Metabolism

اعداد: ا.م.د. همت محمد دردير قليعي

كلية العلوم

قسم الكيمياء

2023/2022

- **Faculty of Science**
- **Second Year**
- **Second Semester**
- **Biotechnology Program**

Content

- **Digestion and absorption of lipids**
- **Triglyceride storage**
- **Hormonal control of lipolysis**
- **Digestion of lipids in diet**
- **Oxidation of fatty acid**

Carbohydrate Metabolism

Definition of Metabolism:

The chemical processes occurring within a living cell or organism that are necessary for the maintenance of life. All these are called anabolism and catabolism.

Metabolism

Anabolic reaction	**catabolic reaction**
1. synthesis of complex molecules from simple compound.	1.break down of large molecules Such as polysaccharides, proteins
2. energy is needed for synthesis (endergonic reaction)	Into small molecules like, CO_2, NH_3, H_2O.
	2. liberated energy. (exergonic reaction)

Digestion and absorption:

Digestion of CHO is accomplished by the enzymes of digestive fluids, saliva, pancreatic juice and intestinal juice.

1. mouth: salivary glands secrete saliva

Saliva contains: **α- amylase** (ptyalin), **water** 99.5% and **glycoprotein** as food lubricant.

α- amylase, hydrolysis **starch** to dextrin and maltose.

PH of α- amylase = 5.8 – 7.1 less than 4.0 is in active

2. stomach ---------- no digestion is seen in stomach , amylase is in active

Because the PH of stomach (1 - 2) very acidic.

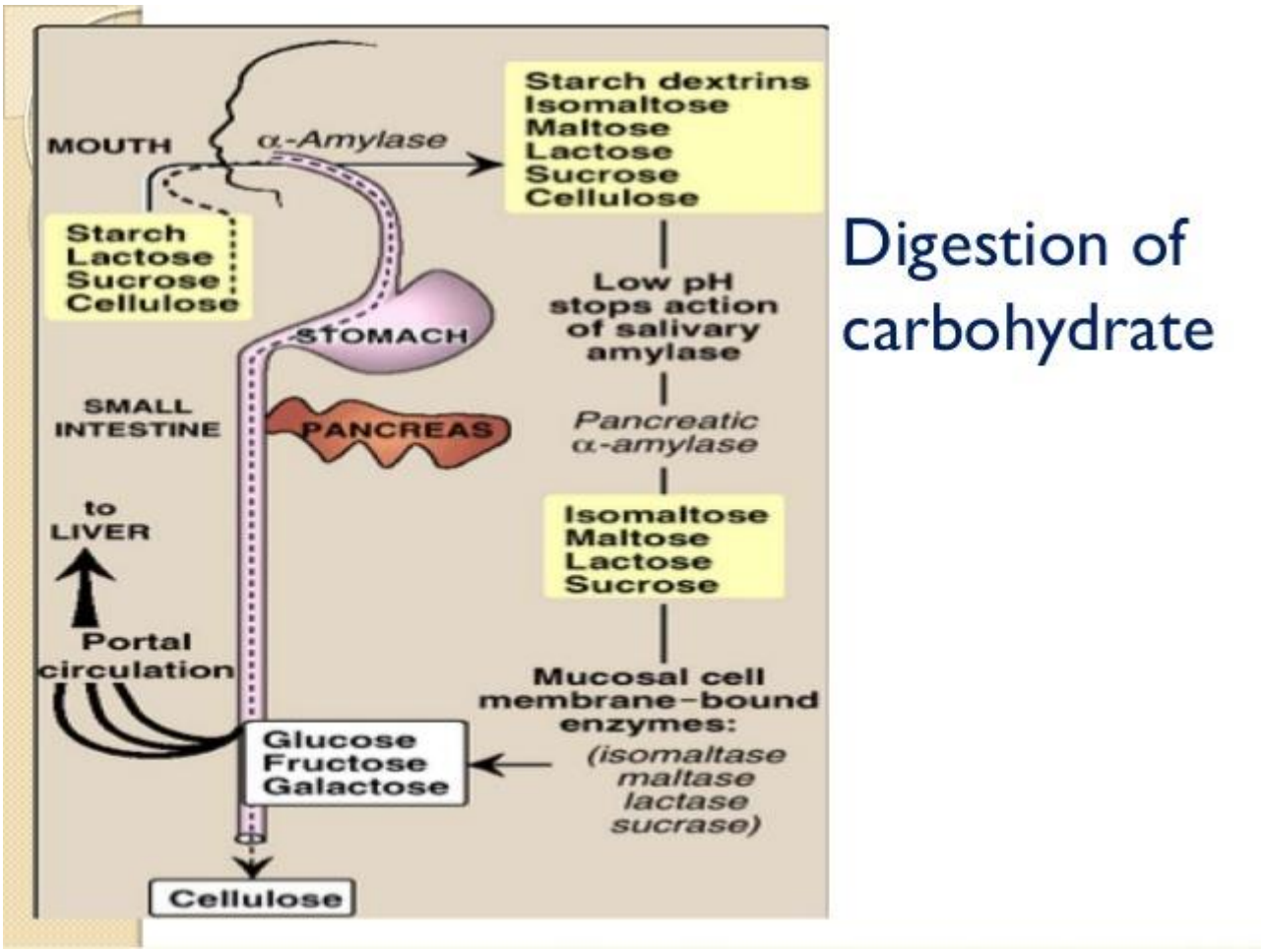
3. small intestine: it is the major site of digestion of CHO, pancreatic amylase hydrolyze dextrin into maltose. The optimum PH of amylase = 7.1

4. intestinal mucosal : mucosal cell membrane – bound enzymes , the site where disaccharides hydrolyze.

Maltose $\xrightarrow{\text{maltase}}$ glucose + glucose

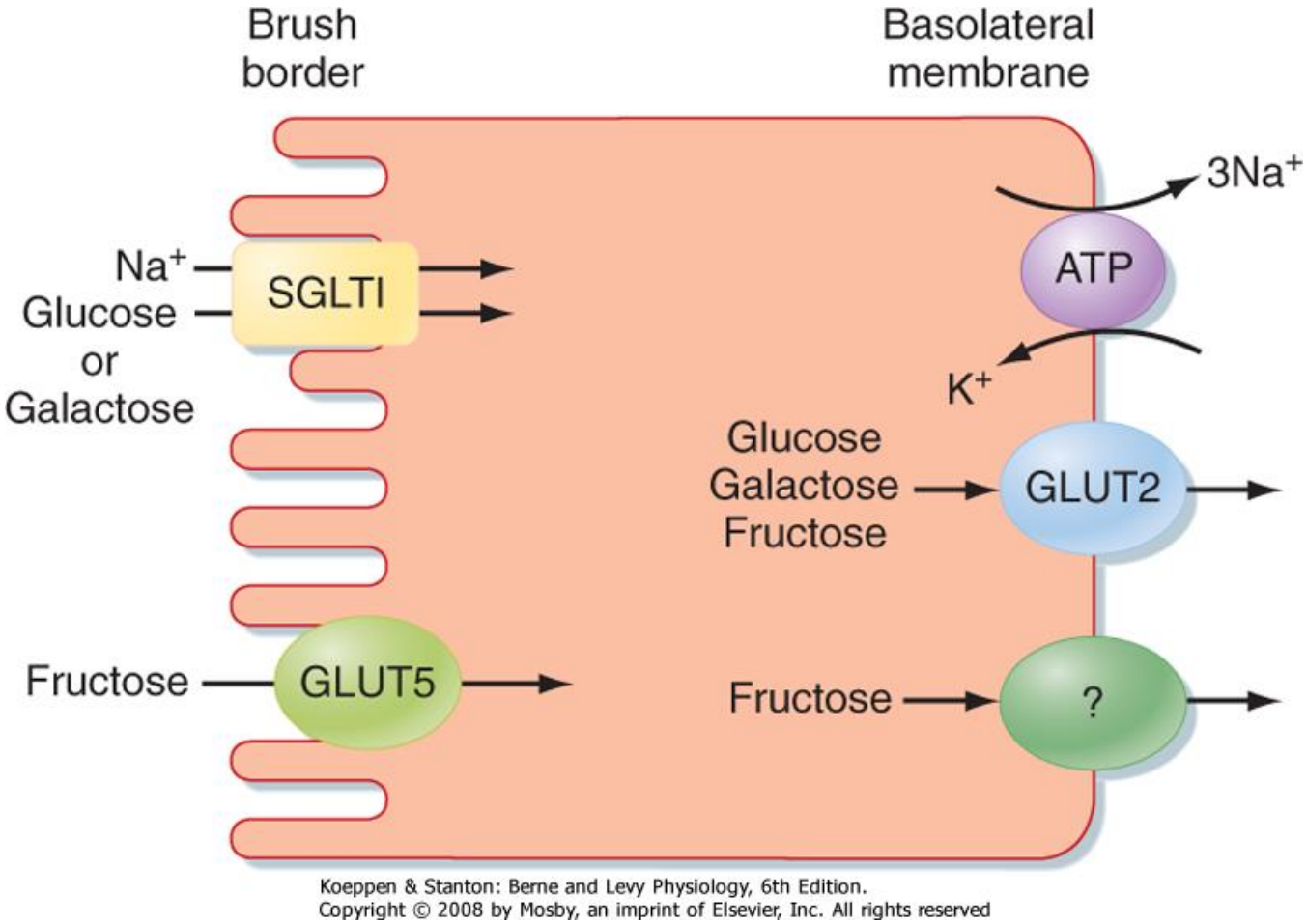
Sucrose $\xrightarrow{\text{sucrase}}$ glucose + fructose

Lactose $\xrightarrow{\text{lactase}}$ glucose + galactose



Absorption of Carbohydrates

Intestine



Absorption of Carbohydrates:

1. transport into epithelial cells (of the villi)

glucose and galactose are transported by **active transport**, while **fructose** is transported by **facilitated diffusion.**

2. transport from epithelial cells into the blood stream is by **facilitated diffusion.**

Fate of glucose after absorption

In the liver, glucose undergoes **variety of chemical changes depending upon the physiological need of the body.**

1. Body need for energy: glucose oxidized completely to **CO2, H2O and energy** by (**glycolysis** and **citric acid cycle**).

2. Excess glucose may be converted to glycogen, deposit in liver, muscle tissues By **(glycogenesis**).

3. To maintain glucose blood level, liver glycogen reconverted to glucose enters blood By **(glycogenolysis).**

4. excess glucose after conversion to glycogen , **convert to fatty acids stored in adipose tissue as triglycerides (lipogenesis).**

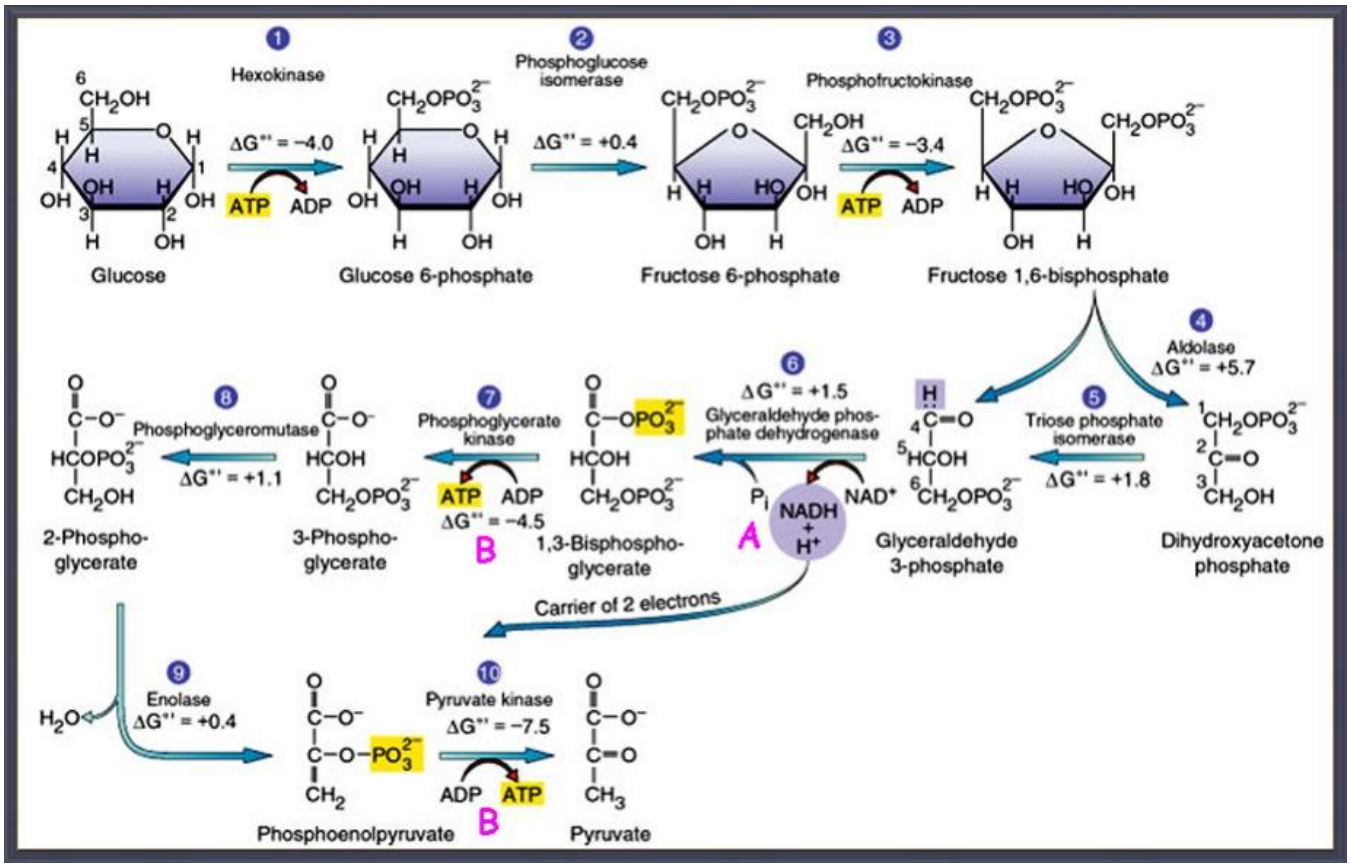
5. small amounts of glucose may be utilized for the synthesis of ribose and deoxyribosee for synthesis of nucleic acids.

6. in muscle contraction, only partial degradation of glucose may take place, resulting in formation of lactic acid disposed off by the liver.

The metabolism of CHO may be subdivided in the following categories.

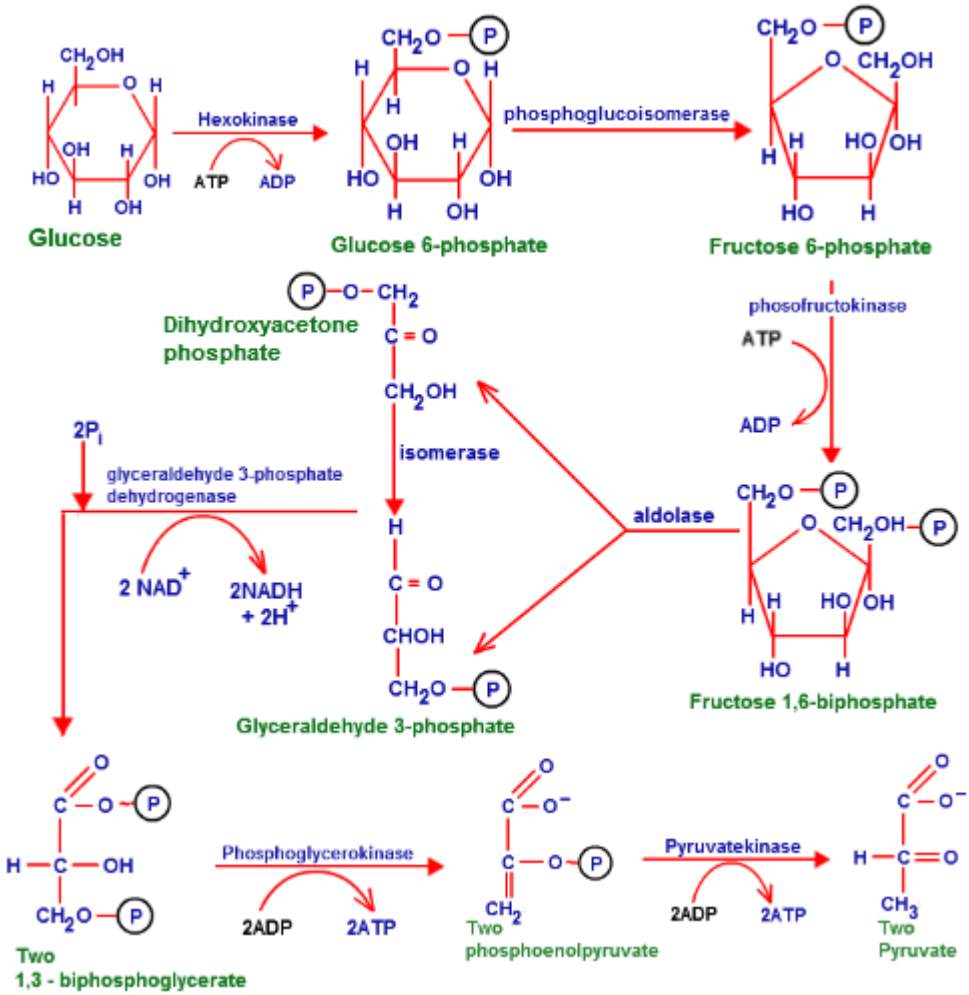
Glycolysis: (from *glycose*, an term for glucose + *-lysis* degradation)

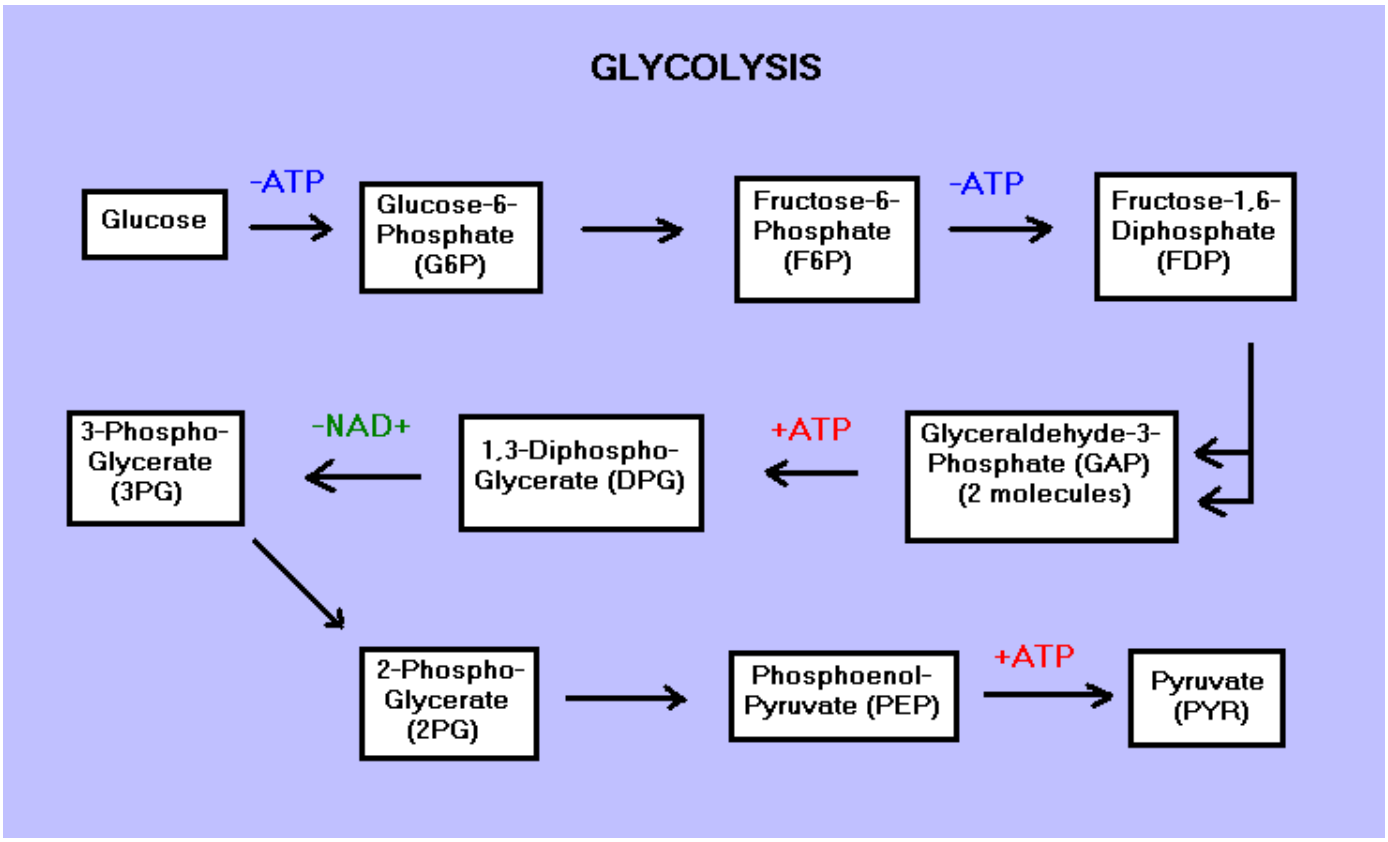
1. It is the metabolic pathway that converts glucose $C_6H_{12}O_6$, into pyruvate.
2. The free energy released in this process is used to form the high-energy molecules ATP and NADH.
3. Glycolysis is an oxygen independent metabolic pathway, said to be anaerobic.
4. Glycolysis occurs in the cytosol (cytoplasm) of the cell.
5. The most common type of glycolysis is the Embden–Meyerhof–Parnas (EMP), which was discovered by Gustav Embden, Otto Meyerhof, and Jakub Karol Parnas.
6. The glucose in the blood circulation, when enter the cell become phosphorylated given by ATP (Activation by phosphate group).
7. This phosphorylation occurs on the cell membrane by the action of two enzymes.
    1. specific enzyme (glucokinase) in the liver.
    2. nonspecific enzyme (hexokinase), Present in liver and other extra hepatic cell
8. Glu-6- p is an important compound for several metabolic pathways. The reaction is irreversible.

