Metabolism

Metabolism is the sum of all chemical reactions occurring within a cell or organism. Through metabolism, living cells use nutrients in many chemical reactions that provide energy for vital processes and activities.

As the body uses nutrients to create energy, metabolism takes place.

Types of Metabolism

There are two types of metabolism: catabolism and anabolism.

Catabolism is a type of metabolic process occurring in living cells by which complex molecules are broken down to PRODUCE ENERGY. Catabolic reactions are normally exothermic….. heat and energy yielding.

Anabolism is a constructive metabolic process that USES ENERGY to combines simple substances such as amino acids in the creation of complex cell structures and compounds.

Molecules break down; energy is produced

Compounds are created; is used

Parts of Cell

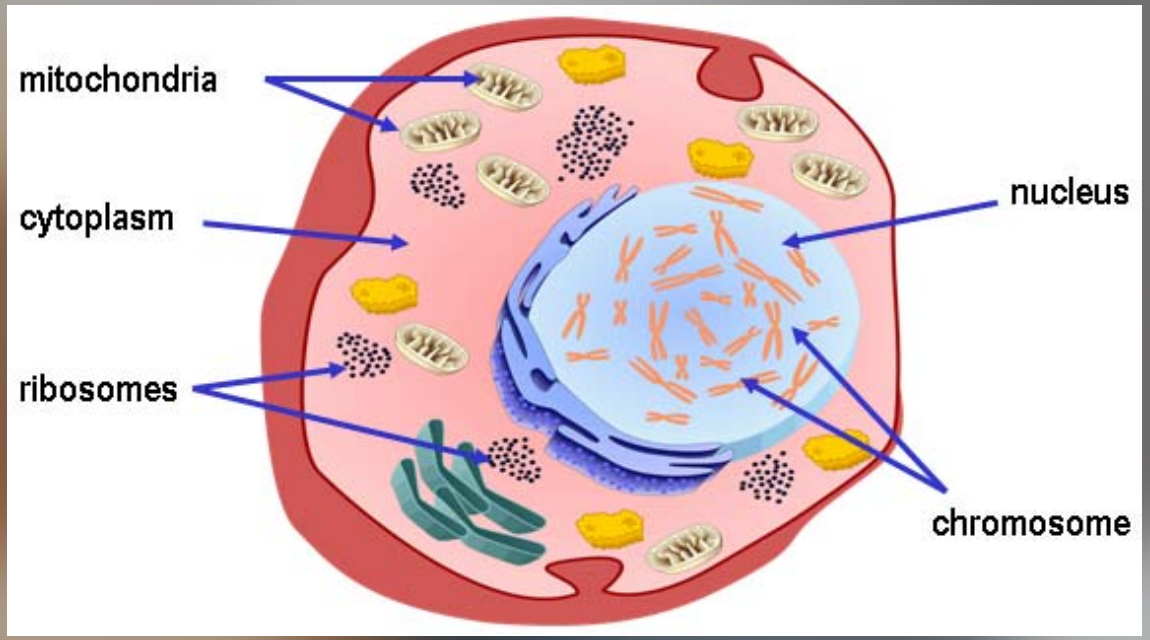
The nutrients are absorbed through the walls of the small intestine into the bloodstream.

They travel through the bloodstream to the liver. They are eventually released from the liver back into the bloodstream, and delivered to the cells. Nutrients are then transported through the outer membrane into the interior of the body's cells.

where energy is generated

the primary substance of the cell

converts stored genetic information



control center of the cell

strands of genetic information

Calories

- In chemistry, a calorie (small c) is not a 'thing'…but a unit of heat measurement. One calorie is the amount of energy needed to raise the temperature of 1.0 gram of water 1.0° Celsius.
- Most people use the word calorie incorrectly. They are actually talking about kilocalories (kcal). A kcal equals 1,000 calories and is referred to as a Calorie (capital C).
- Suppose your favorite snack food or drink label reports that a serving contains 0 Calories. Does that always mean it is calorie-free? (remember… it takes 1,000 calories to equal 1 Calorie)
- A joule is another unit of heat energy.
- 1 joule (J) is equal to 0.239 calories.

