletal muscles) for this to happen?

_____

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Diabetes (Type 2) = insulin resistance. Cells ignore insulin & don't take in glucose, so blood glucose high..

Treatments:

1. Diet & exercise (doesn't always work, especially with genetic predisposition).

2. Pharmaceuticals:

Ex.

Ozempic (semaglutide injection) OR *Rybelsus* (semaglutide pill form)

= increases insulin production AND inhibits glucagon

Click here for Wiki mechanism of action

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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 to make ATP

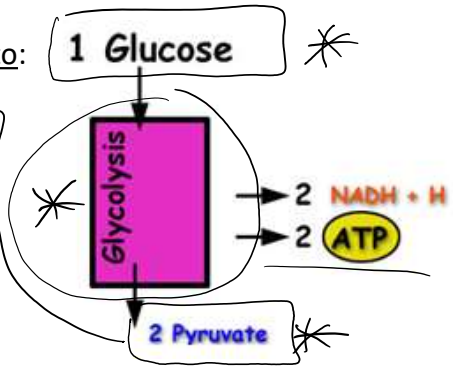
- Occurs in cell cytoplasm

- Conversion of 1 glucose molecule into:

> 2 pyruvate

> 2 $NADH_2$

> 2 ATP



Pyruvate then can go one of 2 ways

- depends on if O^2 is present or not

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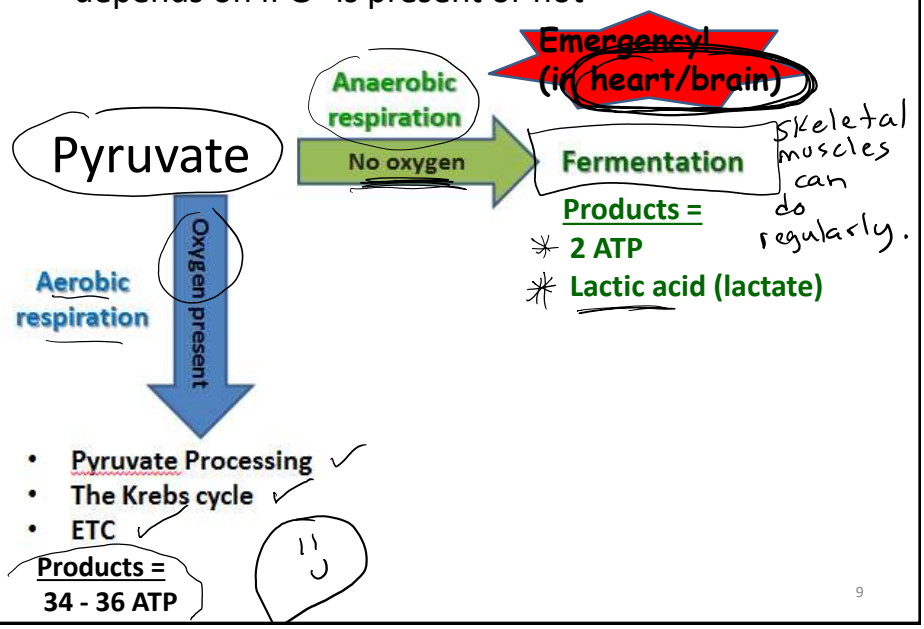
Pyruvate from glycolysis then can go one of 2 ways
- depends on if **O^2** is present or not



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Ischemia, Serum Lactate, and Heart Attack

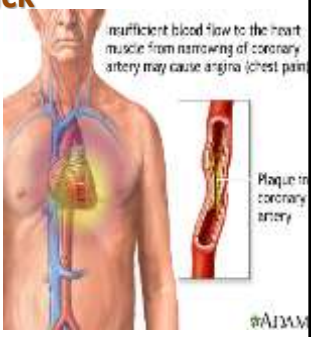
loss of blood flow.

Ischemia & Angina Pectoris – Click HERE for Clinical App reading.

"Ischemia" = loss of Blood Flow

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 in Left chest & arm (from lactic acid) in myocardial infarction.