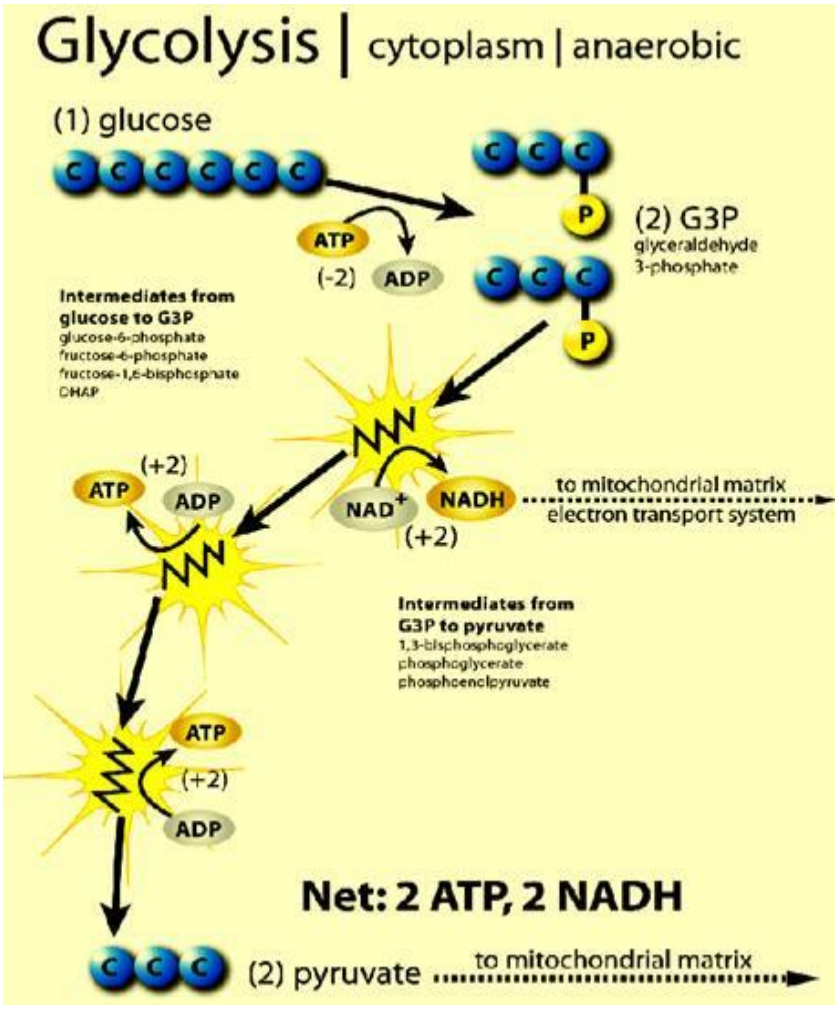


The overall process of glycolysis is:

$$\text{Glucose} + 2\ NAD^+ + 2\ ADP + 2\ P_i \rightarrow 2\ \text{Pyruvate} + 2\ NADH + 2\ H^+ + 2\ ATP + 2\ H_2O$$




GLYCOLYSIS
Glucose
-ATP
Glucose-6-Phosphate (G6P)
Fructose-6-Phosphate (F6P)
-ATP
Fructose-1,6-Diphosphate (FDP)
Glyceraldehyde-3-Phosphate (GAP) (2 molecules)
+ATP
1,3-Diphospho-Glycerate (DPG)
-NAD+
3-Phospho-Glycerate (3PG)
2-Phospho-Glycerate (2PG)
Phosphoenol-Pyruvate (PEP)
+ATP
Pyruvate (PYR)


Glycolysis | cytoplasm | anaerobic
(1) glucose
ATP
(-2)
ADP
(2) G3P
glyceraldehyde 3-phosphate
Intermediates from glucose to G3P
glucose-6-phosphate
fructose-6-phosphate
fructose-1,6-bisphosphate
DHAP
(+2)
ATP
ADP
NAD+
NADH
(+2)
to mitochondrial matrix
electron transport system
Intermediates from G3P to pyruvate
1,3-bisphosphoglycerate
phosphoglycerate
phosphoenolpyruvate
ATP
(+2)
ADP
Net: 2 ATP, 2 NADH
(2) pyruvate
to mitochondrial matrix

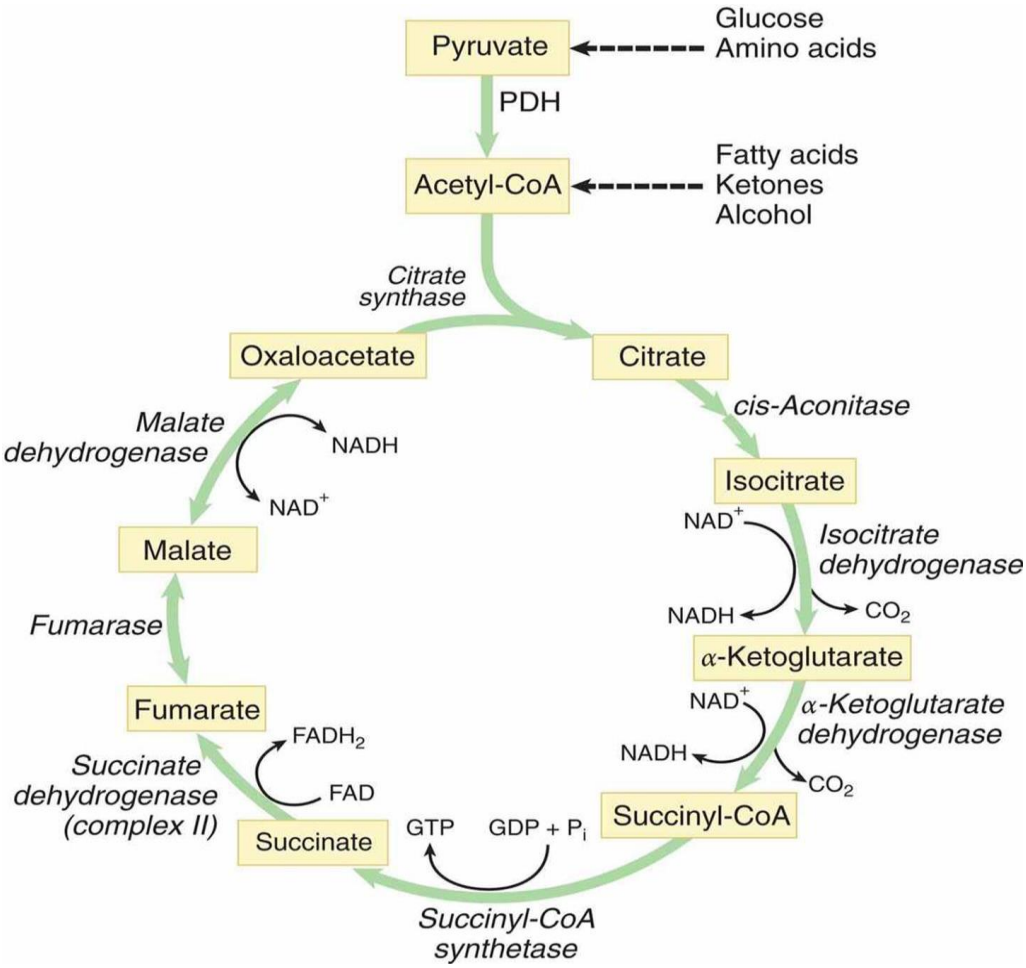
Energy production: The net of ATP molecules during glycolysis is equal to (8).

ATP used	1.	(glu ⟶ glu-6-pho)	1 ATP
	2.	(F-6-pho ⟶ F-1,6 - di pho)	1 ATP
ATP gain	Gly-3- pho ⟶	1,3-diphoGly	NADH × 2
	1,3 -diphoGlyc ⟶	3phoGly	1 ATP × 2
	PEP ⟶	pyruvate	1 ATP × 2

Net of ATP from anaerobic glycolysis 10 – 2 = 8 ATP

Formation of lactate from pyruvate is the major steps in **RBCs, lens and cornea, kidney, medulla, and leukocytes.**

Tricarboxylic Acid Cycle (TCA) OR Krebs Cycle:



.

ATP generated in TCA cycle

Convertion of :

pyruvic acid to acetyl COA 1 NADH = 3ATP

Isocitric acid to α-ketoglutarate	1NADH	=3ATP
α –ketoglutarare to succinyl COA	1NADH	=3ATP
Succinyl COA to succinic acid	1GTP	=1ATP
Succinic acid to fumeric acid	1FAD	=2 ATP
Malic acid to oxaloacitic acid	1NADH	=3ATP
	total	15 ATP

Net ATP produced per glucose molecule = 15 × 2= 30 ATP

Total ATP per glucose (aerobic oxidation + anaerobic) 30 + 8= 38 ATP

Citric acid cycle

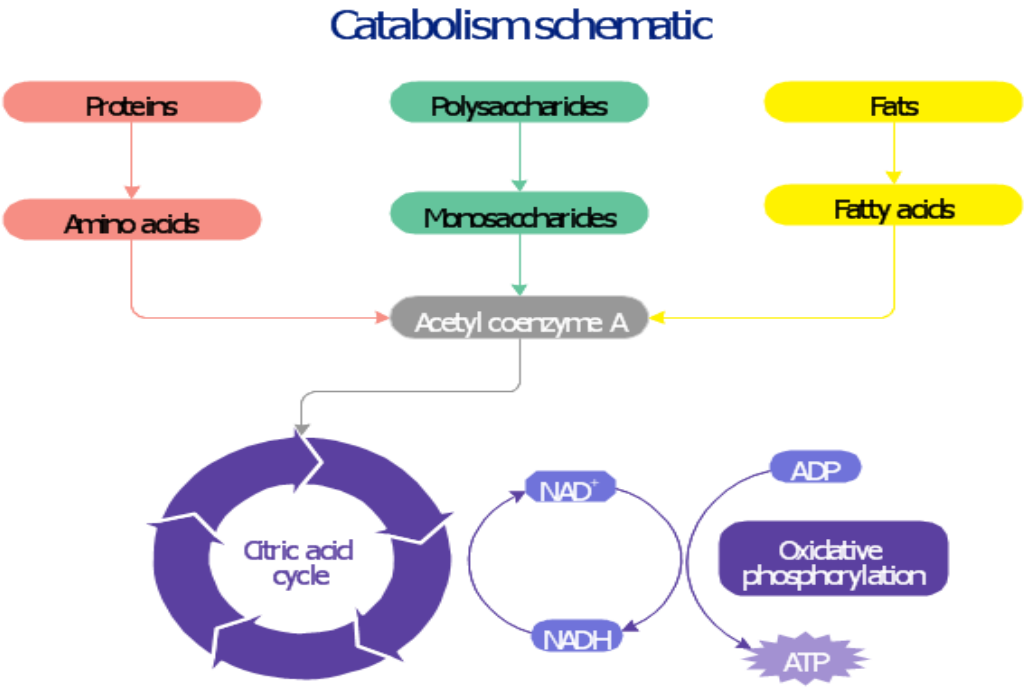
Krebs cycle, tricarboxylic acid cycle TCA

The central function is the oxidation of acetyl CoA to CO2

- It is the final common pathway for oxidation of fuel molecules
- Acetyl Co is derived from the metabolism of fuel molecules as amino acids, fatty acids, and carbohydrates.
- Citric acid cycle is also an important source of precursors
  - Some intermediates are precursors of amino acid
  - One of the intermediates is used in the synthesis of porphorins
  - Another is used in the synthesis of fatty acids and sterols.
- Citric Acid Cycle located in the mitochondrial matrix

(c) Glycolysis and citric acid cycle

Glycolysis		**Citric acid cycle (Krebs cycle)**	
1.	It is a linear pathway.	1.	It is a cyclic pathway.
2.	It occurs in the cell cytoplasm.	2.	It occurs in the mitochondrial matrix.
3.	It occurs in both aerobic and anaerobic respiration.	3.	It occurs in aerobic respiration.
4.	One glucose molecule breaks down to generate 2 $NADH_2$ and 2 ATP molecules.	4.	It produces 6 $NADH_2$, 2 $FADH_2$, and 2 ATP molecules on breakdown of two acetyl-coA molecules.



Glycogenesis (glycogen synthesis): formation of glycogen from glucose.

1. Glycogen is serves as an energy store primarily in muscle and liver, when glucose and ATP are present in relatively high amounts.

2. the excess of insulin promotes the glucose conversion into glycogen for storage in liver and muscle cells.

3. It is stored in the form of granules **cytoplasm** in the cell.

4. The concentration of glycogen in **muscle is low** (1-2 % fresh weight) compared to the levels **stored in the liver** (up to 8% fresh weight).

5. Glycogen is an **energy reserve** that can be quickly mobilized to meet a sudden need for glucose.

Difference between muscle and liver glycogen

	Liver glycogen	Muscle glycogen
Amount	-	More
Source	Glucose and other precursors	Glucose only
Hydrolysis	Give blood glucose	Give lactic acid
Starvation	Converted into blood glucose	Not affected
Muscular exercise	Depleted later on	Depleted first

Glycogenolysis: biochemical breakdown of glycogen to glucose.

1. take place in the cells of muscle and liver tissues in response to hormonal and neural signals.

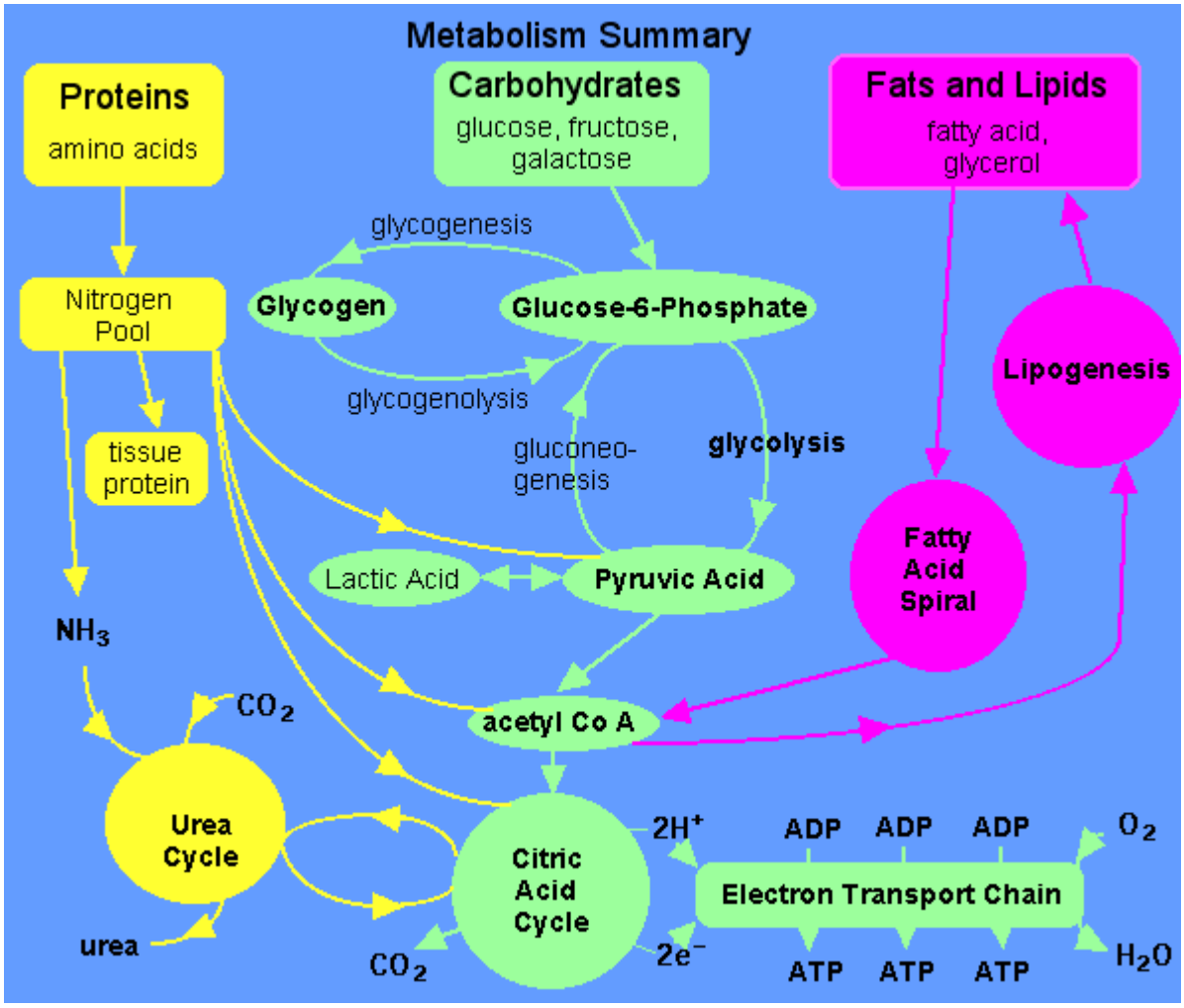
2. Glycogenolysis occurs in the cytoplasm and is stimulated by **glucagon** and **adrenaline hormones.**

3. glycogenolysis plays an important role in the **adrenaline-induced fight-or-flight** response and the **regulation of glucose levels in the blood.**

4. The enzymes required for this process are **glycogen phosphorylase**, **debranching enzyme, and amylo-α-1, 6-glucosidase.**

Gluconeogenesis: is the process of producing glucose from non-carbohydrate sources.

1. 6 ATP molecules are consumed per molecule of glucose produced.
2. most reactions of the gluconeogenesis take place in the ***cytoplasm*** while two reactions occur in the **mitochondria**
3. It mainly occurs in hepatocytes in liver.
4. The molecules that provide substrates for gluconeogenesis include ***proteins***, ***lipids*** and **pyruvate.**
5. Muscle proteins are degraded to form ***amino acids***, These amino acids are called '**glucogenic amino acids.**
6. **Pyruvate** is produced by ***glycolysis*** under ***anaerobic*** conditions.
7. ***glycerol*** produced during the ***hydrolysis*** of fat stores or ingested fats



Regulation (homeostasis) of blood glucose level:

The blood sugar level is maintained by two factors .

a.factors adding glucose to blood (increase blood glucose level).

- from diet (intestinal absorption).
- glycogenolysis (liver).
- gluconeogenesis.
- lipolysis
- conversion of fructose and galactose into glucose

b. factors remove glucose from blood (decrease blood glucose level).

- glycogen formation in liver and muscle (glycogenesis).
- glycolysis in liver(oxidation of glucose).
- convertion of glucose to fat in adipose tissue(lipogenesis).
- B-oxidation (supply energy).
- synthesis of glycoprotein.
- excretion in urine (diabetes)

Hormones decrease blood glucose level

1. insulin secreate from β-cells of pancreas.

causes the liver to convert more glucose into glycogen (this process is **called glycogenesis**).

2. about **2/3 of body cells (primarily muscle and fat tissue cells)** take up glucose from the blood, thus decreasing blood sugar..

Hormones increase blood glucose level

1.glucagon

in very heavy exercise or lack of food for extended periods, the Alpha cells of the pancreas release glucagon, a hormone act to increase blood glucose levels. They convert **glycogen** into glucose (this process is **called glycogenolysis).**

2. Epinephrine, also known as **adrenalin** or **nor adrenaline**, is a hormone, neurotransmitter and medication

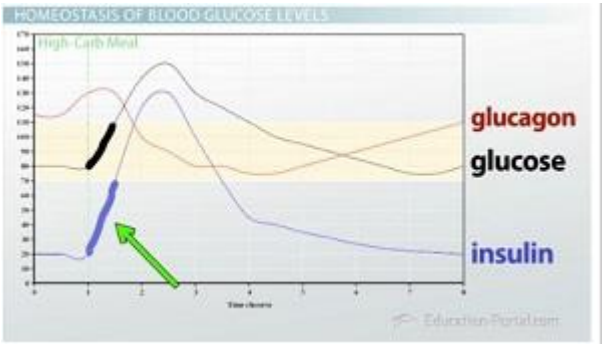
a. Enhances release of glucose from glycogen **(glycogenolysis**).

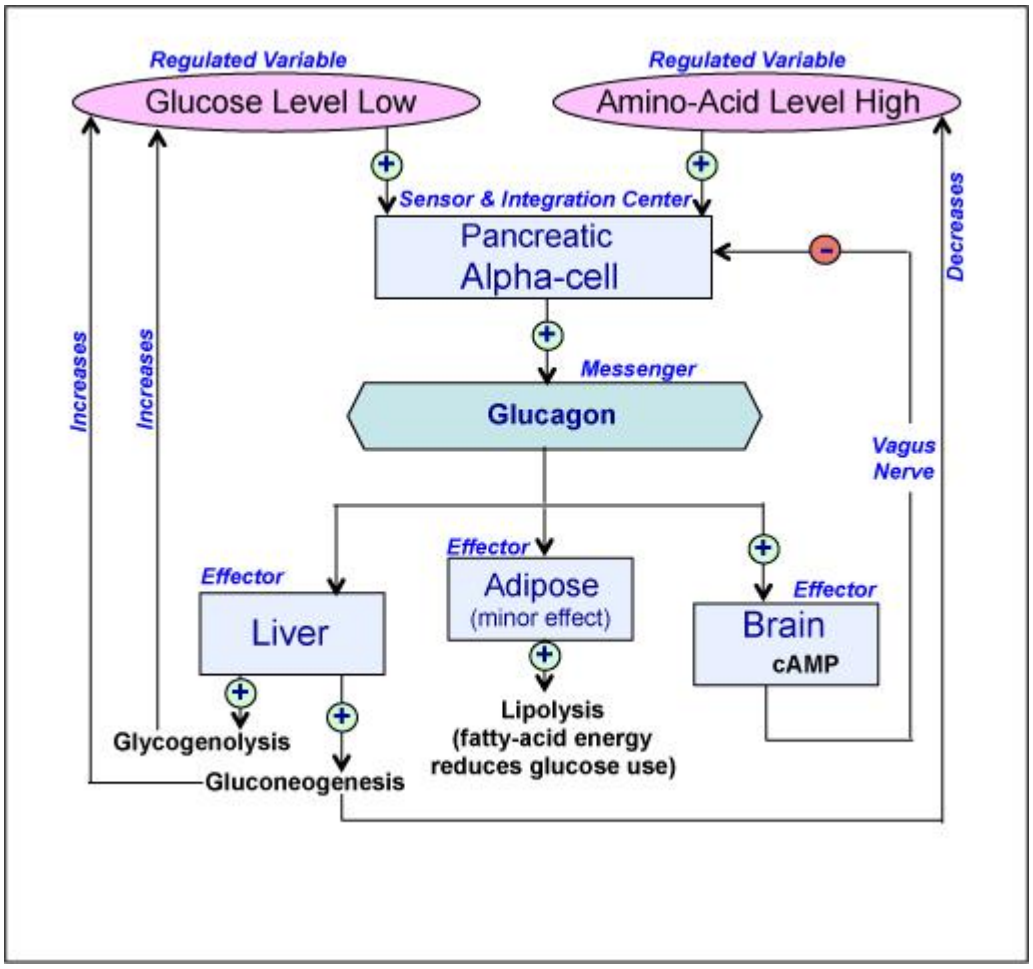
b. Enhances release of fatty acids from adipose tissue **(lipolysis).**

3. Cortisol, Enhances **(gluconeogenesis)** ; Antagonizes **Insulin.**

4. Thyroxine, Enhances release of glucose from glycogen; Enhances absorption of sugars from intestine

5. ACTH, Enhances release of fatty acids from adipose tissue **(Lipolysis).**





BLOOD SUGAR LEVEL CHART

	FASTING	JUST ATE	3 HOURS AFTER EATING
NORMAL	80-100	170-200	120-140
PRE-DIABETIC	101-125	190-230	140-160
DIABETIC	126+	220-300	200+

Abnormalities in blood glucose level:

- **1.Hyperglycemia:** Hyperglycemia is an abnormally high blood glucose (blood sugar) level.
- Hyperglycemia is a hallmark sign of **diabetes** (both **type 1 diabetes** and **type 2 diabetes)** and **prediabetes.**
- **Diabetes** is the most common cause of hyperglycemia.