Basal metabolism

- Basal metabolism is energy used by a body at rest to maintain involuntary, life-supporting processes such as breathing, regulating heartbeat, growing new cells, and maintaining body temperature.
- About 2/3rds of the energy your body produces is spent on basal metabolism.
- Basal metabolism is expressed as basal metabolic rate, or BMR.
- BMR is a measure of heat given off per time unit… usually as kcalories per hour. You can use your BMR to estimate your daily kcalorie needs.

Calculating your basal metabolic rate (BMR)

- Calculating your basal metabolic rate (BMR) can help you determine your nutrition and energy needs for the day.
- Although a precise measurement of BMR takes special equipment and/or procedures, you can get an estimate.
- Find your mass in kilograms.
- Divide your weight in pounds by 2.2.
- Find your basal metabolic rate (BMR) or the kcalories you use per hour. If you are female, multiply your mass by 0.9.
- If you are male, multiply by 1.0
- Determine kilocalories (Calories) used per day by multiplying your BMR by 24.
- A 130 pound female would use about 1,272 Calories per day "at rest". A 180 pound male would use 1,416 Calories per day "at rest".

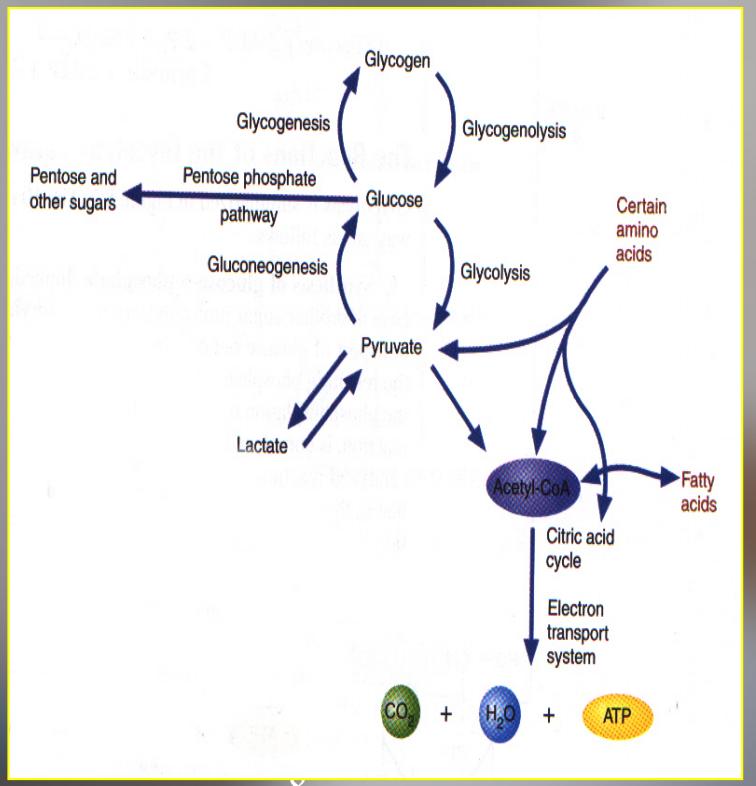
- With 2/3rds of the body's energy used on basal metabolism the remaining 1/3rd is used for voluntary activities.
- The number of Kcalories a voluntary activity uses will depend on how physical the activity is, the amount of time you spend doing it, and your own level of fitness.
  - To determine your daily kcalorie needs for both basal metabolism and voluntary activities, take your kcalories needed for basal metabolism…
  - Multiplied by 1.20 for a sedentary lifestyle
  - Multiplied by 1.30 for a lifestyle of light activity
  - Multiplied by 1.40 for a lifestyle of moderate activity
  - Multiplied by 1.50 for a lifestyle of vigorous activity

Major Pathways of CHO Metabolism

CHO metabolism in mammalian cells can be classified into:

1. **Glycolysis**: Oxidation of glucose to pyruvate (aerobic state) or lactate (anaerobic state)
2. **Krebs cycle:** After oxidation of pyruvate to acetyl CoA, acetyl CoA enters the Krebs cycle for the aim of production of ATP.
3. **Hexose monophosphate shunt:** Enables cells to produce ribose-5-phosphate and NADPH.
4. **Glycogenesis:** Synthesis of glycogen from glucose, when glucose levels are high
5. **Glycogenolysis**: Degradation of glycogen to glucose when glucose in short supply.
6. **Gluconeogenesis:** Formation of glucose from noncarbohydrate sources.

Glucose is the major fuel of most organisms. The major pathways of CHO metabolism either begin or end with glucose.



Glycolysis (Embden-Meyerhof Pathway)

[glycolysis: from the Greek *glyk*-, sweet, and *lysis*, splitting]

Glycolysis occurs in all human cells. Glycolysis is believed to be among the oldest of all the biochemical pathways.

Aerobic: Glucose → Pyruvate

Anaerobic: Glucose → Lactate (or ethanol & acetic acid)

Glycolysis (10 reactions in 3 stages, all in cytoplasm)

1) Priming stage: D-Glucose + 2ATP → D-fructose 1,6-biphosphate + 2ADP + $2H^+$

2) Splitting stage : D-Fructose 1,6-biphosphate → 2 D-Glyceraldehyde 3-phosphate

3) Oxidoreduction – Phosphorylation stage:

2 D-Glyceraldehyde 3-phosphate + 4ADP + 2Pi + 2H+ → 2Lactate + 4ATP

Sum:

Glucose + 2ADP + 2Pi ----- 2 Lactate + 2ATP + 2H2O (Anaerobic)

Glucose + 2ADP + 2Pi + $2NAD^+$ ---- 2 pyruvate + 2ATP + 2NADH + $2H^+$ + $2H_2O$ (Aerobic)

What effects do fluoride and magnesium have on glycolysis ?

Comments on Glycolysis

- ✓ Glycolysis is the only pathway that produce ATP in absence of O_2.
- ✓ The best known inhibitors of the glycolytic pathway include:

  2-Deoxyglucose: causes inhibition of hexokinase.

  Sulfhydryl reagents (e.g. Hg-compounds and alkylating agents as iodoacetate); inhibit glyceraldehydes-3-phosphate dehydrogenase which has cysteine residue in the active site.