- Prelude to "**myocardial infarction**" (heart attack)

- Normal serum lactate = 1- 0.5 mmol/L
- **Hyperlactatemia** = high blood lactate = > 4mmol/L

Serum Lactate as a Marker of Acute Myocardial Infarction
http://www.aafp.org/afp/1998/0415/p1993.html

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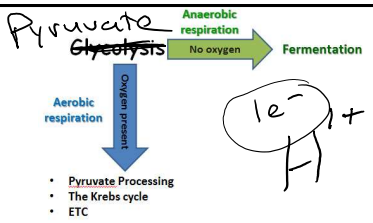
Aerobic respiration



Glucose → Glycolysis → 2 Pyruvate

3 Steps of aerobic respiration (AFTER GLYCOLYSIS):

1. Pyruvate processing (pyruvate conversion)

2 pyruvate enter → **2** Acetyl CoA, 2 $NADH_2$, 2 CO_2

2. Kreb's cycle (citric acid cycle)

2 Acetyl CoA enter → **2** ATP, 6 $NADH_2$, 2 $FADH_2$, 4 CO_2

H's

3. Electron transport chain (ETC)

2 $NADH_2$, 6 $NADH_2$, 2 $FADH_2$ enter → **30 – 32 ATP**, 10 NAD^+, 2 FAD^+, 12 H_2O

Plus 2 NADH2 from glycolysis and
2 NADH2 from pyruvate processing

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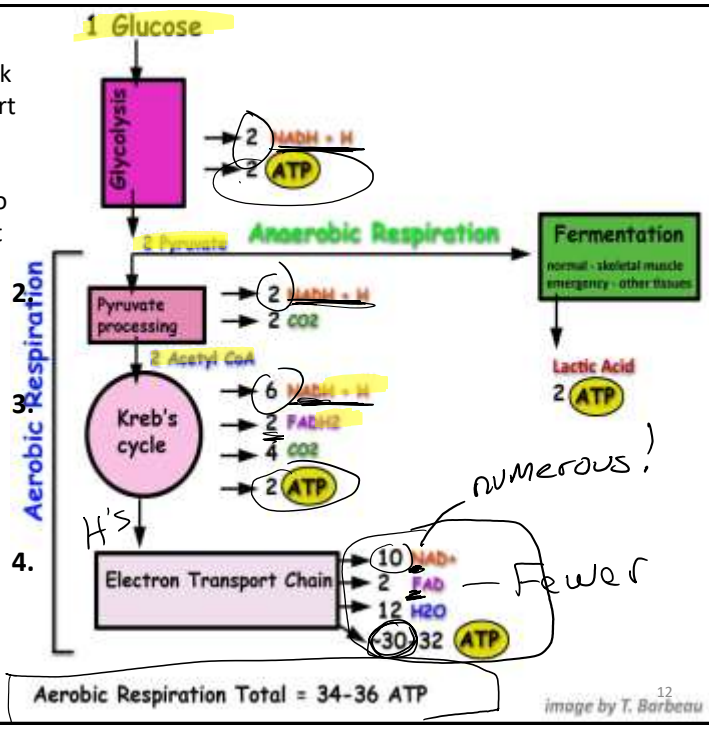
Click **HERE** for blank Glycolysis flow chart

Click **HERE** for KEY to Glycolysis flow chart



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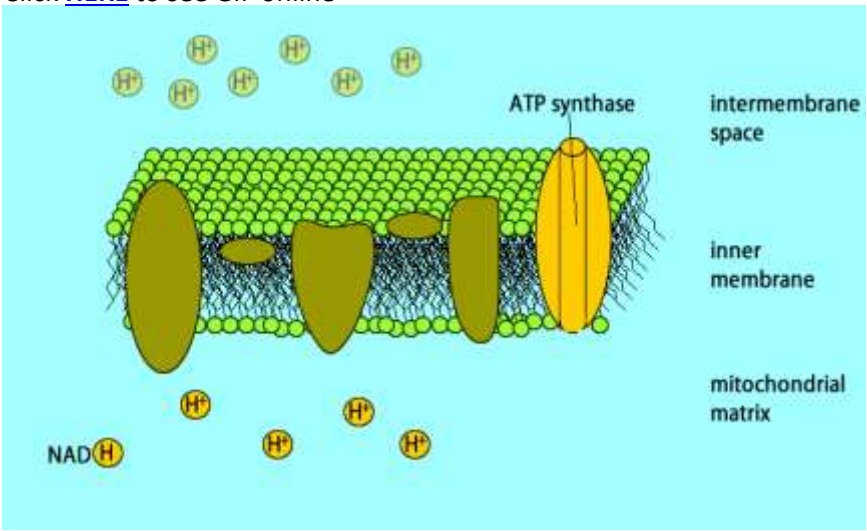
Electron Transport Chain within the cell mitochondria – ATP production!

