

Gluconeogenesis(abbreviated GNG)

Gluconeogenesis is a metabolic pathway that results in the generation of **glucose** from non-carbohydrate carbon substrates such as pyruvate, lactate, glycerol, glucogenic amino acids, and odd-chain fatty acid.

It is one of the two main mechanisms (with glycogenolysis), humans use to keep blood glucose levels from dropping too low (hypoglycemia).

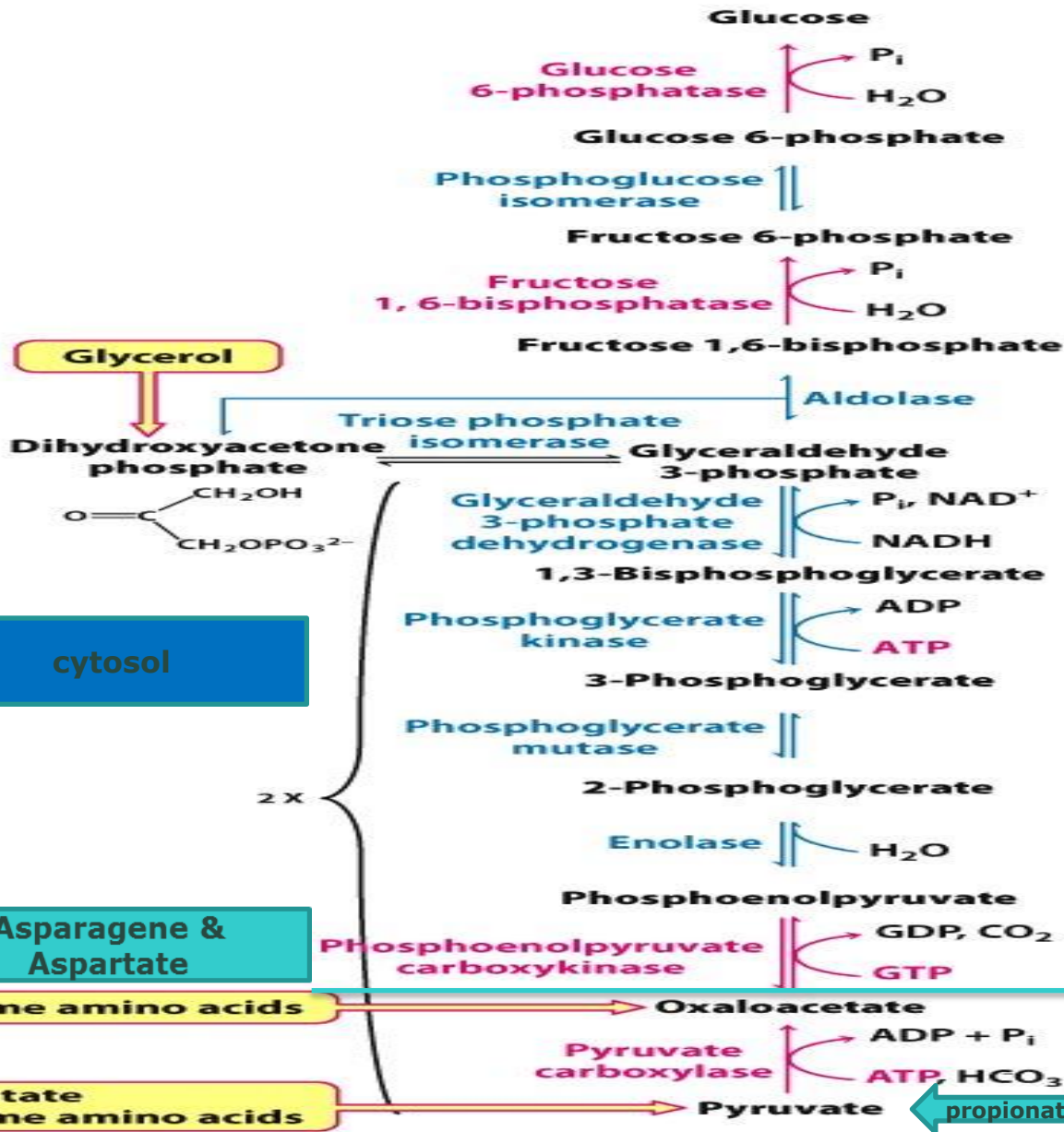
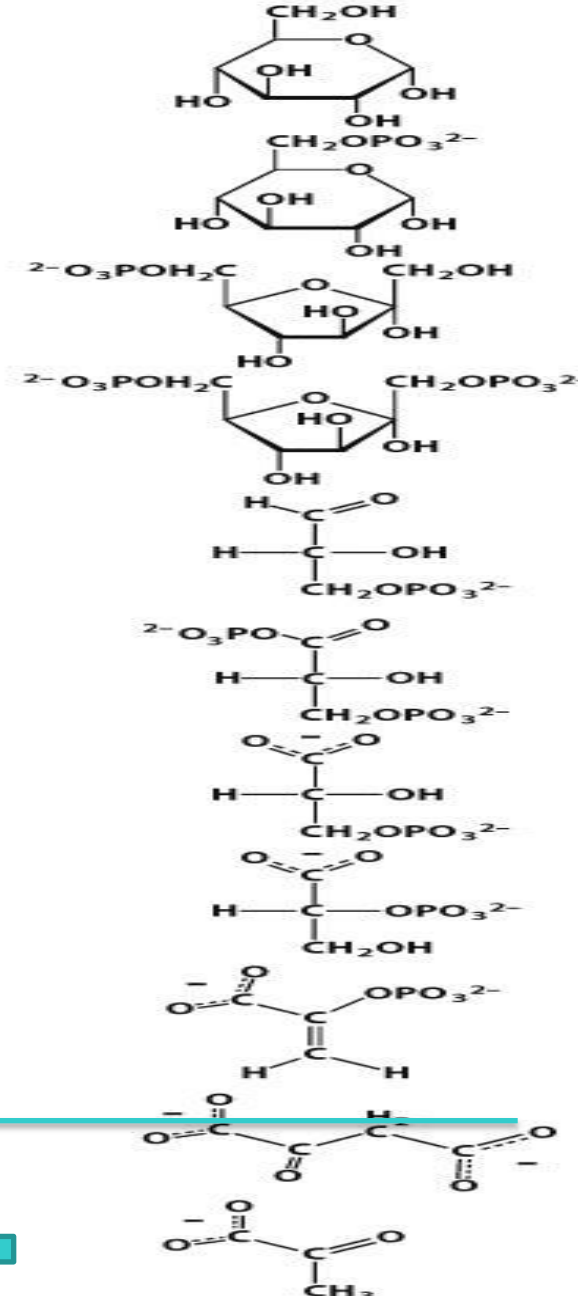
gluconeogenesis takes place mainly in the liver and, to a lesser extent, in the kidneys.