- **Causes of hyperglycemia**
- **pancreatitis**, **Cushing's syndrome**, **pancreatic cancer, certain medications**, and **severe illnesses.**
- **Common symptoms of diabetes:**
- 1. Urinating often. 2. Feeling very thirsty. 3. Feeling very hungry - even though you Eating.
  4. Extreme fatigue. 5. Blurry vision. 6. Weight loss - even though you are eating more (type 1)
  7. Tingling, pain, or numbness in the hands/feet (type 2)
  8. Cardiac arrhythmia

Treatment: This is done by a combination of proper **diet**, **regular exercise**, and **insulin** or other medication such as **metformin.**

2. Hypoglycemia:

abnormally low level of sugar (glucose) in the blood. Hypoglycemia is not a disease in itself.

The brain needs a continuous supply of glucose to **function** because it can neither store nor manufacture glucose.

Hypoglycemia is not a disease, it is commonly linked with **diabetes** or caused by other conditions.

Common symptomes of low sugar levels: include **hunger, trembling, heart racing, nausea**, and **sweating**.

Causes of hypoglycemia:

1. medication:

Quinine, a drug used for **malaria**, can also cause hypoglycemia. Salicylates, which are used for treating **rheumatic disease**, and propanolol for (**high blood pressure**)

2. Alcohol abuse if somebody has been drinking heavily.

3. Some liver diseases -hepatites can cause hypoglycemia.

4. Kidney disorders

5. Some disorders of the **adrenal and pituitary glands** can lead to hypoglycemia.

6. Not eating enough - people with eating disorders, such as **anorexia nervosa**, may find that their blood sugar levels drop dramatically.

7. Insulinoma - this is a **tumor in the pancreas** which can make the pancreas produce too much insulin.

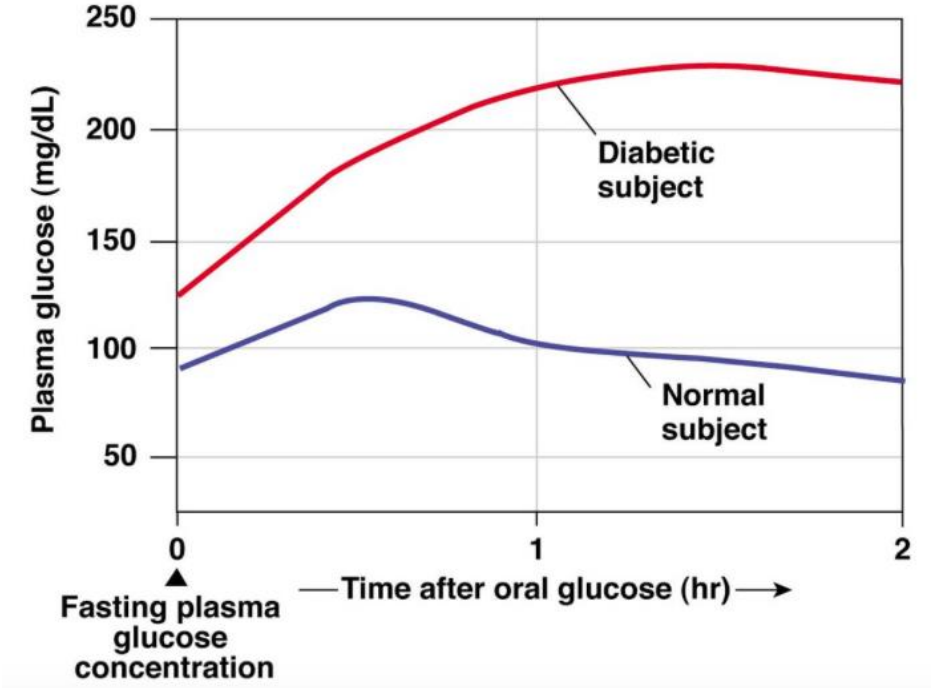
Test used in determining blood sugar:

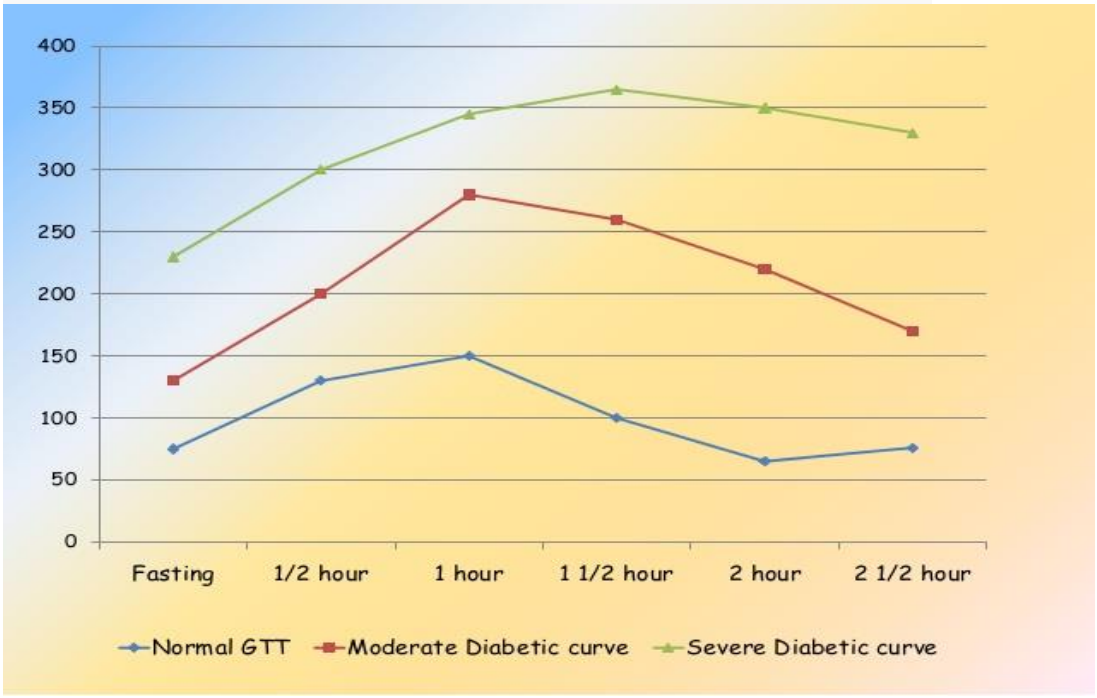
1. Fasting blood sugar (F.B.S).

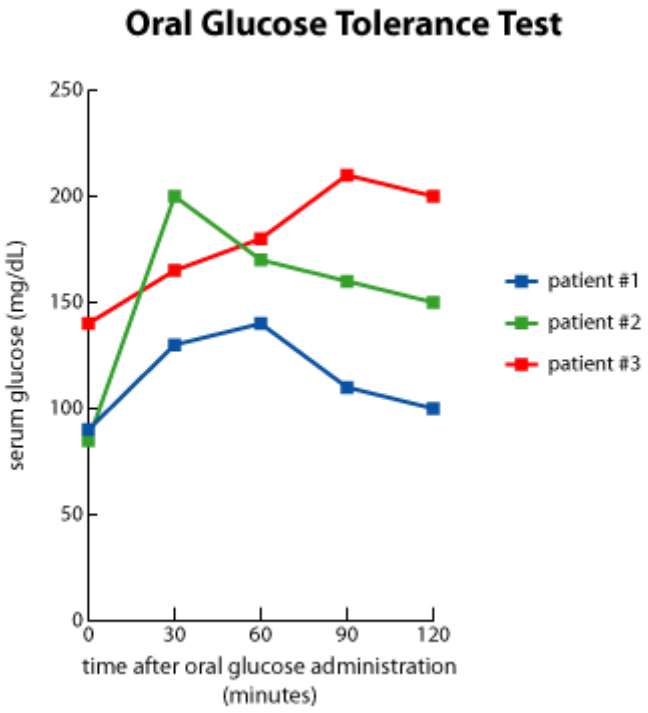
2. Random blood sugar (R.B.S).

3. 2hrs postprandial test

4. Oral glucose tolerance test (OGTT).


250
200
150
100
50
Plasma glucose (mg/dL)
Diabetic subject
Normal subject
0
1
2
Fasting plasma glucose concentration
Time after oral glucose (hr)


400
350
300
250
200
150
100
50
0
Fasting
1/2 hour
1 hour
1 1/2 hour
2 hour
2 1/2 hour
Normal GTT
Moderate Diabetic curve
Severe Diabetic curve



A. Normal blood sugar level= 70 – 100 mg/ dl or 80 – 110 mg/dl

B. Conditions in which blood sugar level is raised.

1.diabetes melletus 2.hyperthyrodism. 3.hyperadrenalism 4.thyrotoxicosis

C. Conditions in which blood sugar level is low.

1. Overdose of insulin treatment of diabetes melletus.
2. hypothyrodism

D. Kidney threshold of glucose equal = 180 mg/dl

E. Hormones regulate blood glucose level (insulin).

F. **The functions of insulin are:**

1. excess glucose in the bloodstream, known as hyperglycemia, insulin encourages the storage of glucose as glycogen in the liver, muscle (glycogenesis).
2. in fat cells(adipose tissues) synthesis of triglycerides (lipogenesis).
3. Build muscle following sickness or injury.
4. Enhance learning and memory of the brain functions.

Disorders in CHOs metabolism

1.Lactose intolerance:It is a condition in which people have symptoms due to the decreased ability to digest lactose, a sugar found in milk products.

Symptoms:

Abdominal pain, bloating, diarrhea, gas, and nausea. **These typically start between half and two hours after drinking milk**.

Severity depends on the amount a person eats or drinks. It does not cause damage to the gastrointestinal tract

Causes.

1. due to not enough of the enzyme lactase present in the small intestine to break lactose down in to glucose and galactose.

2. Primary lactose intolerance is when the amount of lactase decline as people age.

3. Secondary lactose intolerance is due to injury in the small intestine from **infection**, **celliac disease**, **inflammatory bowel disease.**

4. Developmental lactose intolerance may occur in premature babies and usually improves over a short period of time.

2. Galactosemia It is a hereditary disease that results in a **defect in, or absence of, galactose-metabolizing enzymes**. This inborn error leaves the body unable to metabolize galactose, **allowing toxic levels of galactose to build up in human body blood, cells, and tissues or urine .**

Symptoms: lethargy, vomiting, diarrhea, failure to thrive, and jaundice. None of these symptoms are specific to galactosemia.

A galactosemia test: is a blood test (from the heel of the infant) or urine test that checks for three enzymes that are needed to change galactose sugar that is found in milk into glucose.

endogenous production of galactose can cause symptoms development of:

cataract, renal failure, cirrhosis, cognitive, neurologic, and female reproductive complications.

3. Glycogen storage disease (GSD):

Accumulation of glycogen in liver or muscle or other tissues, due to the defects in the processing of glycogen synthesis or breakdown within muscles, liver.

GSD has two types of causes:

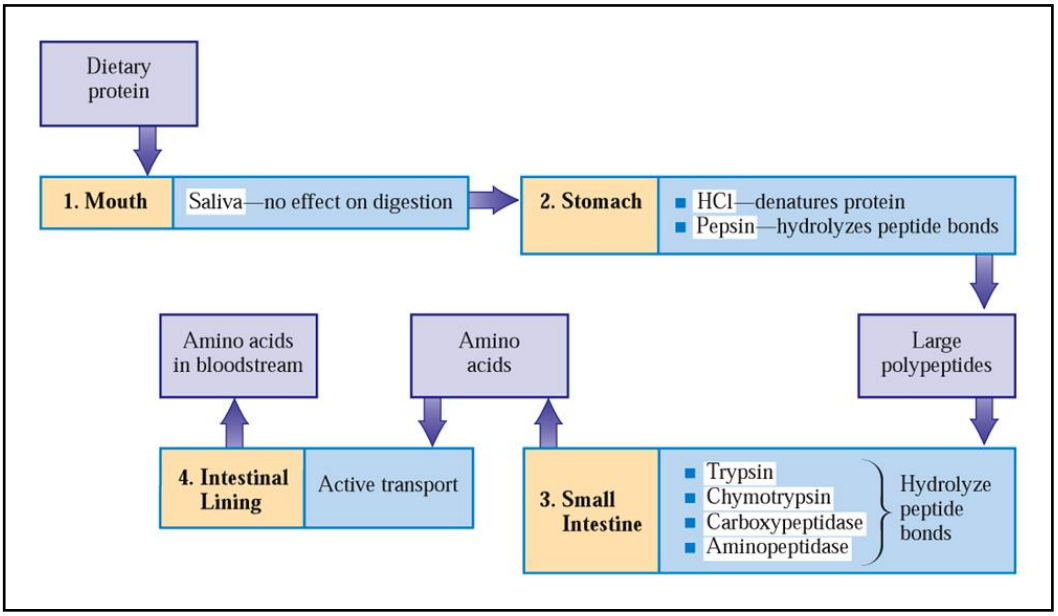
1. Genetic GSD is caused by any inborn error of metabolism (genetic defect of enzymes).
2. Acquired GSD is caused by intoxication.

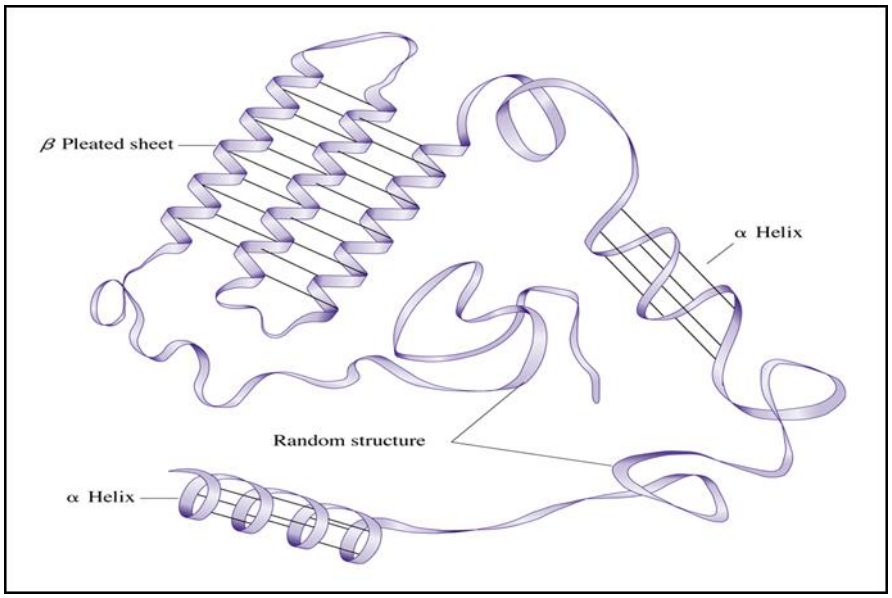
Proteins Metabolism

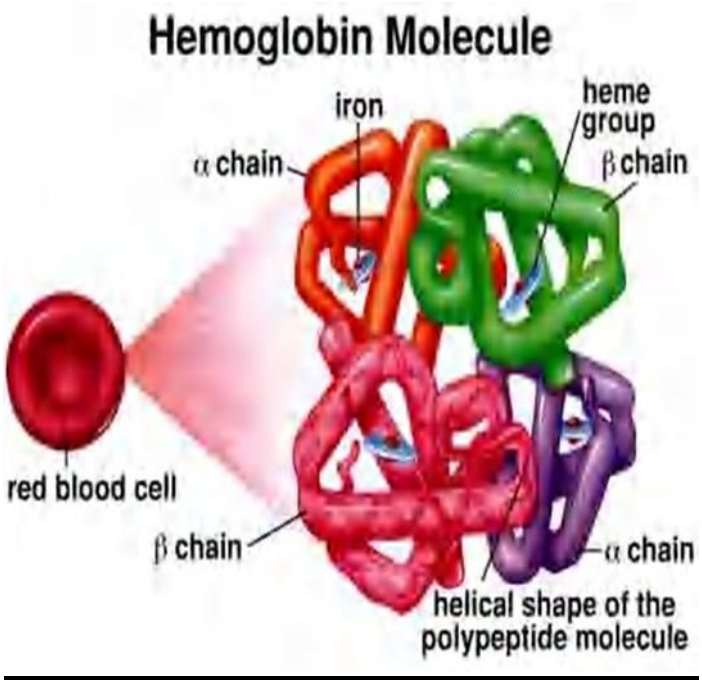
Protein Digestion

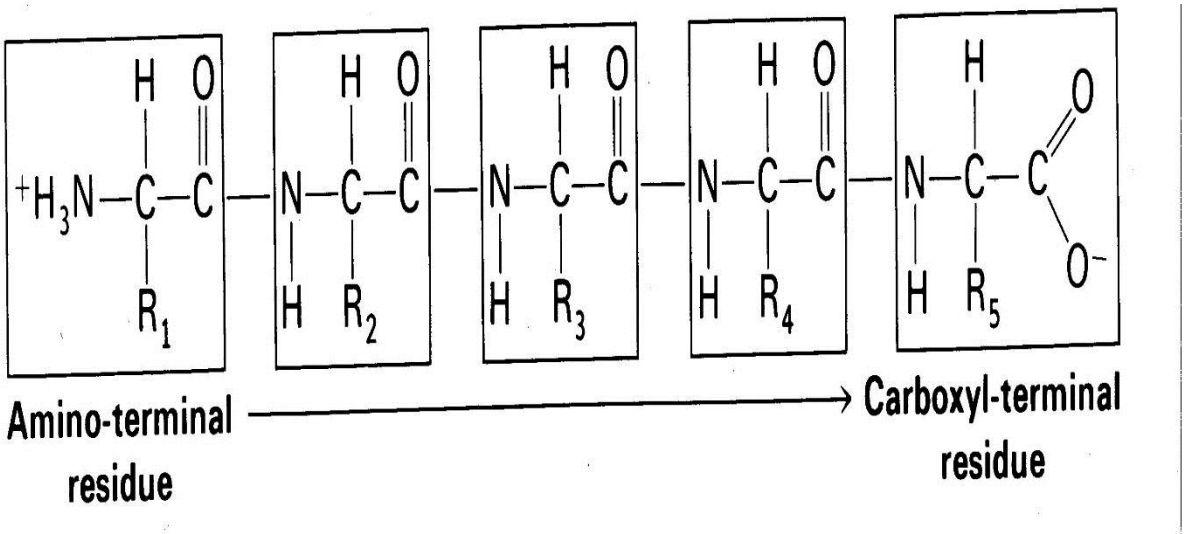
Protein breakdown begins in the **stomach**.

No protein hydrolyzing enzymes are found in saliva.






Hemoglobin Molecule
iron
heme group
α chain
β chain
red blood cell
β chain
α chain
helical shape of the polypeptide molecule


Amino-terminal residue
Carboxyl-terminal residue

Hydrolysis (10% of peptide bonds) & **denaturization** by pepsin enzyme & HCl acid produce **short chain polypeptides** in the stomach.

Trypsin, chymotrypsin, & carboxypeptidase from Pancreatic juices, and **Aminopeptidase** from cells in the small intestine Brush Zone create "free" **amino acids**.

Free amino acids are absorbed thru intestinal wall via active transport. Enter bloodstream and are brought to cells.

The total supply of free amino acids available is called: the **Amino Acid Pool**.