Click **HERE** to see GIF online



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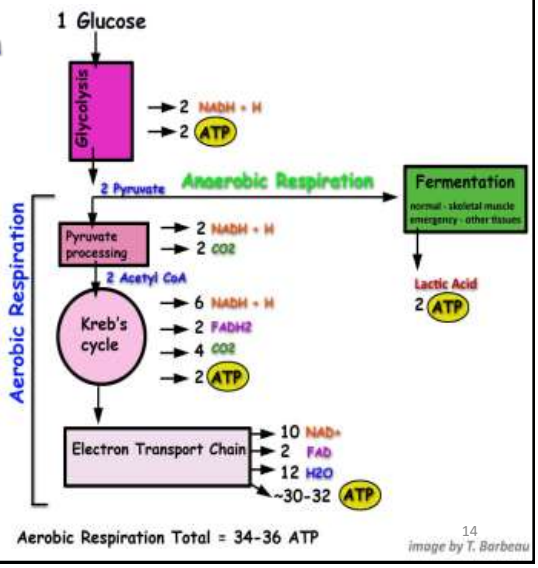
Question:
Why do we need oxygen???

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



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When aerobic respiration goes wrong!

Read online Clinical App: cyanide

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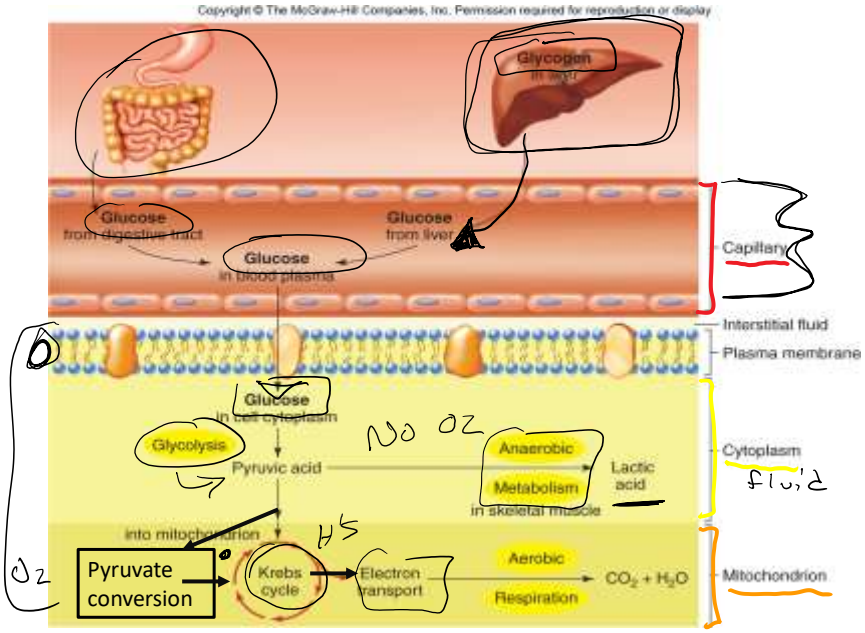
Where Cell Respiration Occurs



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Review (Whew! That's a lot!)

- 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 34 – 36 ATP
- Glycolysis occurs in cytoplasm, but pyruvate conversion, Kreb's cycle, and ETC occurs in mitochondria

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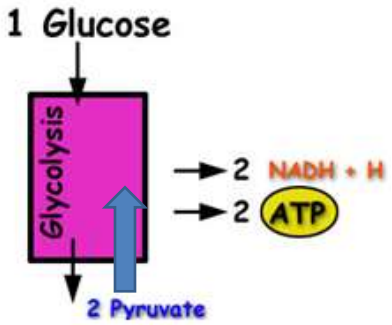
glucose create

Gluconeogenesis = making glucose from a novel (not carbohydrate) source.

new

lipids
amino acids ⇒ Glucose
lactate



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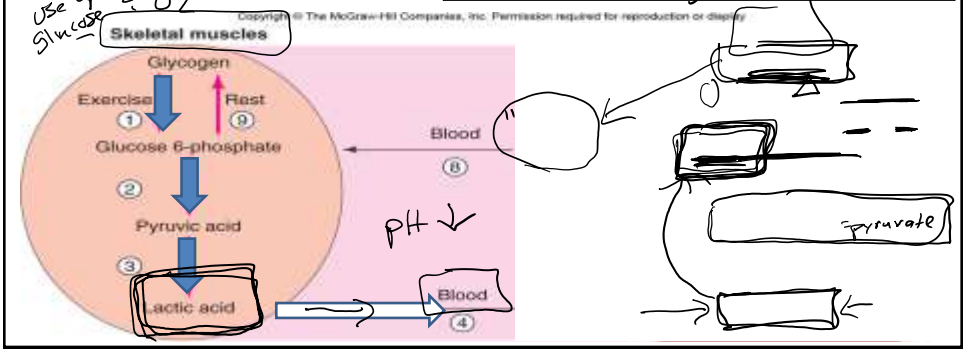
Lactic acid (lactate) metabolism = "The Cori cycle"

= 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

What is the term for when non-carbohydrate molecules (like lactic acid) are turned into glucose? Gluconeogenesis



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Lipid Metabolism:

"**Lipogenesis**" = making lipids.