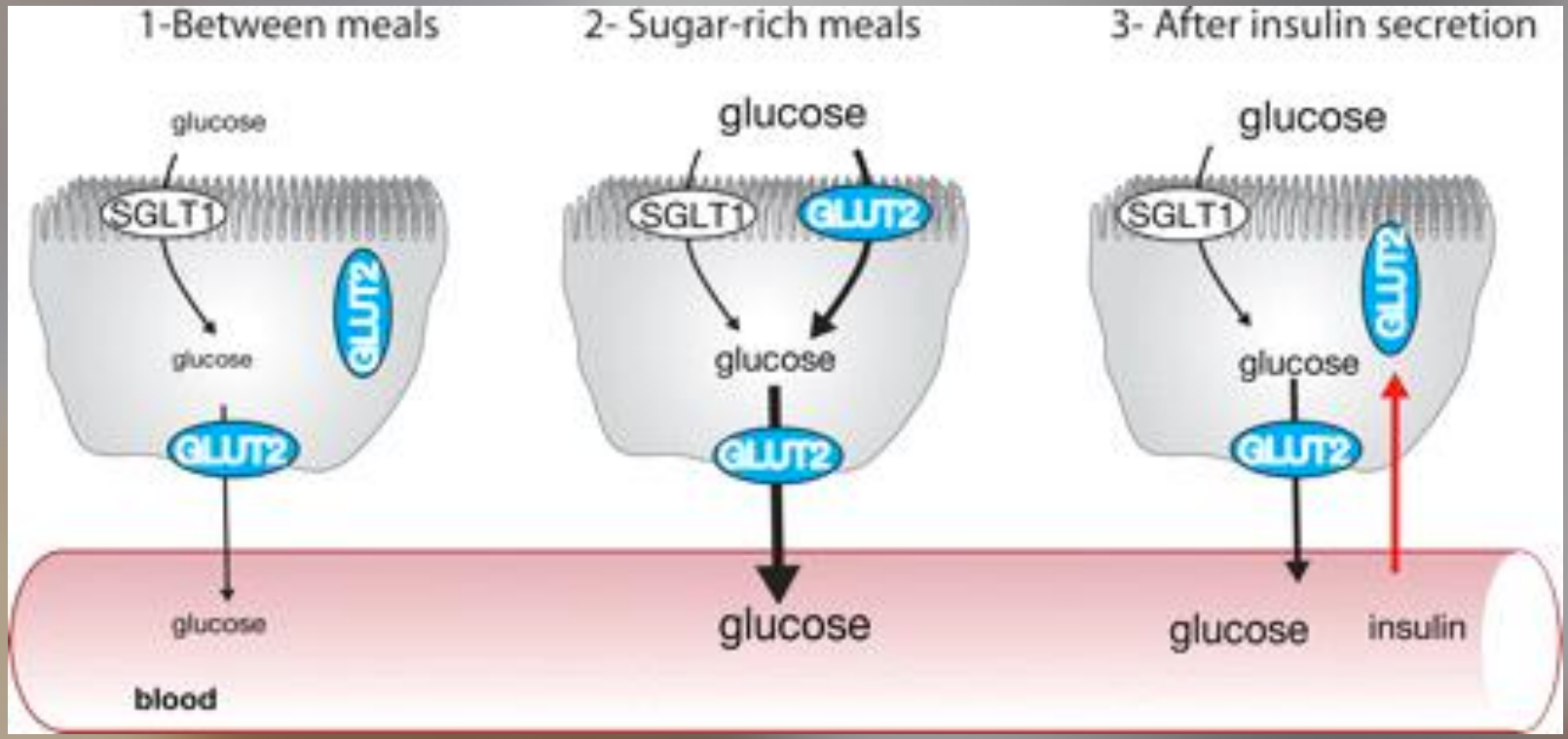
  Fluoride: a potent inhibitor of enolase. Thus, fluoride is usually added to blood samples to inhibit glycolysis before estimation of blood glucose.
- ✓ Magnesium: required for kinase reactions by forming Mg-ATP complex.
- ✓ Accumulation of lactate is responsible for muscle fatigue and cramps observed under heavy exercise (anaerobic glycolysis).
- ✓ In RBCs, glycolysis is the major source of ATP since RBCs lack mitochondrial oxidation.

GLUT classes	GLUT isoforms	Gene name	Tissue distribution	Substrate specificity	Trans-acceleration	Crystal structure/ computer model
I	GLUTI	SLC2A1	Red blood cells, Ubiquitous	Glucose/Galactose/ Dehydroacetic Acid	Yes	Crystal structure
I	GLUT3 (GLUT14)	SLC2A3 (SLC2A14)	Neurons (Testis)	Glucose/Galatose/ Dehydroacetic Acid	Yes	Computer model
I	GLUT4	SLC2A4	Muscle cells, Fat cells (Adipocytes)	Glucose/Dehydroacetic Acid	No	Computer model
I	GLUT2	SLC2A2	Intestine, Liver, Kidney, Beta cells	Glucose/Fructose/ Galatose/Glucosamine/ Dehydroacetic Acid	No	N/A
II	GLUT5	SLC2A5	Intestine, Kidney Muscle, Sperm, Brain	Fructose	N/A	Computer model
II	GLUT7	SLC2A7	Intestine, Colon	Fructose/Glucose	N/A	Computer model
II	GLUT9	SLC2A9	Kidney, Liver, Placenta, Colon	Urate/Fructose/Glucose	Yes	Computer model
II	GLUT11	SLC2A11	Muscle, Heart, Placenta, Kidney, Pancreas, Fat	Glucose	N/A	N/A
III	GLUT6	SLC2A6	Brain, Spleen	Glucose	N/A	N/A
III	GLUT8	SLC2A8	Testes, Brain, Fat, Liver, Spleen	Glucose/Fructose	N/A	N/A
III	GLUT10	SLC2A10	Heart, Lung	Glucose	N/A	N/A
III	GLUT12	SLC2A12	Insulin-sensitive tissues	Glucose/Fructose	N/A	N/A
III	GLUT13 (HMIT)	SLC2A13	Brain	Myo-inositol	N/A	N/A