3 sources of "free" amino acids:

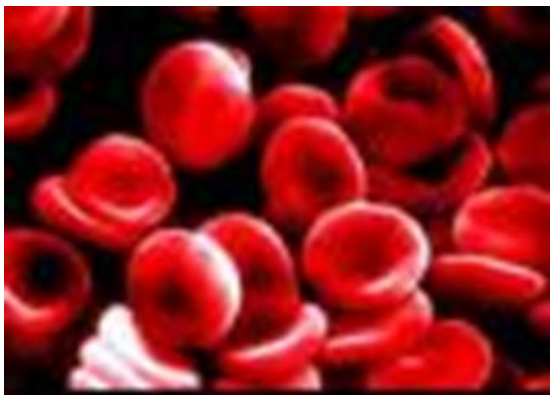
1. Dietary protein breakdown
2. Biosynthesis of amino acids in the Liver
3. Protein turnover (I prefer apple turnovers)

Protein turnover is the breakdown & re-synthesis of body protein:

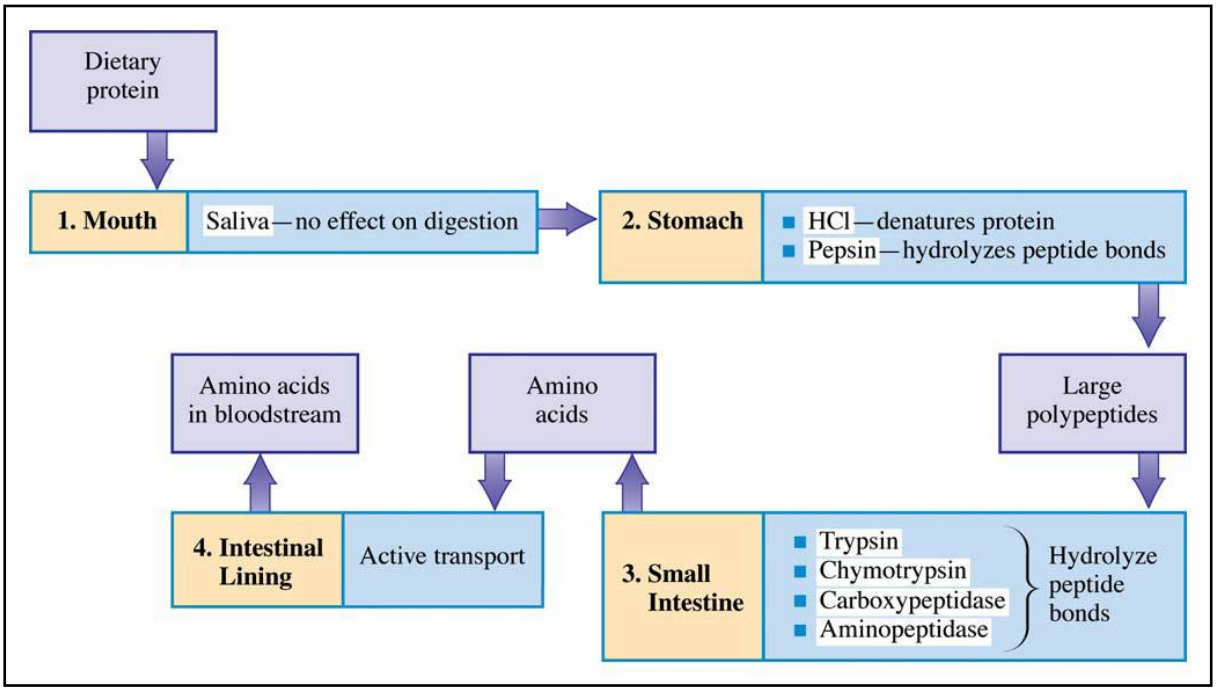
Old tissues

Damage

Recycling enzymes & hormones



Summary of protein digestion in the human body. Possible fates for amino acid degradation products.



Transamination and Oxidative Deamination:

Two steps in degrading amino acids

1) remove a-amino group

2) breakdown & process carbon skeleton

Release of an **amino group** is also two steps:

1) **Transamination**

2) **Oxidative deamination**

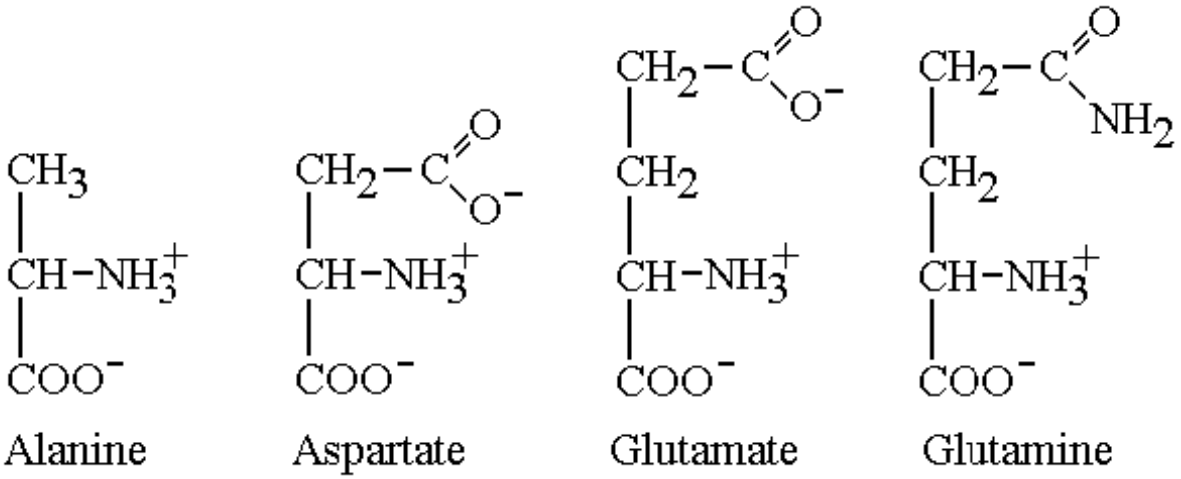
Central role of glutamate:

Amino acids:

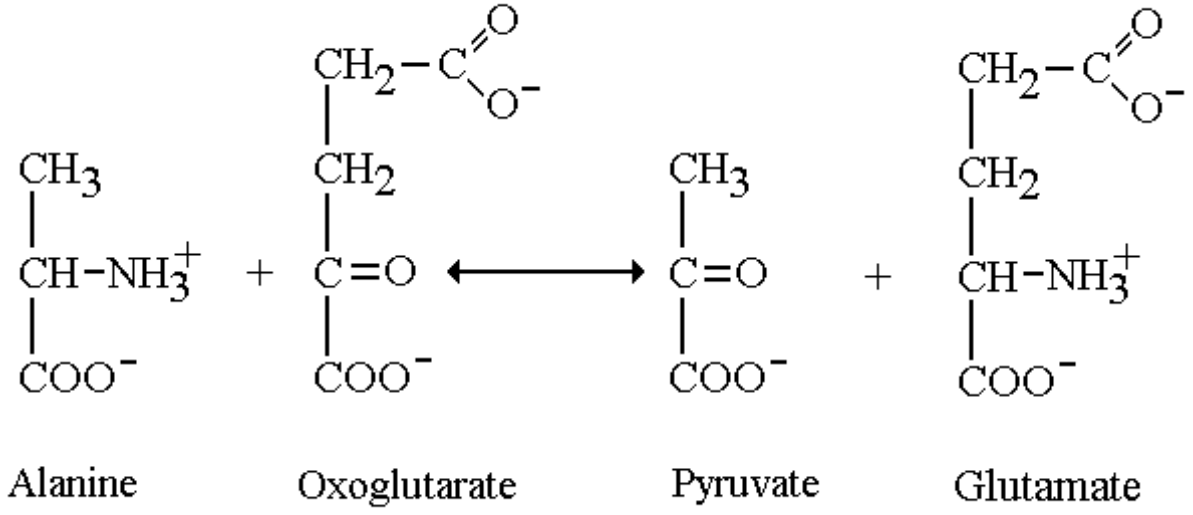
Glutamate, **aspartate**, **alanine** & **glutamine**

present in higher concentrations in mammalian cells. Have metabolic functions as well as roles in proteins.

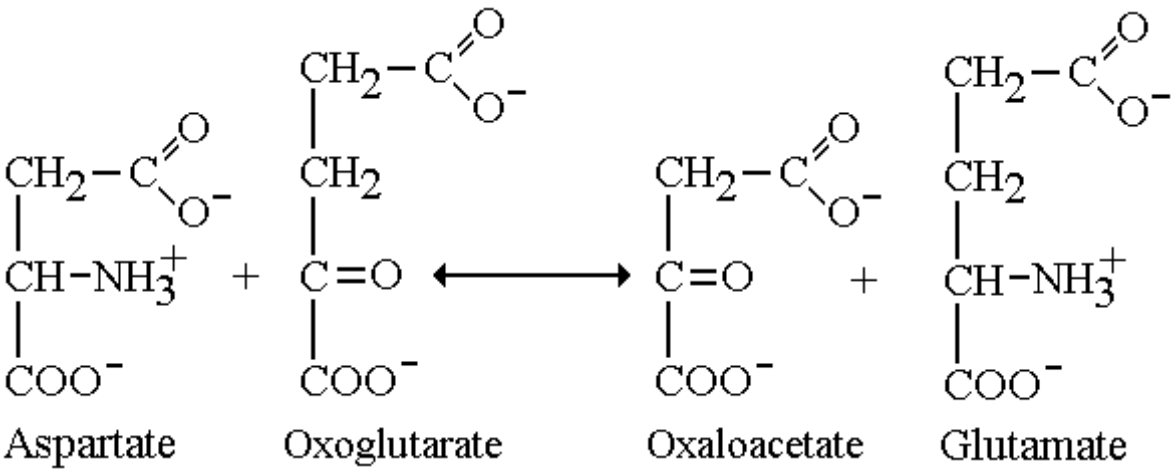
Glutamate is the most important, metabolically



Some **transaminases** are used for diagnosing disorders:
enzyme **alanine aminotransferase**. Escapes in large amounts from dead or dying liver tissue. Measured in blood samples for diagnostic purposes.



Transaminase enzyme **aspartate aminotransferase** very active enzyme inside heart cells. Also escapes in large amounts from dead or dying heart tissues & enters bloodstream. Measured in blood for diagnosing myocardial infarction.

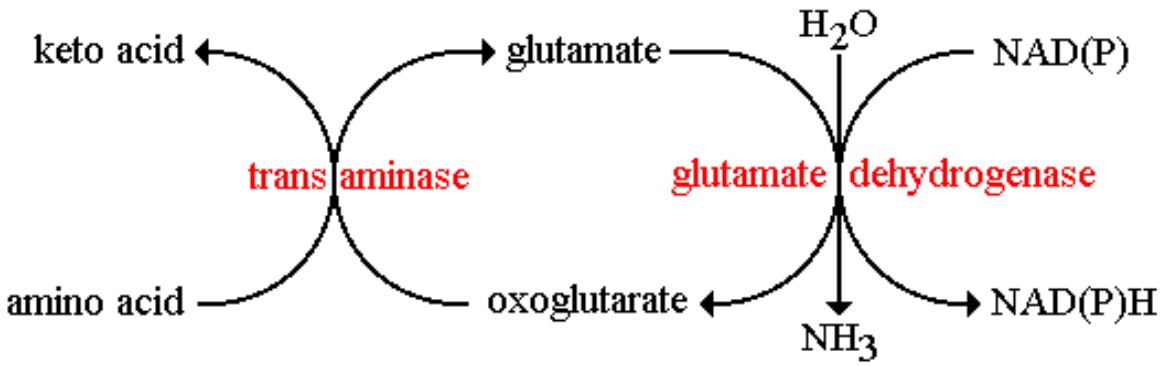


Trans-deamination (sum it up)

Most **transaminases** share a common substrate and product (oxoglutarate and glutamate) with the enzyme **glutamate dehydrogenase**.

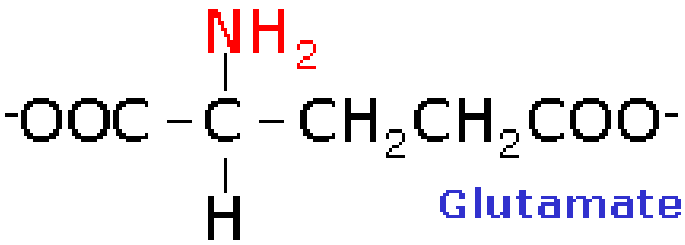
This permits a ***combined*** N excretion pathway for individual amino acids: "trans-deamination."

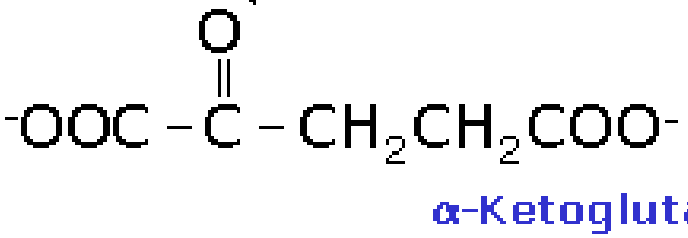
Glutamate has a central role in the overall control of nitrogen metabolism.



Oxidative Deamination

The **glutamate** produced from the transamination step is then deaminated by **oxidative deamination** using the enzyme **glutamate dehydrogenase**



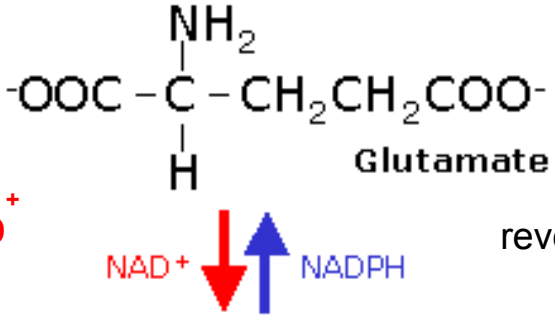


Recycles back to a ketodiacid & releases ammonia

Glutamate dehydrogenase [GluDH] will reversibly convert

glutamate to **a-ketoglutarate** and **a-ketoglutarate** to **glutamate**.

Deamination reaction uses **NAD**$^+$



reverse reaction uses **NADPH**

Uses ***both*** **NAD**$^+$ and **NADPH** – how to regulate it?

Urea cycle:

Ammonium salts (NH_4^+) are toxic compounds.

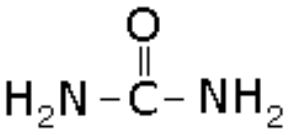
Oxidative deamination converting glutamate to a-ketoglutarate is an easily shifted equilibrium reaction.

Ammonium ions building up favors the synthesis of excessive amounts of glutamate, decreasing the Krebs cycle intermediate

a-ketoglutarate.

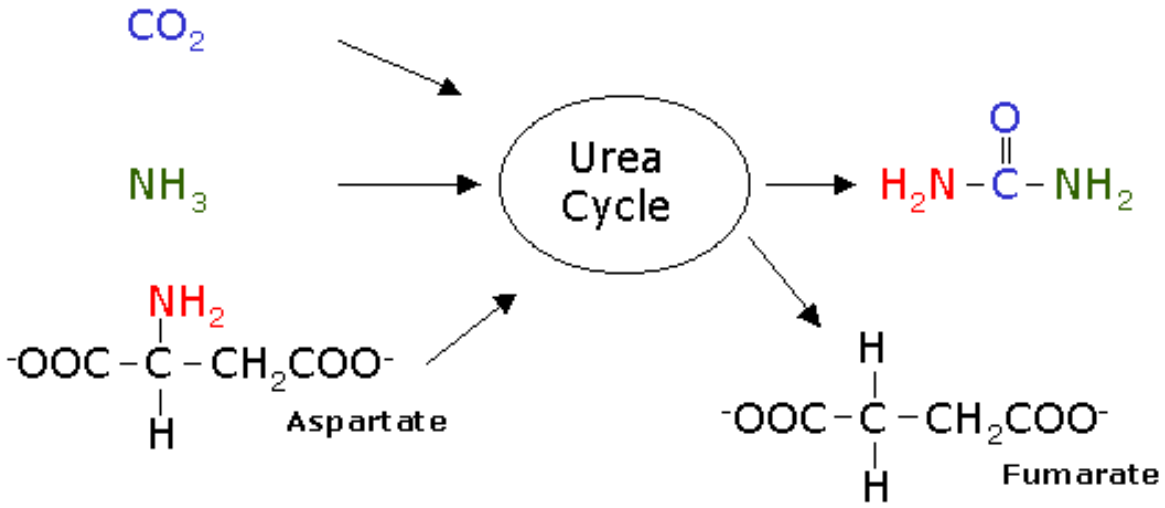
This in turn decreases **ATP production**, and that affects the nervous system.

The answer is Urea:

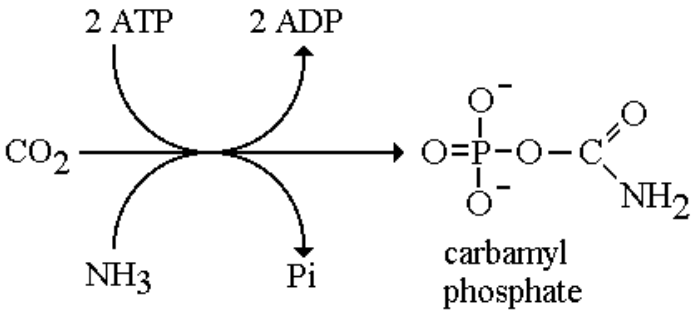


The **inputs** to the urea cycle are NH_3, CO_2 and aspartic acid and ATP.

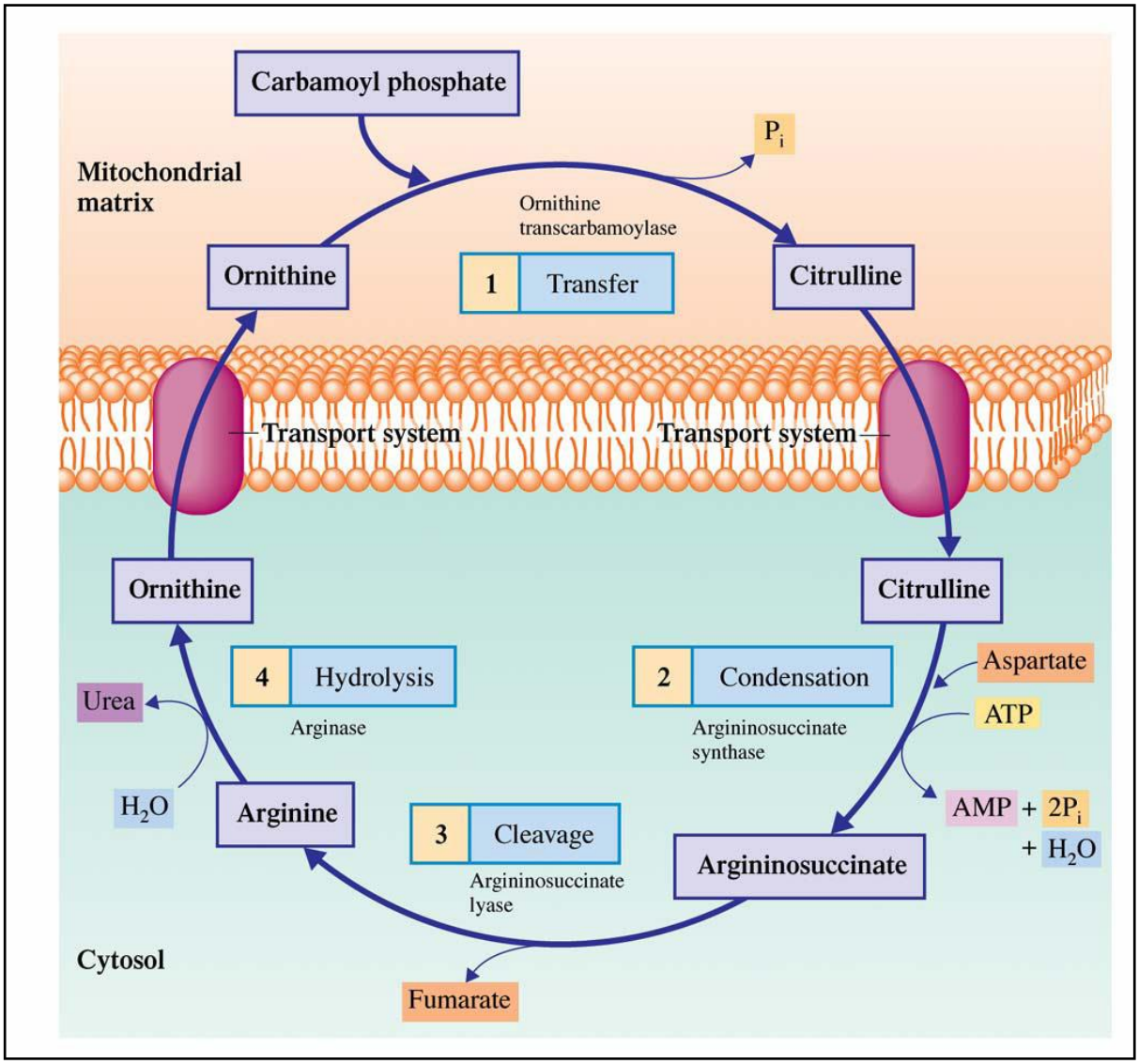
The **outputs** are urea, ADP and fumaric acid.