"**Lipolysis**" = breaking down lipids.

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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 through pyruvate conversion into **Acetyl CoA** (Gallstones (cholelithiasis))

and fat cells

3. Acetyl CoA used by liver to make:

a) cholesterol – used to make 1. cell membranes, 2. Steroid hormones 3. Bile

b) ketones –

c) fatty acids – which will be converted to triglycerides (stored white fat)

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Lipid Metabolism:

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

stored fat

A) Triglycerides turned into Ketones by liver

Process of making ketones = (Ketogenesis)

Ketones metabolized for energy (ATP) if no carbs

Process of using ketones for energy, or ketones in blood = (Ketosis)

using fat for ATP

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

thru Pyruvate conversion

OR Acetyl CoA can be converted back into Pyruvate, and then changed into:

Glycolysis

- glucose (**gluconeogenesis**)
- glucose can be stored as glycogen (**glycogenesis**)

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Lipid Metabolism, contin…

Ketogenesis = making ketones

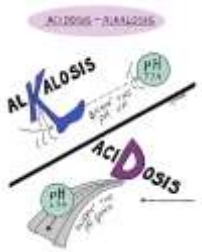
Ketosis = ketones in blood

Click HERE for clinical app on ketosis.

Ketoacidosis = ↓ blood pH from ketosis

Metabolic acidosis = metabolism of substances that ↓ blood pH.

Ex. diabetic ketoacidosis



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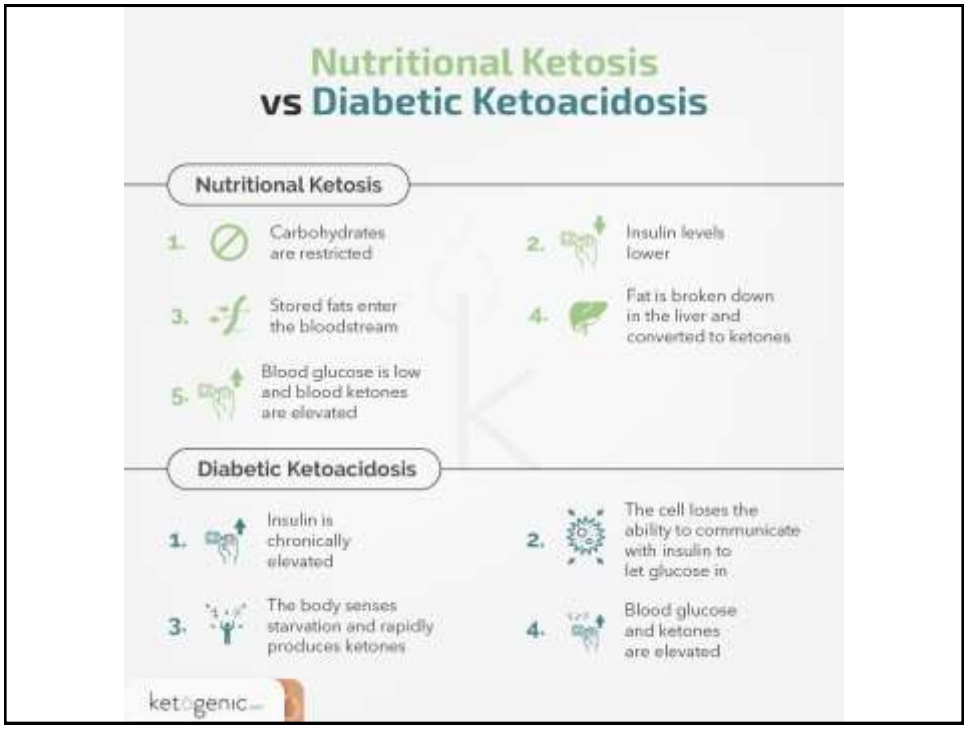
Nutritional Ketosis
vs Diabetic Ketoacidosis
Nutritional Ketosis
1. Carbohydrates are restricted
2. Insulin levels lower
3. Stored fats enter the bloodstream
4. Fat is broken down in the liver and converted to ketones
5. Blood glucose is low and blood ketones are elevated
Diabetic Ketoacidosis
1. Insulin is chronically elevated
2. The cell loses the ability to communicate with insulin to let glucose in
3. The body senses starvation and rapidly produces ketones
4. Blood glucose and ketones are elevated
ketogenic