SGLT type	Location	Function
SGLT1	Apical membranes of small intestinal cells	Absorption of glucose from intestinal content
	Straight cells (S_3 cells) of proximal tubule of nephron	Reabsorption of remaining glucose from urine filtrate
SGLT2	Proximal convoluted tubule of nephron (S_1 and S_2 cells)	Reabsorption of bulk plasma glucose from glomerular filtrate
SGLT3	Intestine, testes, uterus, lung, Brain, thyroid	Function as glucose sensor for controlling glucose levels in gut and brain
SGLT4	Intestine, kidney, liver, brain, lung, uterus, pancreas	Absorption and/or reabsorption of mannose, 1,5- anhydro D-glucitol, fructose and glucose
SGLT5	Kidney cortex	Transport of glucose and galactose
SGLT6	Brain, kidney, intestine	Preferred substrate is D-chiro-inositol

SGLT, Sodium–glucose linked transported (sodium-dependent glucose transporter)

[a] Nature not known


1-Between meals
2- Sugar-rich meals
3- After insulin secretion
glucose
SGLT1
GLUT2
glucose
GLUT2
glucose
blood
glucose
SGLT1
GLUT2
glucose
GLUT2
glucose
glucose
SGLT1
GLUT2
glucose
GLUT2
glucose
insulin

Inherited disorders of SGLT1, SGLT2 and GLUT2

Familial renal glucosuria (OMIM 233100) [6, 52]

Benign, rare, autosomal recessive disorder

Presents as isolated glucosuria (1–150 g [1.73 m]$^{-2}$ day^{-1})

Homogenous mutations in *SGLT2* in 60% of patients

Mutations include missense, nonsense, frame shift, splice site and deletion mutations

Those with premature stop mutations (e.g. V347X) have severe glucosuria

Glucose–galactose malabsorption (OMIM 182380) [6, 50]

Rare autosomal recessive defect in intestinal glucose and galactose absorption

Patients have mild renal glucosuria. Newborns (on mother's milk) present with diarrhoea

Homozygous and heterogeneous *SGLT1* missense, nonsense, frame shift, splice site and deletion mutations.

Mutations cause defects in tracking SGLT1 from endoplasmic reticulum to brush border membrane

Therapy is to remove lactose, glucose and galactose from diet

Fanconi–Bickel syndrome (OMIM 227810) [9]

A fatal, rare autosomal recessive disorder

Characterised by hepatomegaly and glucosuria ranging from 40–150 g [1.73 m]$^{-2}$ day^{-1}

Missense, nonsense, frame shift and splice site mutations in *GLUT2*

Those with truncation mutations have severe glucosuria

Syndrome	Major phenotype
GLUT-1 deficiency syndrome	Reduced glucose transport across brain-blood barrier causing infantile seizures, delayed development, and acquired microcephaly
Fanconi-Bickel syndrome	Fasting hypoglycaemia, fed hyperglycemia hypercholesterolemia, and hyperlipidemia hepatorenal glycogen accumulation leading to hepatomegaly, proximal renal tubular dysfunction, dwarfism
Renal hypouricemia, (RHUC2)	Hypouricemia
Arterial tortuosity syndrome	Connective tissue disorder with elongation and tortuosity of the major arteries (incl. Aorta); skin and joint abnormalities (hyperextensibility, hyperlaxity); micrognathia; elongated face