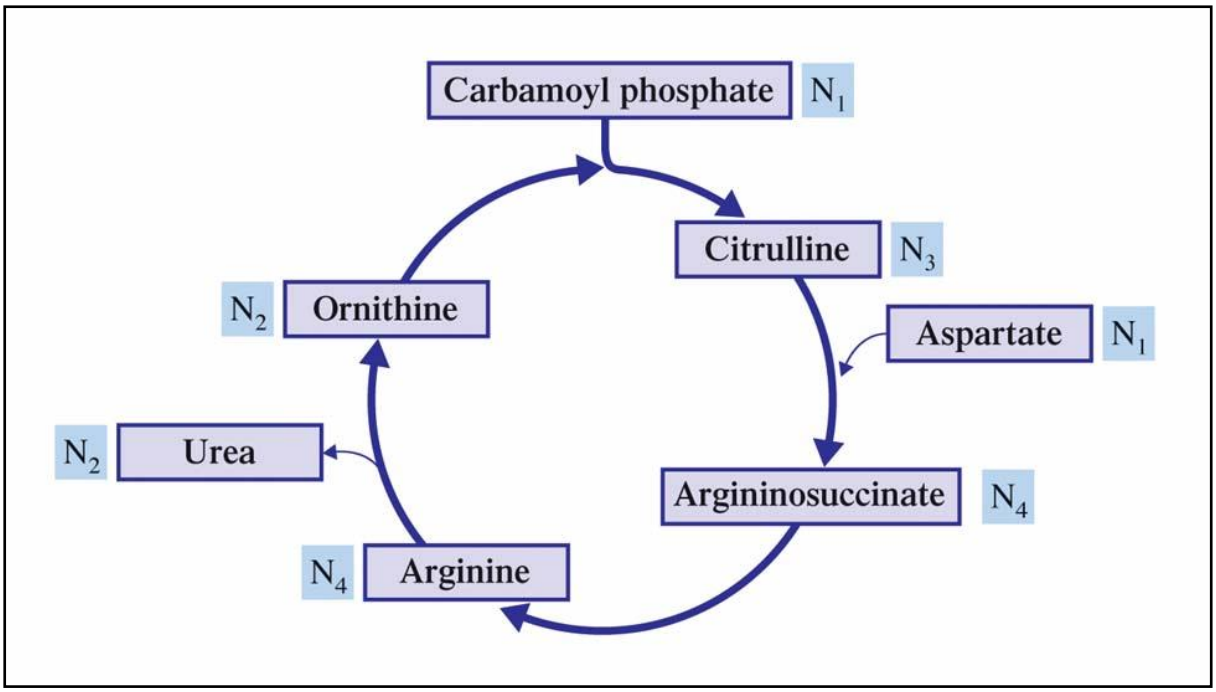
The carbonyl group of urea is derived from **CO_2** , **Ammonia** contributes one of the amine groups on urea



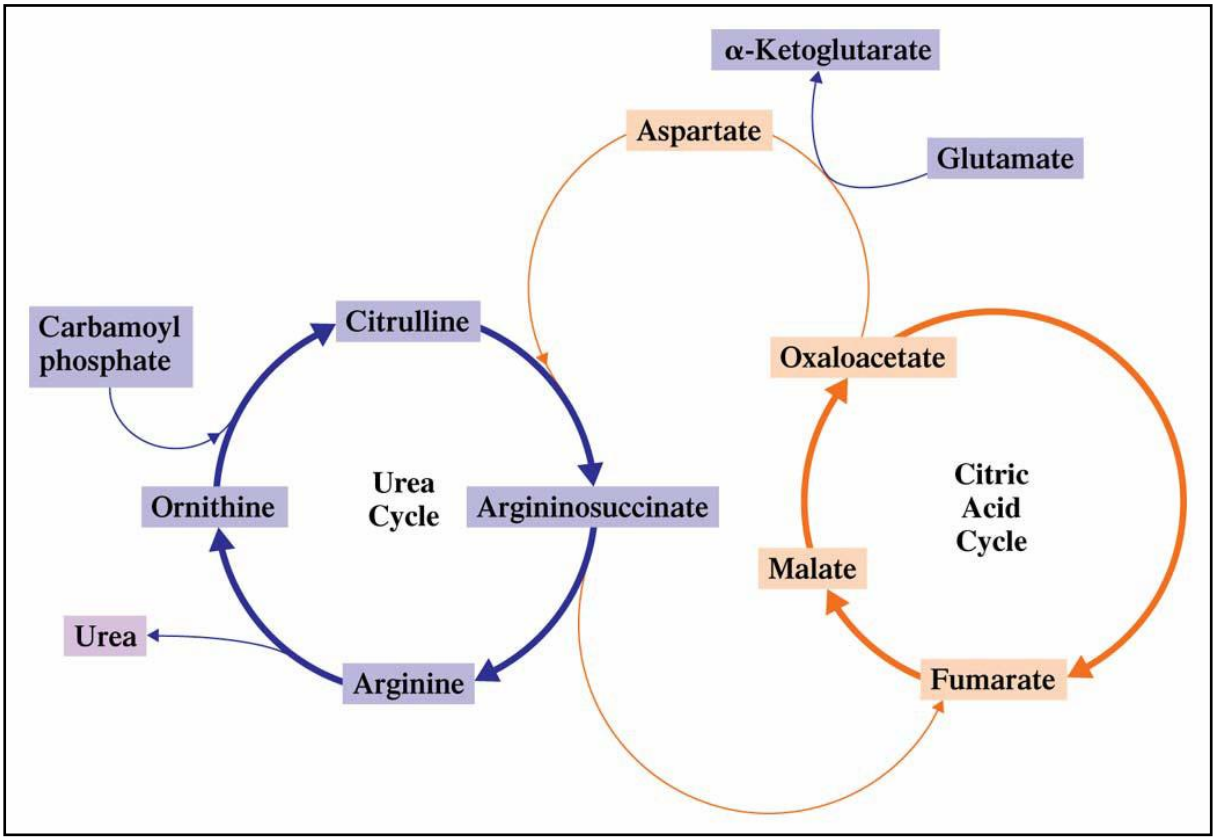
The **four-step** urea cycle in which **carbamoyl phosphate** is converted to **urea**.



The nitrogen content of the various compounds that participate in the urea cycle



Fumarate from the urea cycle enters the Krebs cycle. **Aspartate** produced from **oxaloacetate** of the Krebs cycle enters the urea cycle.



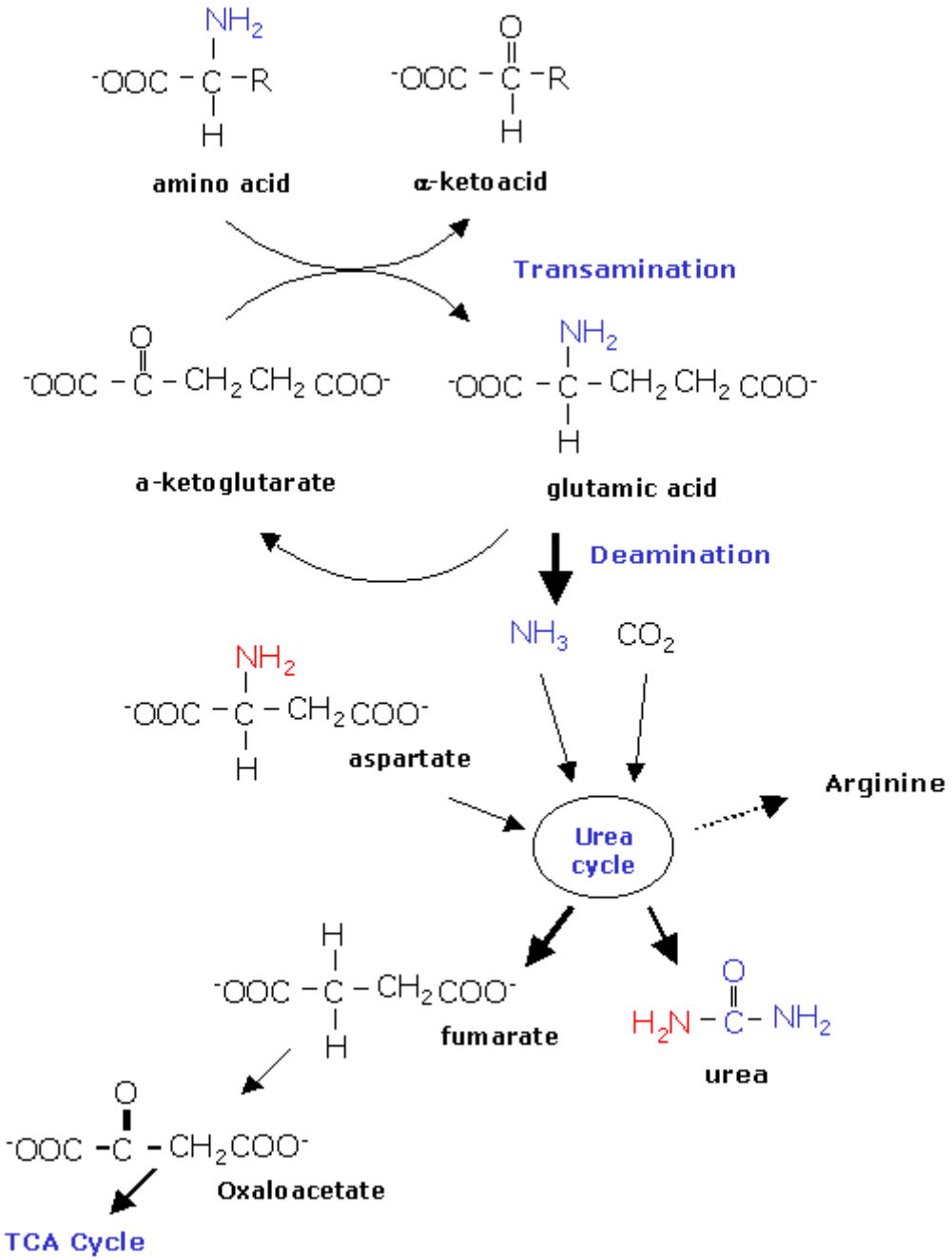
Oxaloacetate has 4 potential fates: transamination; conversion to glucose; formation of citrate; conversion to pyruvate

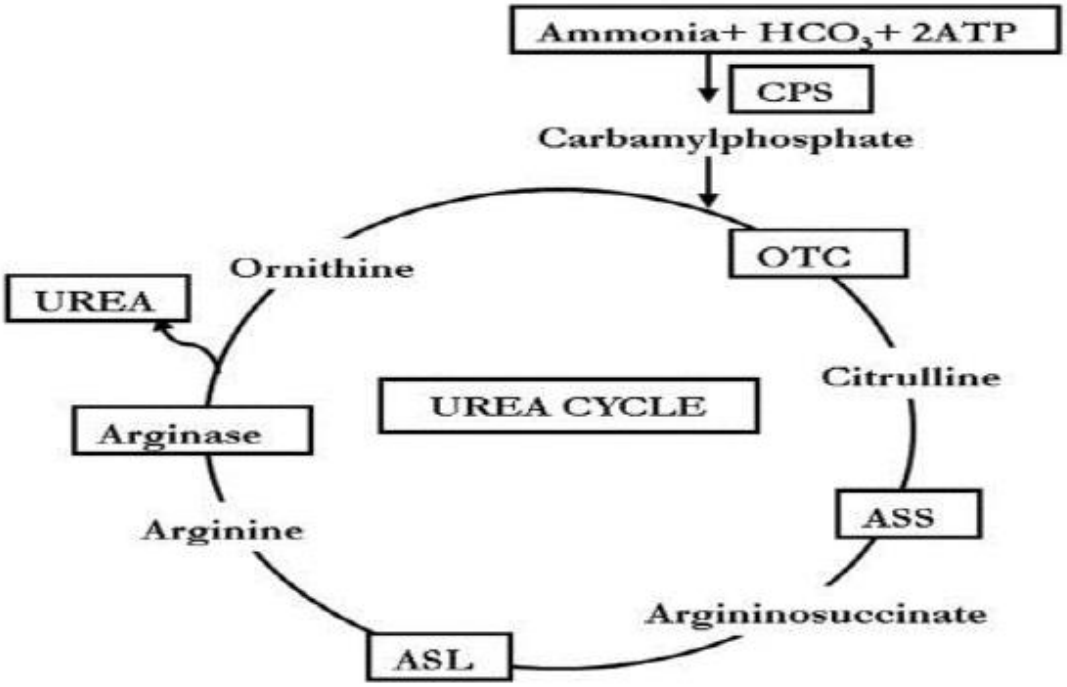
Summary:

Transamination takes off amine groups from amino acids and forms **glutamate**
(ionized glutamic acid)

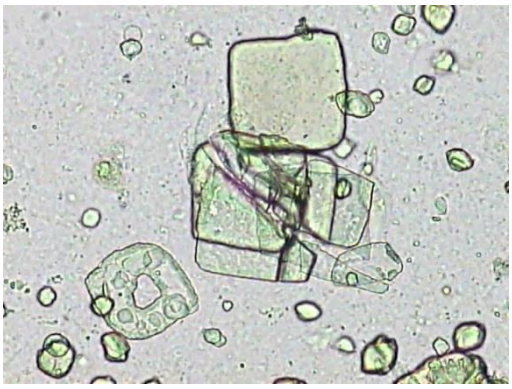
Amine groups form **ammonia** when removed in **deamination**
This combines with **CO_2** & **Aspartate**.

Forms **urea**, **Arginine**,
& **Fumarate**

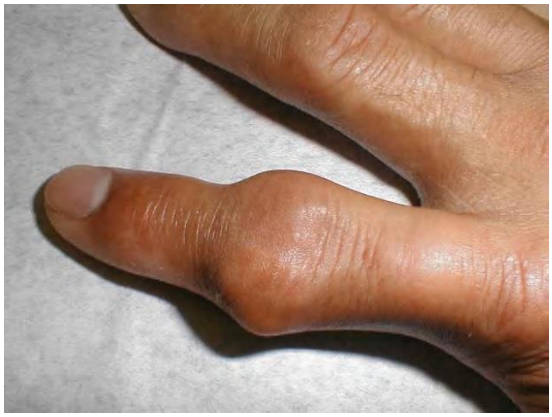


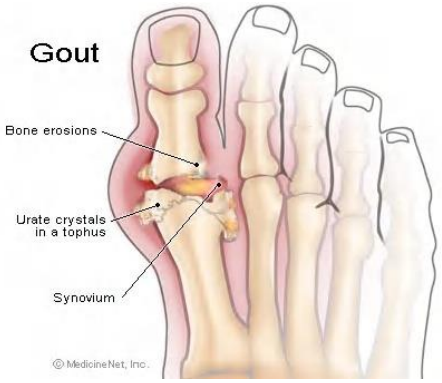


Reptiles & birds excrete **uric acid** – very ***insoluble*** purine compound – forms supersaturated solutions. Concentrated urine, supersaturated with uric acid, goes from cloaca into hindgut – uric acid crystalizes & water is reabsorbed.



In humans uric acid deposits crystals & causes gout





Processing Amino Acid Carbon Skeletons

Transamination or Oxidative deamination both produce a-keto acids

Degradation of these carbon skeletons may take several different pathways:

Amino acid C skeletons that degrade to form a Krebs cycle intermediate can then be used to make glucose via **gluconeogenesis**.

These are called **Glucogenic Amino Acids**.

Amino acid C skeletons that degrade to form **acetyl CoA** or **Acetoacetyl CoA** can form fatty acids or ketone bodies.

These are called **Ketogenic Amino Acids**.

Amino Acid Biosynthesis

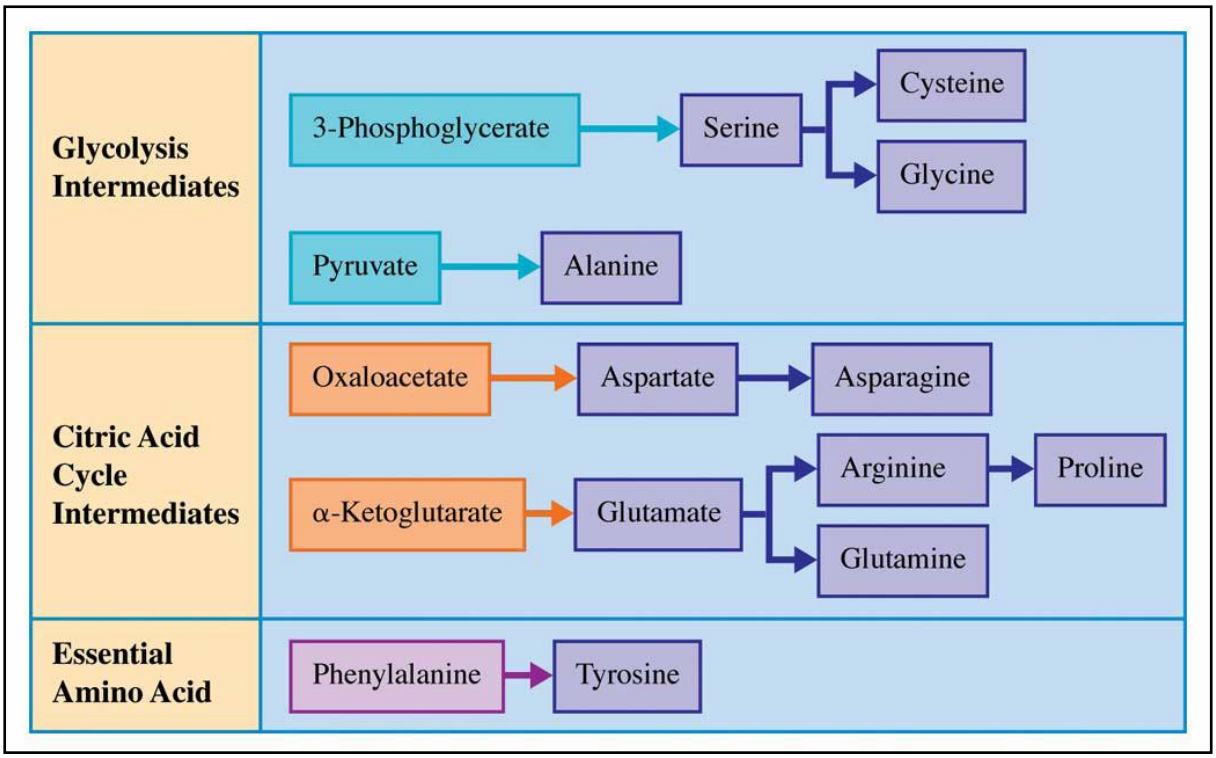
Essential amino acids can be made by plants & bacteria in 7 to 10 steps.

We obtain these amino acids by eating plants.11 Non-essential amino acids synthesized in 1 to 3 steps. Use glycolysis intermediates:

3-phosphoglycerate & pyruvate Krebs cycle intermediates:

Oxaloacetate & **a-ketoglutarate**.

Starting materials for biosynthesis of 11 **nonessential** amino acids: 1 step, 2 steps, or 3 steps



Alanine, aspartate, & glutamate use transamination

Phenylketonuria (PKU):

Defective phenylalanine hydroxylase – **phenylalanine** accumulates in body. Phenylalanine is transaminated to **phenylpyruvate**.

Accumulation of phenylpyruvate leads to severe mental retardation in infants. Persons suffering from phenylketonuria should not consume foods containing high levels of phenylalanine, such as aspartame.

Hemoglobin catabolism

Red blood cells contain oxygen carrying pigments of a conjugated protein: Protein part is ***Globin*** Non-protein prosthetic group is ***Heme***. **Heme** contains four pyrrole (**tetrapyrrole**) groups held together by an **iron** atom. Old red blood cells degraded in the spleen. Globin is hydrolyzed into amino acids. Iron atom stored in a protein (***ferritin***) **Tetrapyrrole** degraded to **bile pigments**.

Review: can you…

- Describe the steps in Protein digestion & absorption
- Explain how Amino Acids are utilized in the body
- Explain **Transamination** and **Oxidative De-amination**
- Describe **The Urea Cycle** – purpose and steps
- Describe how a.a. Carbon Skeletons are processed
- Define and explain Amino Acid Biosynthesis.
- Describe the chemical composition of urine.

Lipid Metabolism

Fatty acids (F.A.s) are taken up by cells.

They may serve as:

- precursors in synthesis of other compounds
- fuels for energy production
- substrates for ketone body synthesis.

Ketone bodies may be exported to other tissues: used for **energy production**. Some cells **synthesize fatty acids** for storage or export.

Energy

Fats are an important source of calories. Typically 30-40% of calories in American diet are from **fat**. Fat is the major form of **energy storage**.

Typical body fuel *reserves* are:

fat: **100,000 kcal.**

protein: **25,000 kcal**.

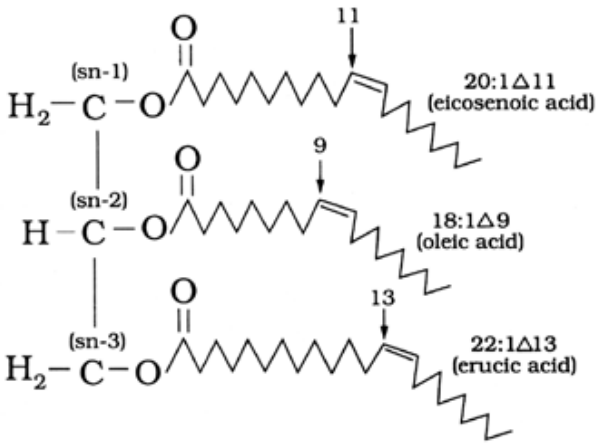
carbohydrate: **650 kcal.**

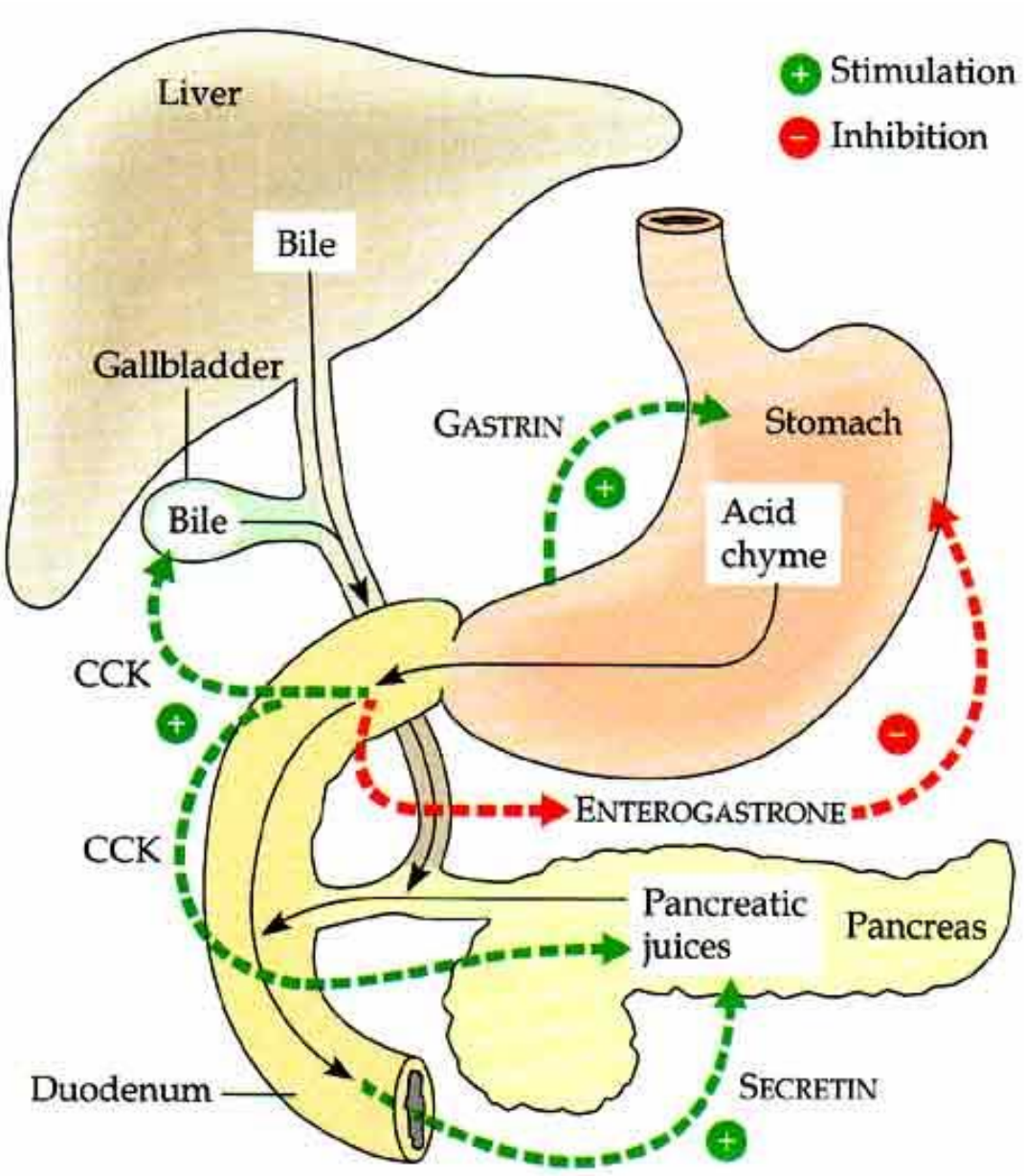
Provides 60% of energy needs for body at restTAG reserves would enable someone to survive starvation for ~30 days.