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Ketosis (new slide 5/29)
SYMPTOMS OF KETOSIS
Fatigue
Weakness
Headache
Intense sugar or carb cravings
Bad breath ("keto breath")
Digestive issues
Insomnia
SYMPTOMS OF KETOACIDOSIS
Nausea
Vomiting
Abdominal pain
Rapid and shallow breathing
Thirst and dehydration
Dry mouth
Confusion
Tiredness
Ketosis compounds
Acetone
Acetoacetate
2-Hydroxybutyric acid
keto mojo
KETONE
150

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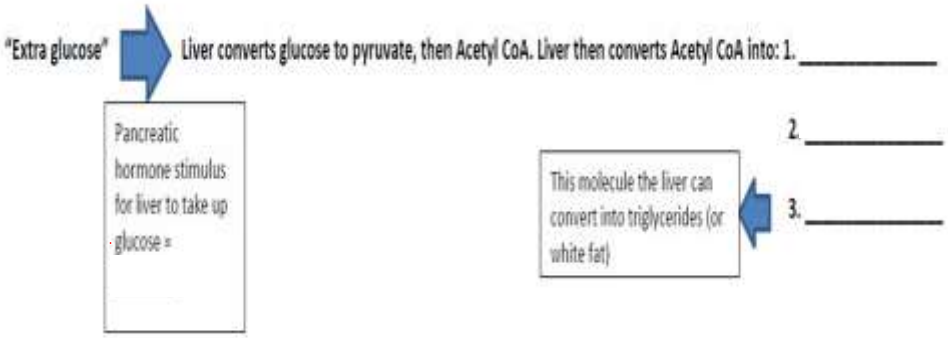
Click **HERE** for blank flow diagram. Click **HERE** for key.

Lipogenesis pathway



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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 Acetyl CoA)
  - **2)** a.a. converted into fat (process called lipogenesis)

    or a.a. converted into glucose (process called gluconeogenesis)

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

- 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.

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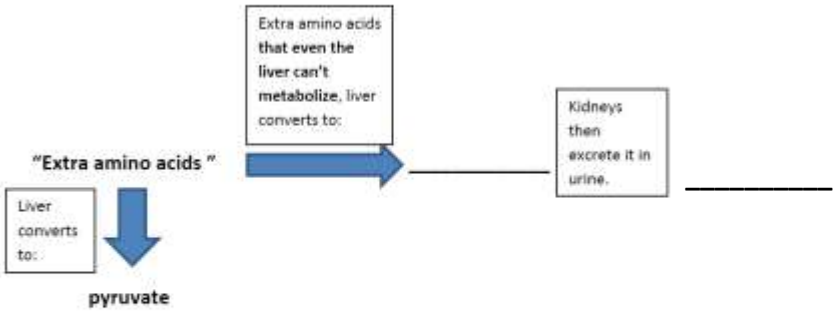
Click **HERE** for blank flow diagram. Click **HERE** for key.

Amino acid metabolism pathway



1. How can pyruvate be used to make ATP? _____

2. What else can pyruvate be changed into?

A) _____ (process called _____)

B) _____ (process called _____)

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Ques:

Metabolism of what molecules can lead to metabolic acidosis?

Answer:

- Ketones
- Fatty acids
- triglyceride
- amino acids
- lactic acid

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Disorder in amino acid metabolism:

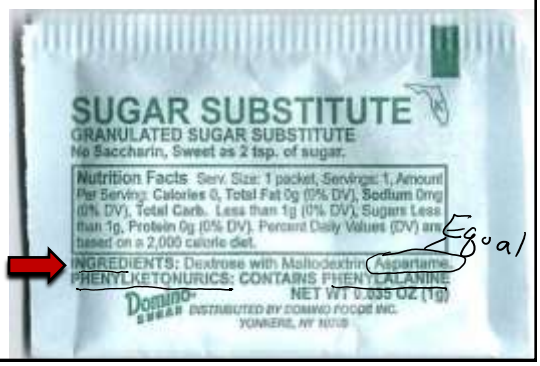
Phenylketonuria (PKU) – Read online Clinical App:

Genetic condiction 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)



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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**. (Gluconeogensis)
- **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 trigylerides 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.

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