Digestion and Absorption of Lipids

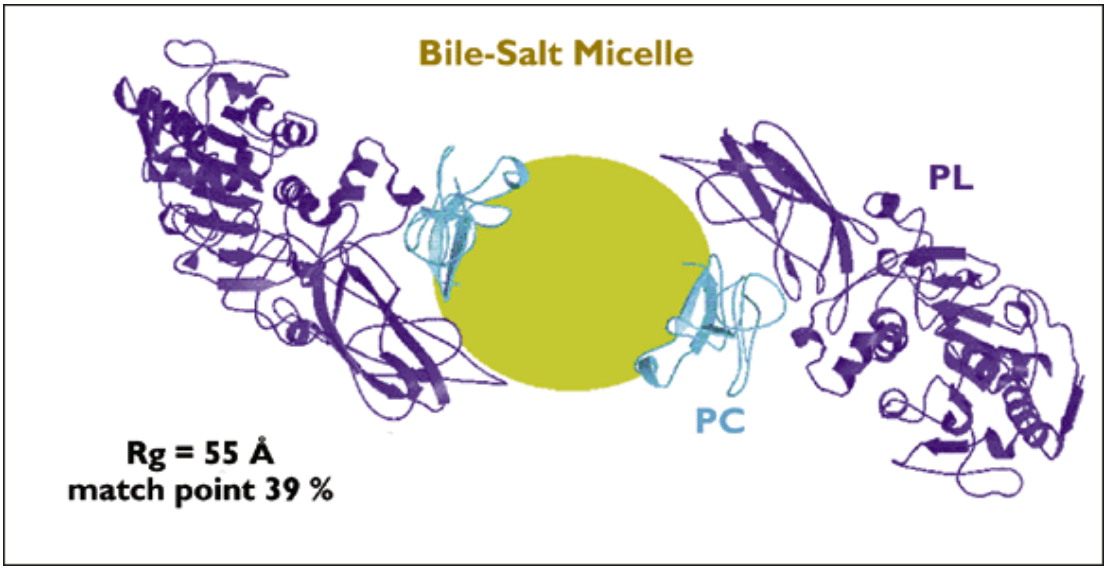
- 98% of ingested lipids are triacylglycerols (TAGs)
- Digestion in the Mouth: enzymes are **aqueous**-little effect on lipids
- Digestion in the Stomach:causes a large ***physical*** change-
  Churned into droplets:
  "Chyme"

TRIACYLGLYCEROL



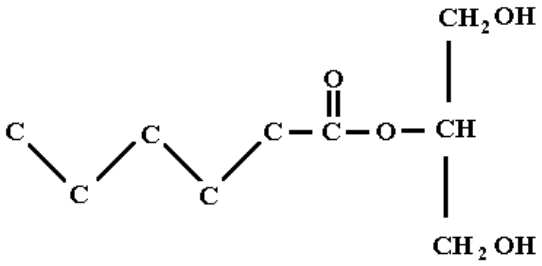


Gastric Lipase: Begins actual lipid digestion.~10% of TAGs are hydrolyzed in the **stomach**.Chyme stimulates **cholecystokinin** (CCK) to release **bile** from gallbladder.Bile is an emulsifier

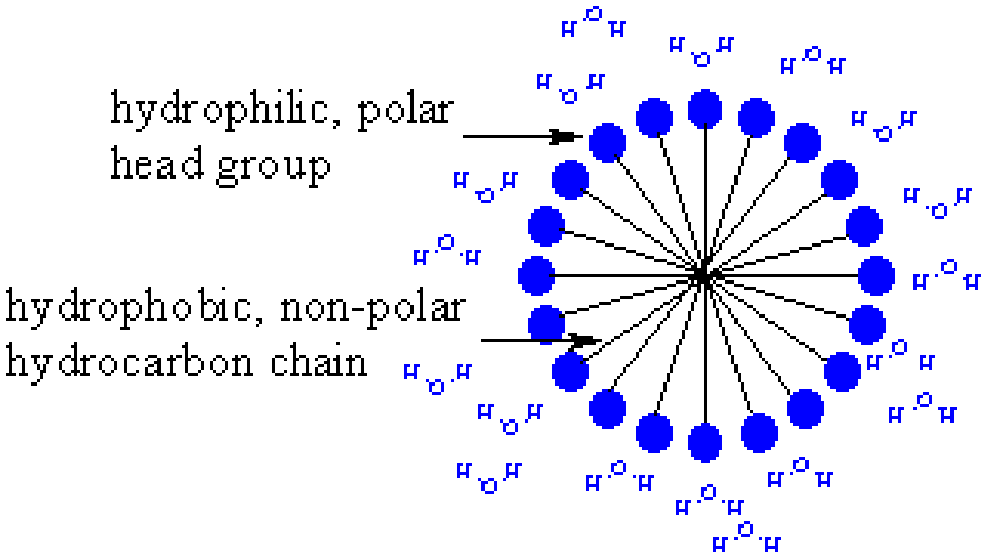


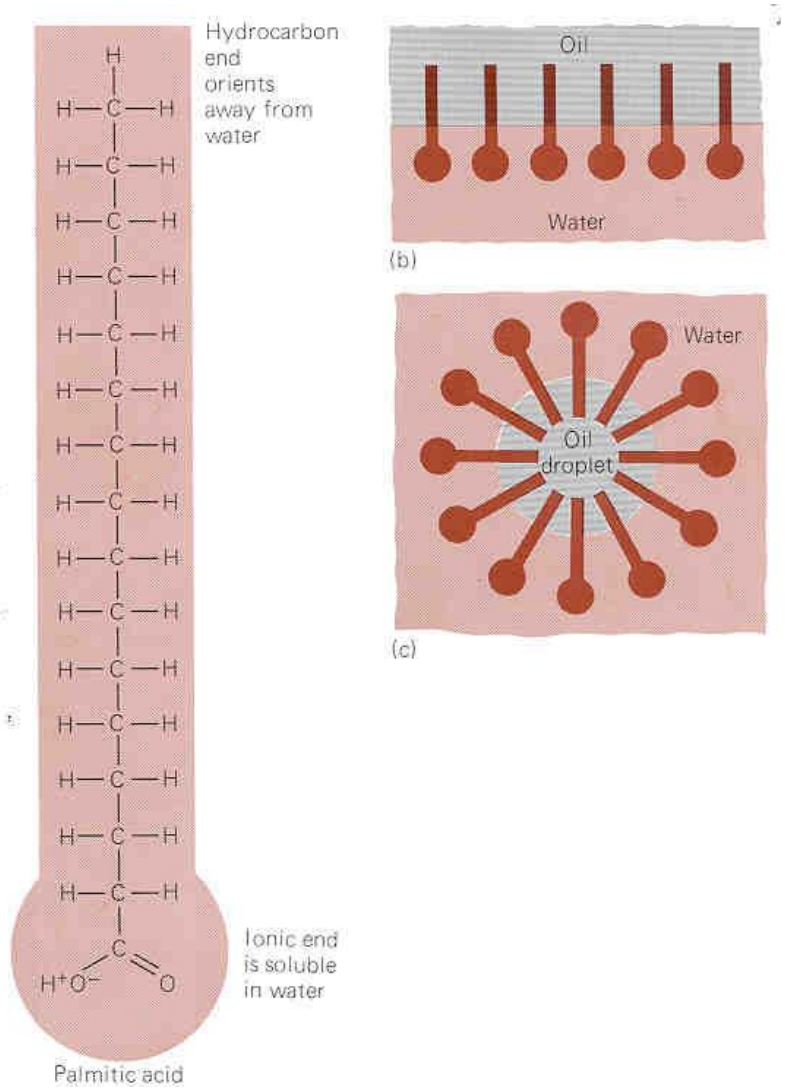
Pancreatic lipase (PL) hydrolyzes insoluble triglyceride by binding to the **bile-salt micelles**TAGs are ***partially*** hydrolyzed: 2 of the 3 F.A.s have ester linkages hydrolyzed and are released.

Monoacylglycerol remains = glycerol and 1 fatty acid



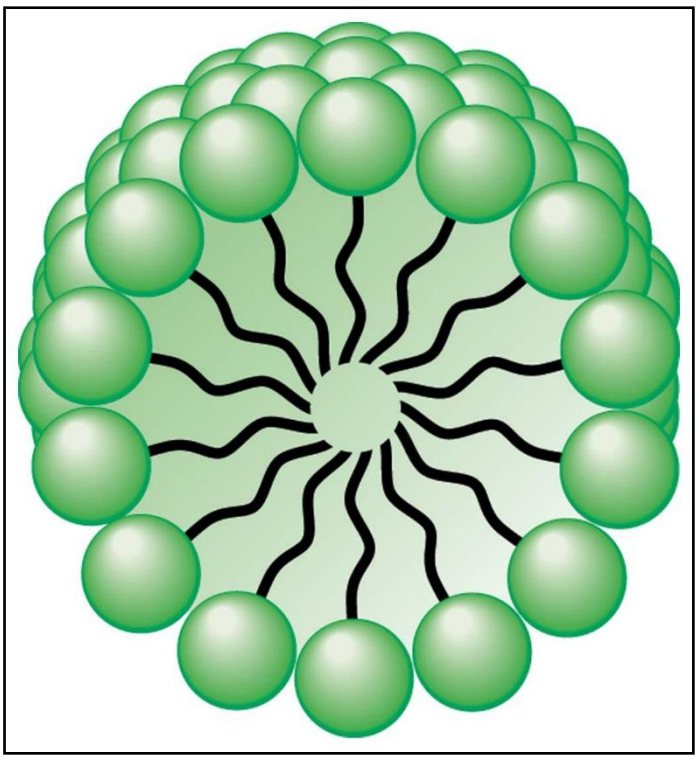
Oil droplets will form spherical **micelle** shapes.Bile salts aid this process clumping fatty acids and monacylglycerols.


hydrophilic, polar
head group
hydrophobic, non-polar
hydrocarbon chain


Hydrocarbon end orients away from water
Ionic end is soluble in water
Palmitic acid
Oil
Water
(b)
Water
Oil droplet
(c)

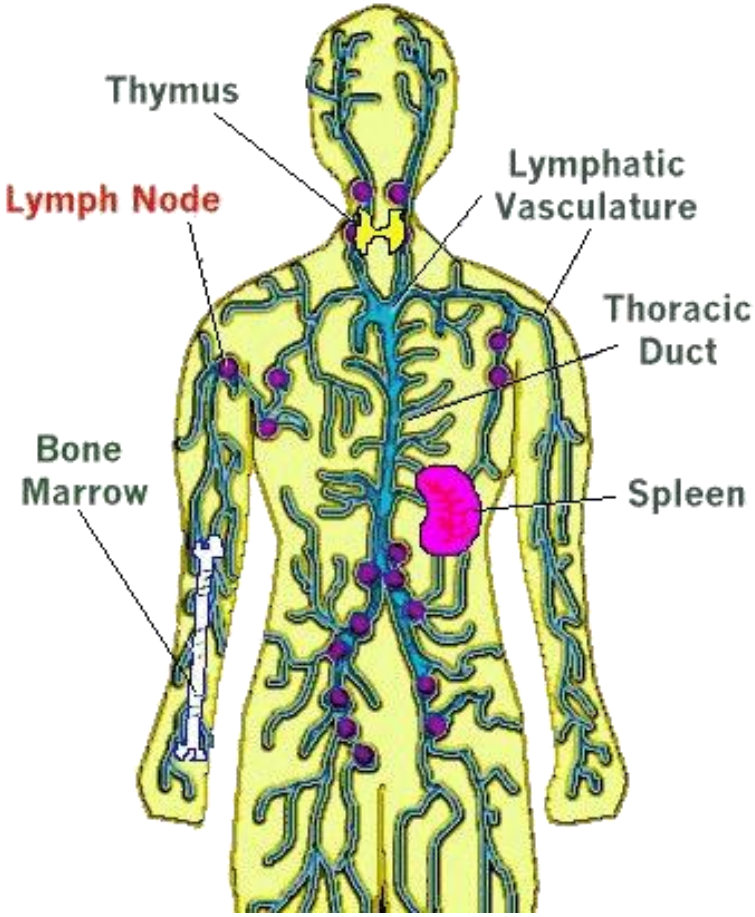
Fatty acid micelle: **hydrophobic** fatty acids & monoacylglycerols are in the interior. Bile salts on exterior.

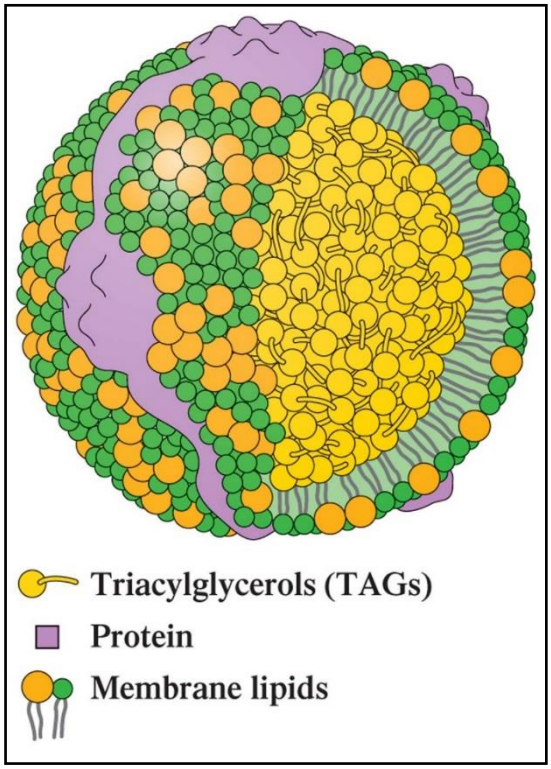
Micelles are small enough to penetrate membrane of intestinal cells. Free fatty acids & monoacylglycerols are reformed into **triacylglycerols**.



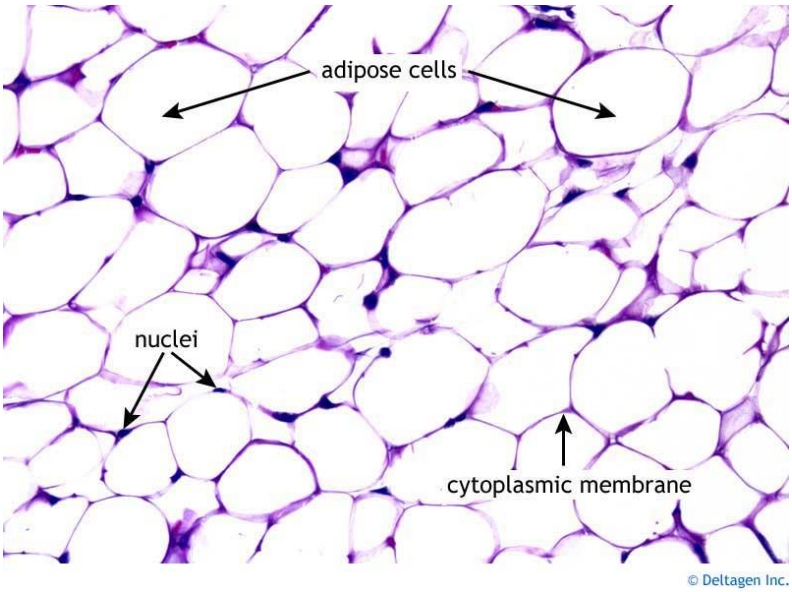
TAGs are combined with membrane & water soluble proteins to form a **chylomicron**, a lipoprotein.

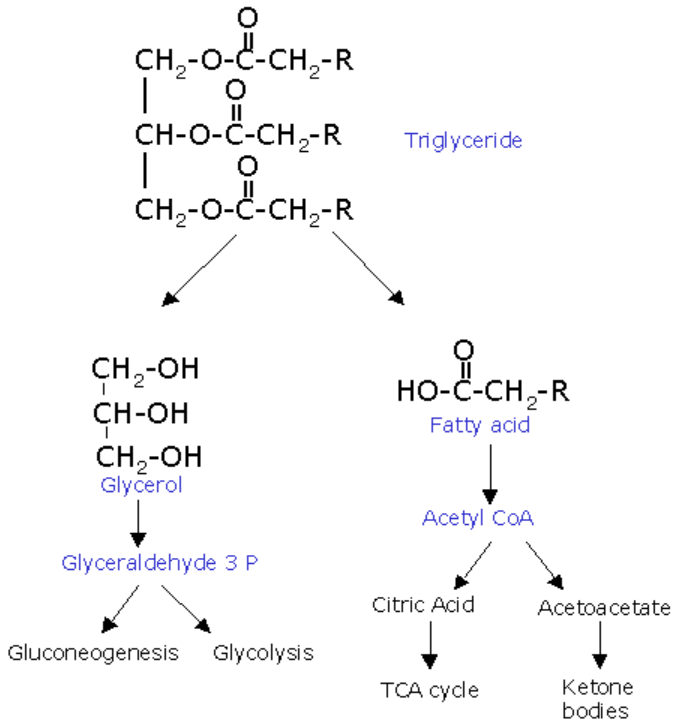
Chylomicrons carry TAGs from intestinal cells into bloodstream via the **lymph system**.


Thymus
Lymph Node
Lymphatic Vasculature
Thoracic Duct
Bone Marrow
Spleen

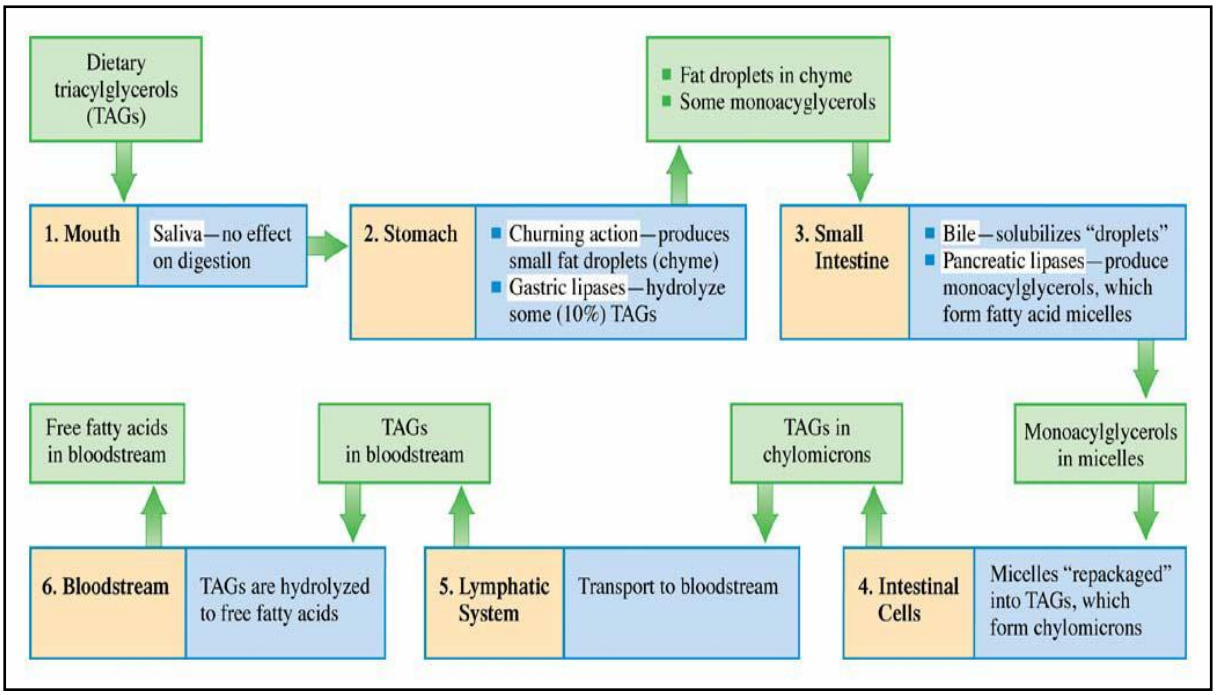

Triacylglycerols (TAGs)
Protein
Membrane lipids

Triacylglycerols reach bloodstream & are hydrolyzed down to **glycerol** and **fatty acids**.These are absorbed by cells and processed further for energy by forming **acetyl CoA**. Or Stored as lipids in fat cells (adipose tissue.



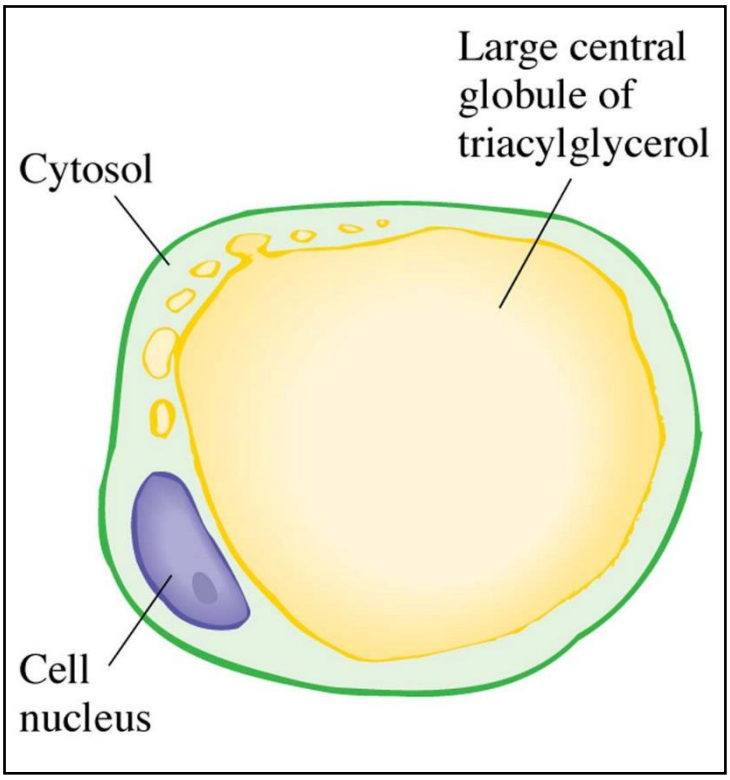


Summary of events that must occur before triacyglycerols (TAGs) can reach the bloodstream through the digestive process.



Triglyceride Storage & Mobilization

Storage of triacylglycerol is in **adipocytes** Fatty acids stored primarily as triacylglycerol.Triacylglycerol is **hydrolyzed** to release **fatty acids** when needed.



Hormonal control of lipolysis

The breakdown of triglycerides by lipases is under hormonal control.

Hormones involved are:

Epinephrine, glucagon, and insulin.

Epinephrine & glucagon:

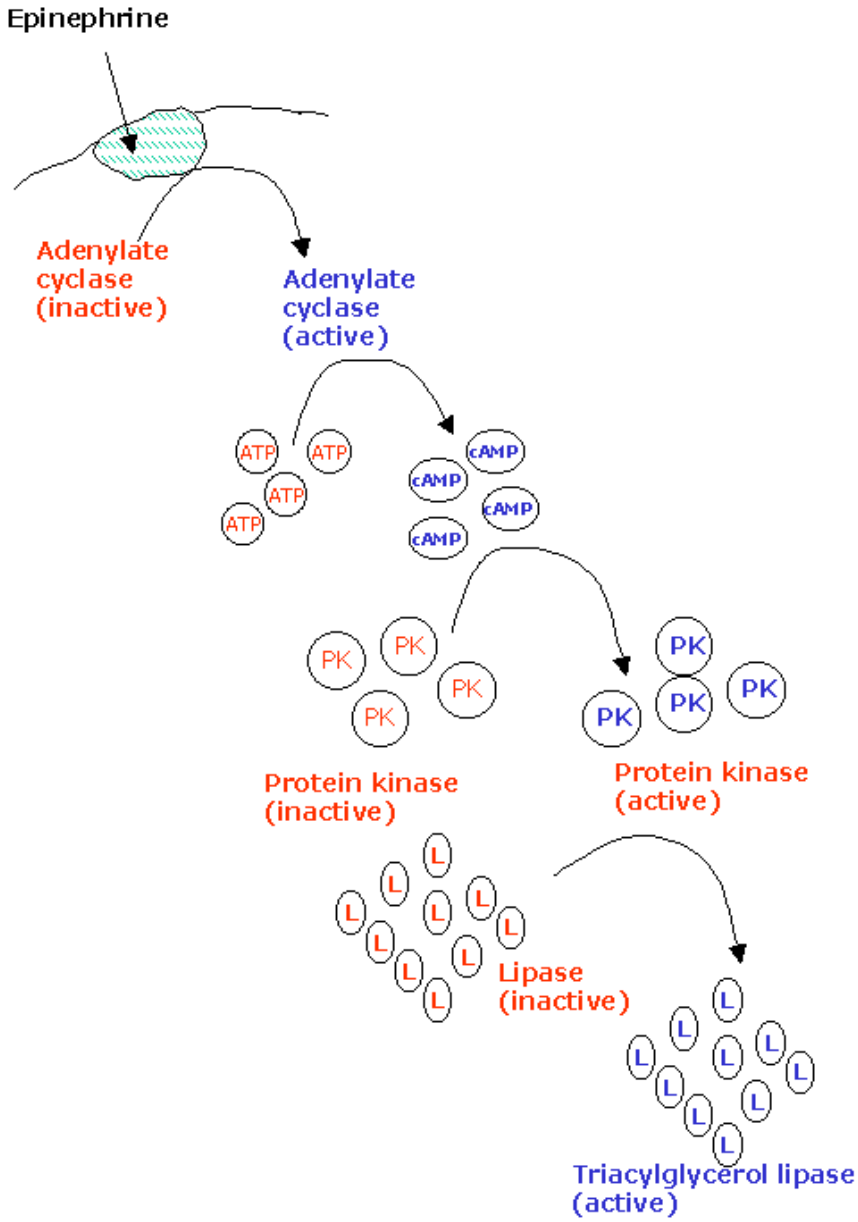
promote breakdown of fat (lipolysis)

Insulin:

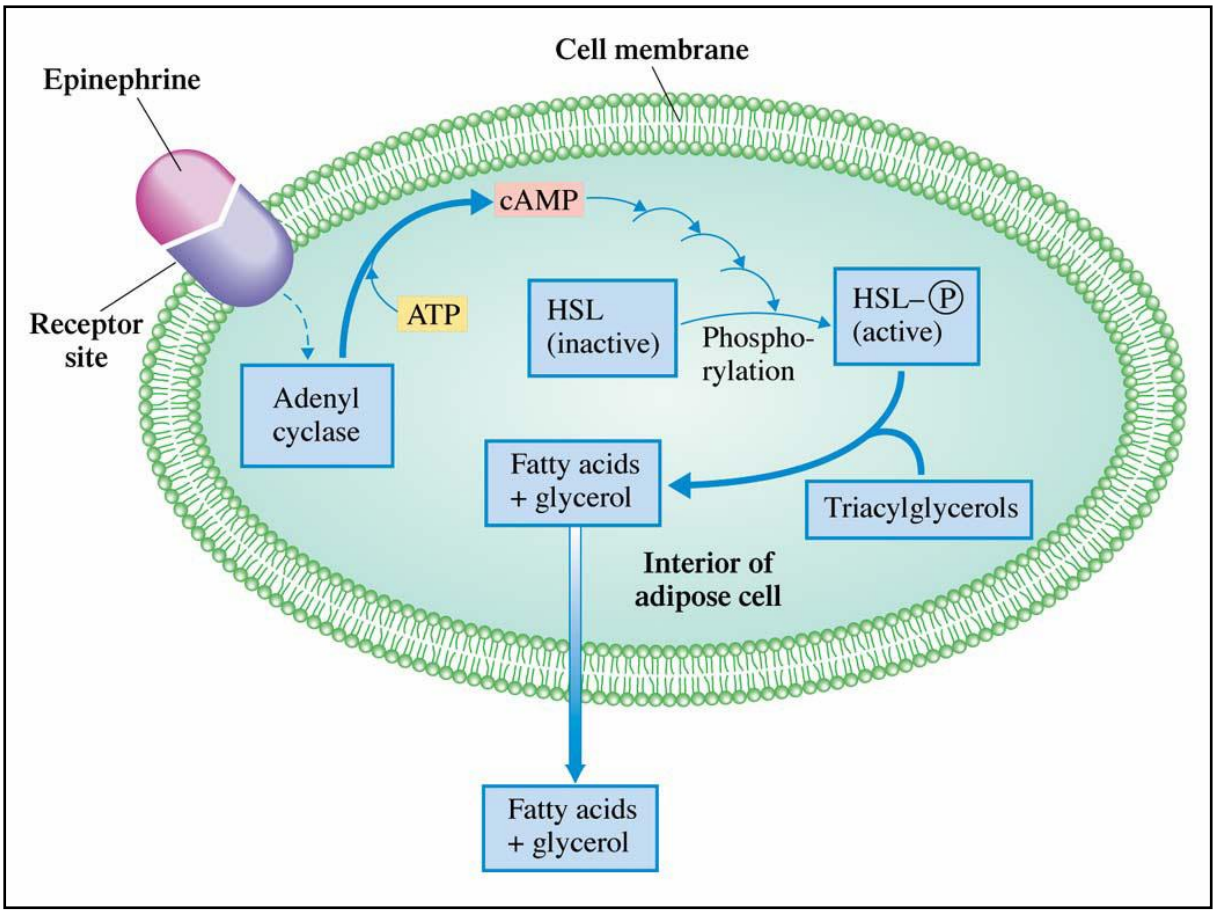
inhibits lipolysis.

Triacylglycerol Mobilization:

Hydrolyzing lipid reserves in adipose tissue for **energy**.Triggered by hormones~10% TAGs replaced in adipose tissue daily as they get used up for energy.



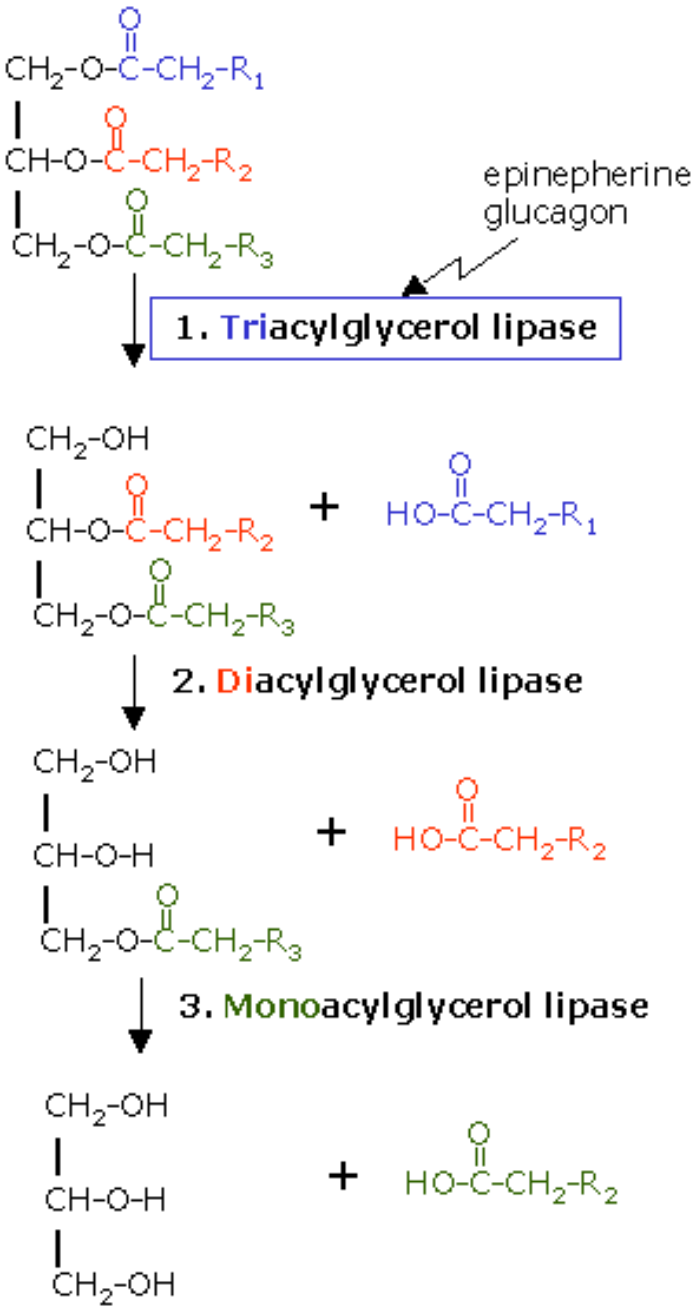
Hydrolysis of stored triacylglycerols in adipose tissue is triggered by hormones that stimulate cAMP production within adipose cells.



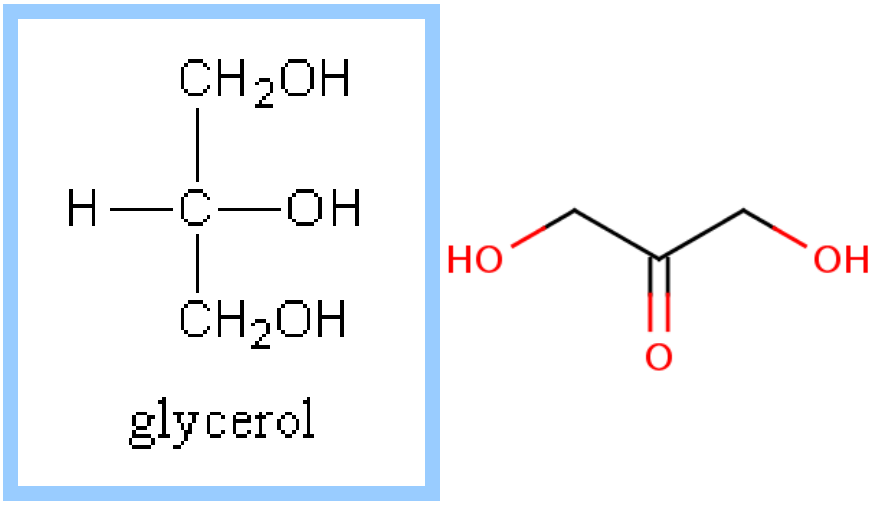
Third time is a charm! TAGs hydrolyzed a 3rd time to form fatty acids.

Triacylglycerol lipase **Di**acyclglycerol lipase **Mono**acylglycerol lipase

Only triacylglycerol lipase is activated by epinephrine.

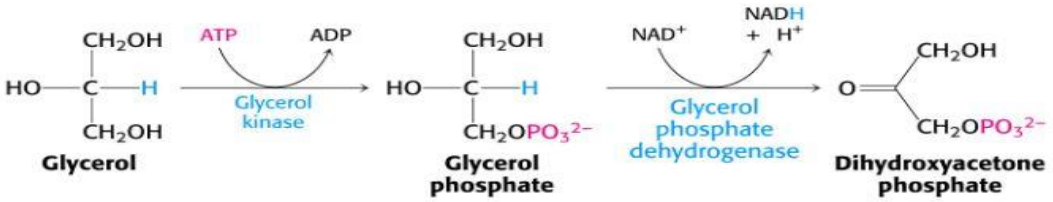


One glycerol formed for each TAG hydrolyzed. Enter bloodstream & go to liver or kidneys for processing. Converted in 2 steps to **Dihydroxyacetone phosphate**



Where will the phosphate be attached?

Uses up one ATP.Reduces one NAD^+ to NADH



Primary hydroxyl group is phosphorylated
Dihydroxyacetone phosphate
is an intermediate for both

Glycolysis:
converted to Pyruvate, then to Acetyl CoA, & eventually to CO_2,

releasing its energy.

Gluconeogenesis:

creates Glucose from **non-carbohydrate** source

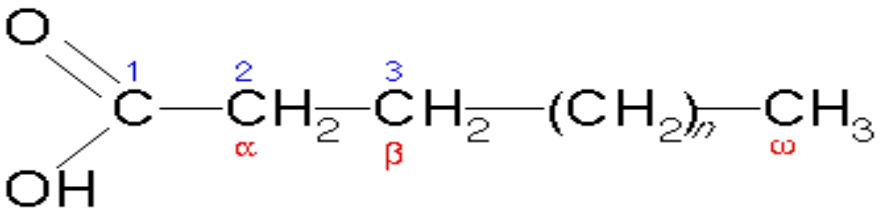
Lipid metabolism & carbohydrate metabolism

are connected.

Fatty acids can also be broken down for energy. What kind of reaction is needed?

Oxidation!

Quick review first on fatty acid numbers & letters:



Fatty acid numbering system

Review Important fatty acids:

Name	# Carbons: (saturation)
Palmitate	16:0
Stearate	18:0
Palmitoleate	16:1 - cis at C9
Oleate	18:1 - cis at C9
Linoleate	18:2 - cis at C9 and C12
Linolenate	18:3 - cis at C9, C12 & C15

Lipid Metabolism

Lipid nomenclature

•Oxidation of Fatty acids

•β-oxidation

•Ketone Bodies

Lipid nomenclature

Fatty acids

•triacylglycerols: know structure

•phospholipids

•waxes

•sphingolipids

•Glycosphingolipids

•Isoprenoids

•Steriods

•Nomenclature

•saturated: palmitate, stearate, no double bonds

•unsaturated: palmitoleate, Oleate: double bond at cis9 position

•polyunsaturated

•Melting points: saturated vsunsaturated

Oxidation of Fatty acids

•Know equation for palmitate: $C_{16}H_{32}O + O_2$ ---> $CO_2 + H_2O$

•Comparison of glucose with palmitatefor ATP production and energy yield

•Mobilization of Triacylglycerols from adipose tissue

–hormonal control: glucagon, epinephrine

–lipases

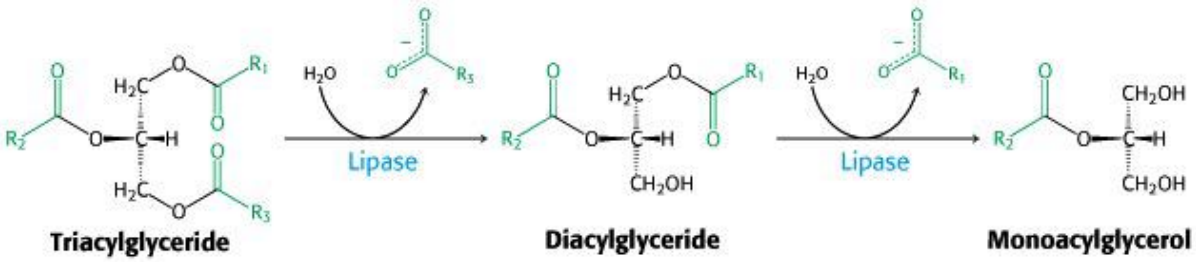
–transport by lipoproteins

–fate of glycerol

•transport into cytoplasm of cell

Digestion of lipid in diet

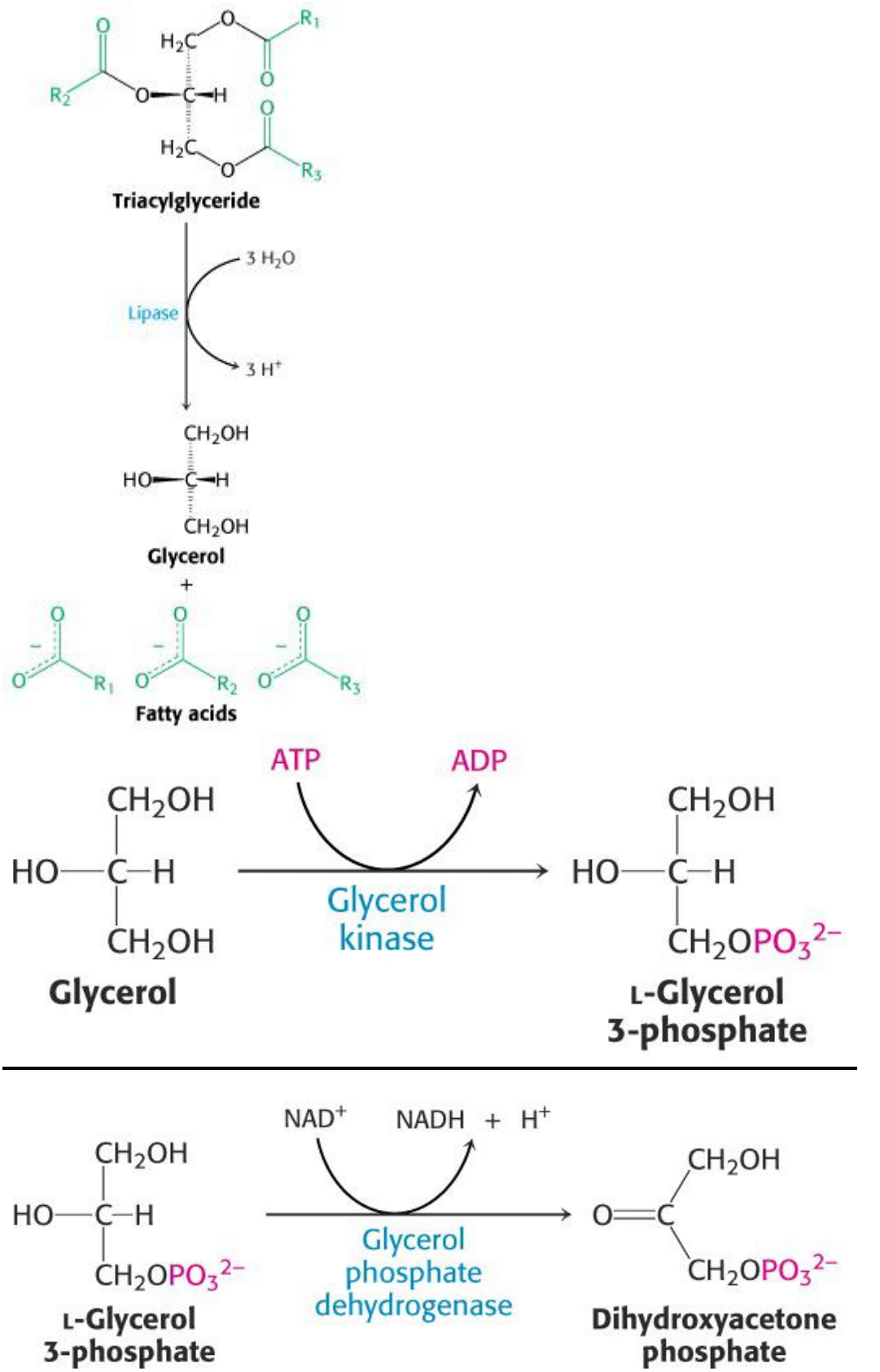
•Triacylglycerolsfrom diet
•broken down in small intestine
•lipases
•bile salts
•transport to adipose tissue



Mobilization of Triacylglycerols

–hormonal control of lipolysis: glucagon, epinephrine
–lipases
–transport by lipoproteins
–transport into cytoplasm of cell
–Insulin inhibits lipolysis

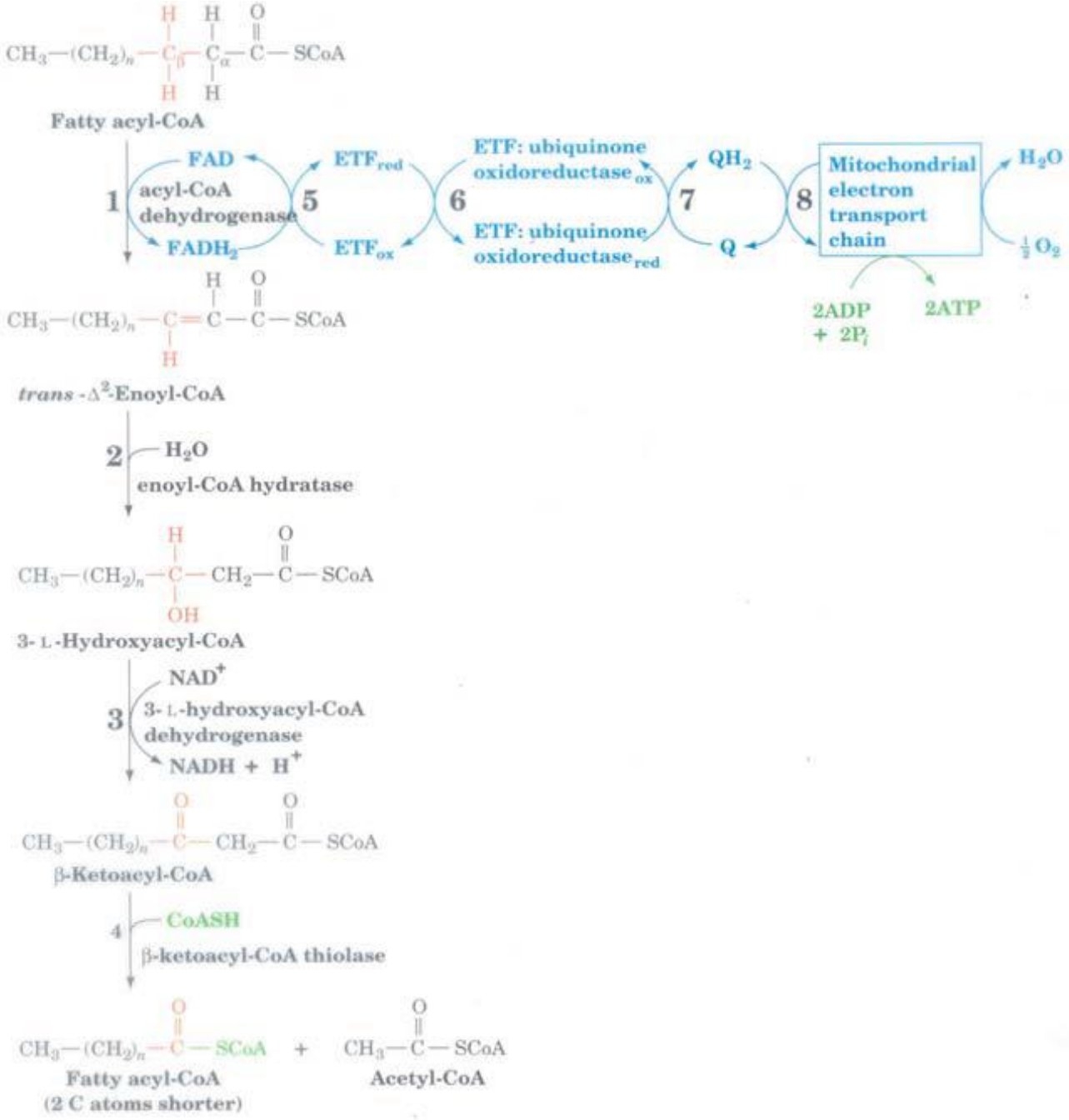
Breakdown of triacylglycerides



fate of glycerol

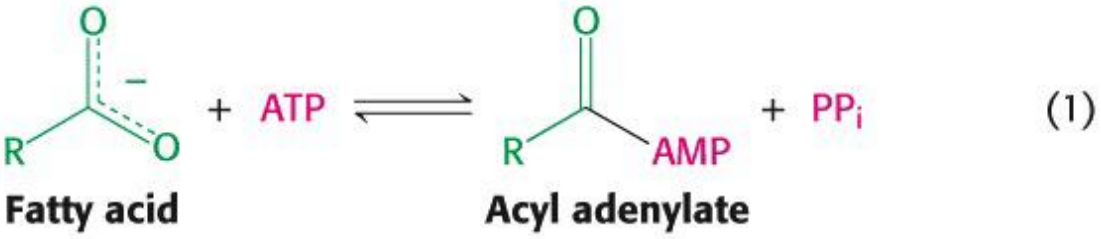
β-oxidation

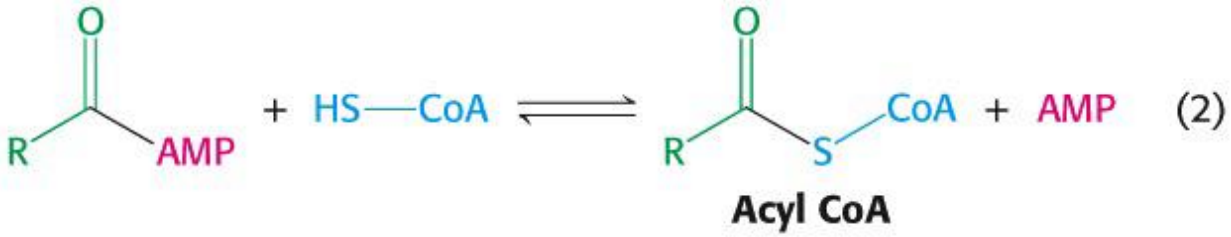
- occurs in mitochondria
- uses FAD and NAD
- produces acetyl CoA



acylCoA synthetase

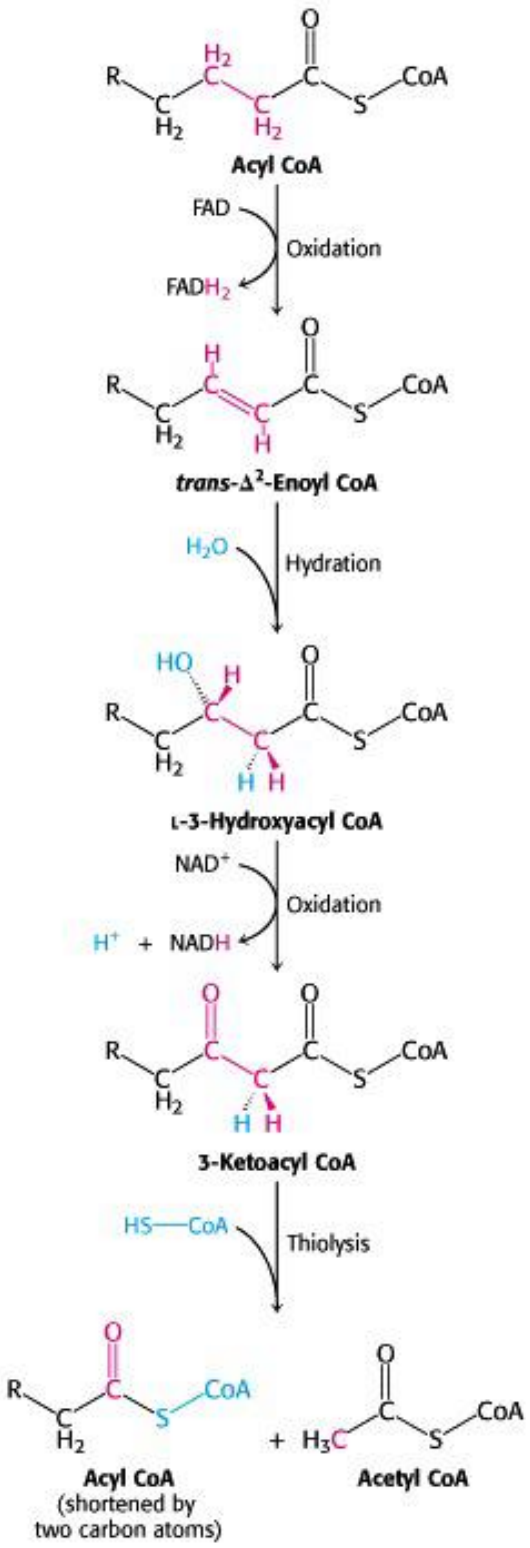
•two step reaction
•ATP + FA ---> AMP-FA
•AMP-FA + CoASH------> FA-CoA + AMP





β-oxidation

AcylCoA dehydrogenase
•enoyl-CoA hydratase
•L-hydroxyacyldehydrogenase
•ketoacyl-CoA thiolase
•Repeat steps



Summary of Reactions

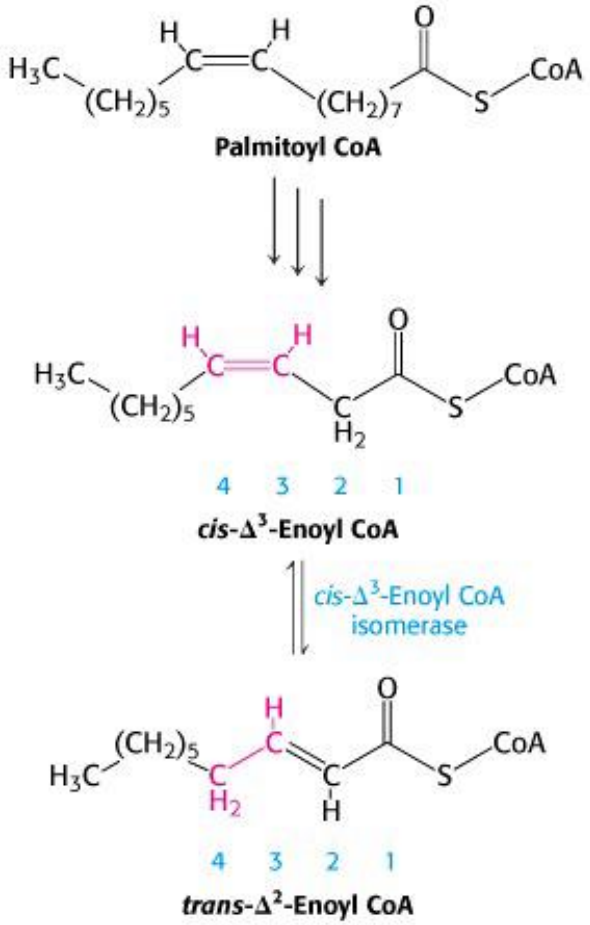
TABLE 22.1 Principal reactions in fatty acid oxidation

Step	Reaction	Enzyme
1	Fatty acid + CoA + ATP ⇌ acyl CoA + AMP + PP_i	Acyl CoA synthetase [also called fatty acid thiokinase and fatty acid:CoA ligase (AMP)]
2	Carnitine + acyl CoA ⇌ acyl carnitine + CoA	Carnitine acyltransferase (also called carnitine palmitoyl transferase)
3	Acyl CoA + E-FAD ⟶ *trans*-Δ^2-enoyl CoA + E-$FADH_2$	Acyl CoA dehydrogenases (several isozymes having different chain-length specificity)
4	*trans*-Δ^2-Enoyl CoA + H_2O ⇌ L-3-hydroxyacyl CoA	Enoyl CoA hydratase (also called crotonase or 3-hydroxyacyl CoA hydrolyase)
5	L-3-Hydroxyacyl CoA + NAD^+ ⇌ 3-ketoacyl CoA + NADH + H^+	L-3-Hydroxyacyl CoA dehydrogenase
6	3-Ketoacyl CoA + CoA ⇌ acetyl CoA + acyl CoA (shortened by C_2)	β-Ketothiolase (also called thiolase)

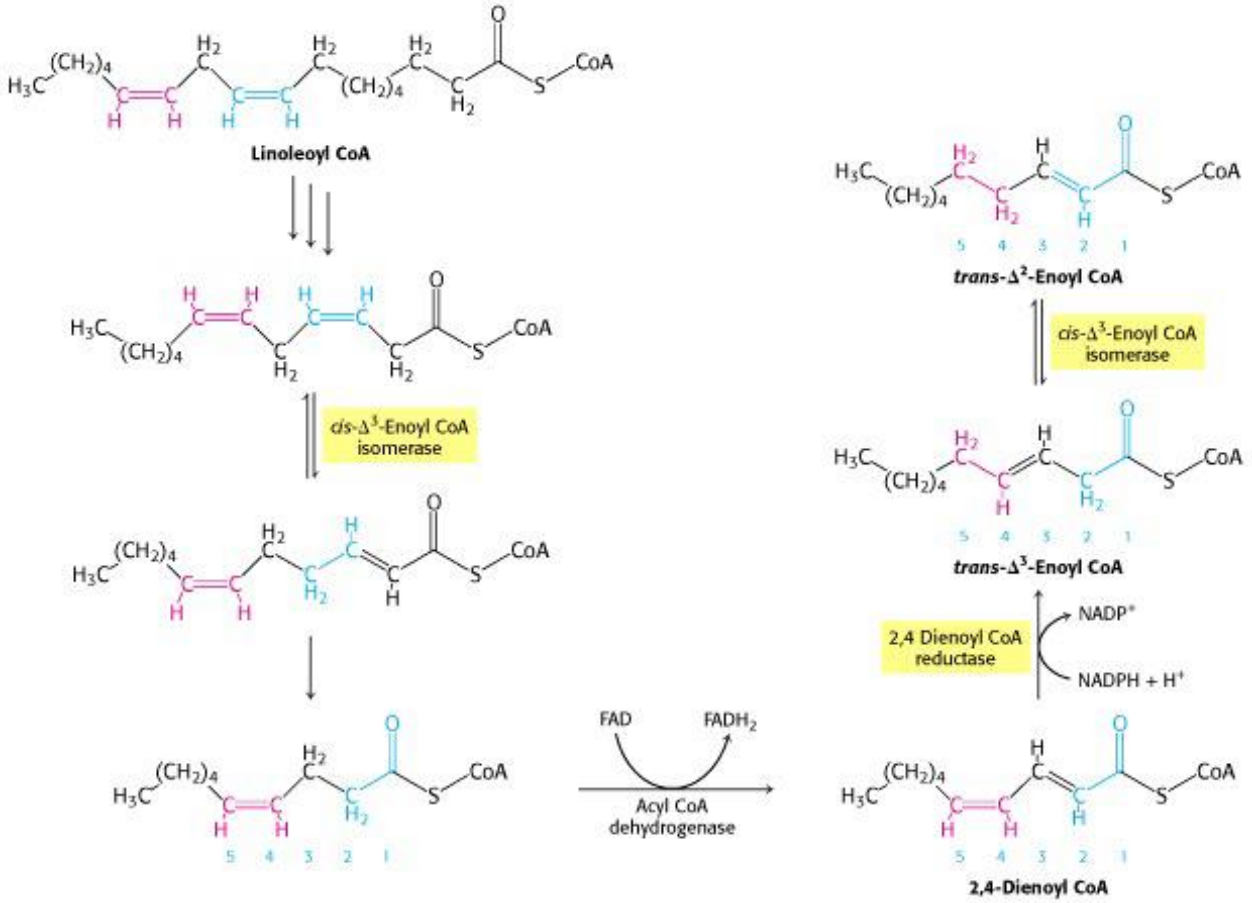
Energy production

- NADH and FADH from B-oxidation
- TCA cycle from acetyl CoA
- Total net yield is minus 2 ATP from activation

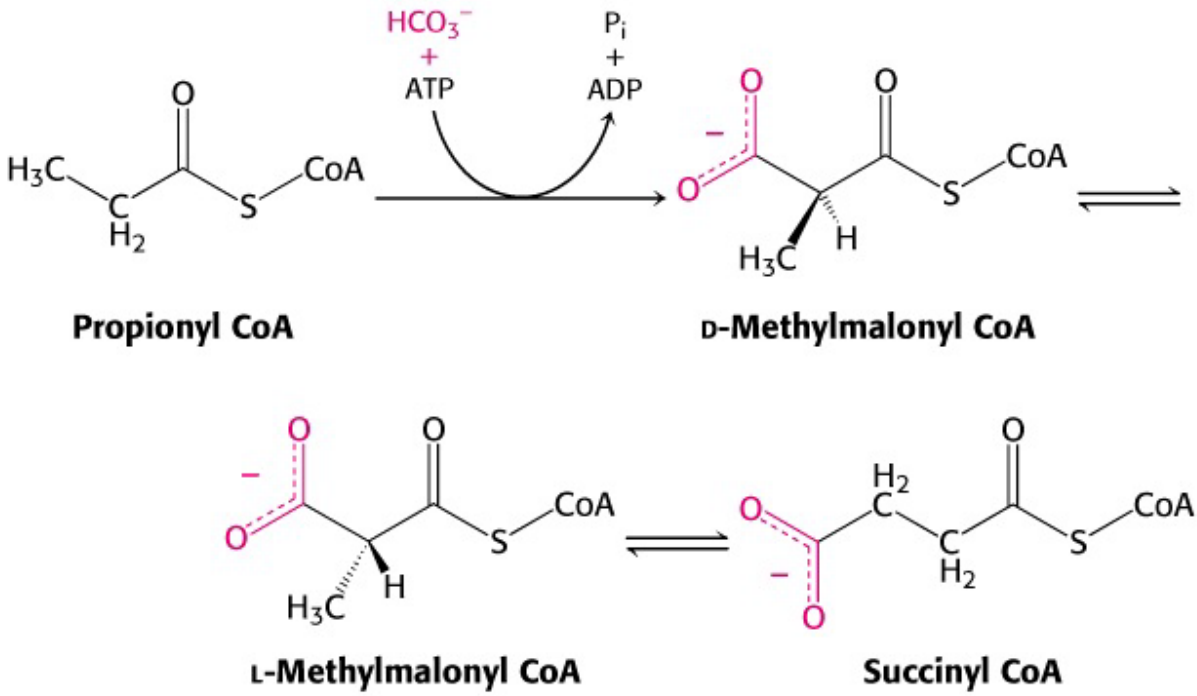
Oxidation of Unsaturated Fatty acids



Unsaturated Fatty acids



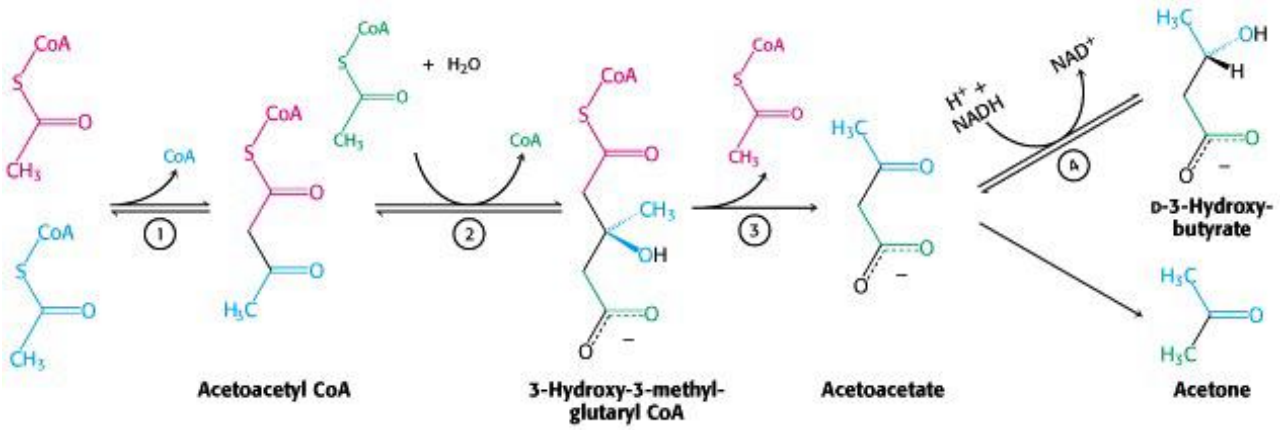
Oxidation of odd chain fatty acids

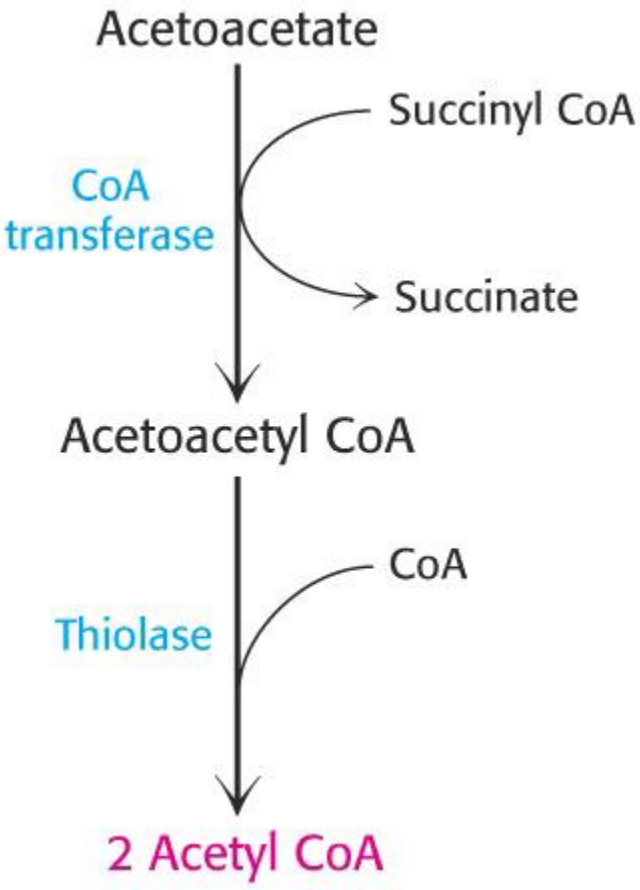


•form propionylCoA

•produce succinylCoA

Ketone Bodies





•Acetoacetate

•Acetone

•B-hyroxybutyrate

•HMG CoA synthase

Referances

Available online

1-BIOCHEMISTRY IN PERSPECTIVE

2-METABOLISM OF CARBOHYDRATES, LIPIDS,PROTEINS AND NUCLEIC ACIDS, Course Team

Prof. Anthony, I. O. Ologhobo(Course Writer)-UI

Prof. Jokthan,G.E. (Programme Leader)-NOUN

Dr. Salisu, B. Abdu (Course Editor)-ABU, Zaria

Dr. Ahmed A. Njidda (Course Coordinator)-NOUN ISBN: 978-978-970-183-4,