The process occurs during periods of fasting, starvation, low-carbohydrate diets, or intense exercise.

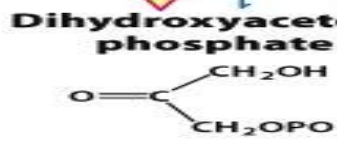
Gluconeogenesis

The main gluconeogenic precursors are **lactate**, **glycerol** (from triacylglycerides), **alanine** and **glutamine** (over 90%). as well as all citric acid cycle intermediates (Transamination or deamination of amino acids facilitates entering of their carbon skeleton into the cycle directly (as pyruvate or oxaloacetate), or indirectly via the TCA cycle).

Lactate is transported back to the liver where it is converted into pyruvate by the Cori cycle using the enzyme lactate dehydrogenase. **Pyruvate**, the first substrate of the gluconeogenic pathway, whether even-chain fatty acids can be oxidized to yield propionyl CoA, a precursor for succinyl CoA, which can be converted to pyruvate and enter into gluconeogenesis.



Glycerol



cytosol

Asparagine & Aspartate

Some amino acids

Lactate
Some amino acids

Alanine, Glycine, serine, Cysteine & Threonine

propionate

Mitochondria

Gluconeogenesis Regulation & overview

- The process is highly **endergonic** until ATP or GTP are utilized, effectively making the process exergonic.
- The pathway leading from pyruvate to glucose-6-p requires 4 molecules of ATP and 2 molecules of GTP.
- Gluconeogenesis is also a target of therapy for type II diabetes, such as metformin, which inhibits glucose formation and stimulates glucose uptake by cells.
- The rate of gluconeogenesis is ultimately controlled by the action of a key enzyme, **fructose-1,6-bisphosphatase**, which is also regulated by cAMP.
- Global hormonal control of gluconeogenesis is mediated by **glucagon**, whose actions oppose those of insulin. Also the **glucocorticoids** secreted from the adrenal cortex increase gluconeogenesis.

Pentose phosphate pathway PPP

(Phosphogluconate pathway or the hexose monophosphate shunt)

Is a process that generates⁽¹⁾ pentoses (5-carbon sugars) used in the synthesis of nucleotides and nucleic acids and⁽²⁾ NADPH used in other biosynthesis reactions within cells. (e.g. fatty acid synthesis) also⁽³⁾ Production of erythrose-4-phosphate (E4P), used in the synthesis of aromatic A.A. It takes place in the cytosol and is found to be most active in the liver, mammary gland, adrenal cortex and Erythrocytes (generate a large amount of NADPH via PPP to prevent oxidative stress of glutathione).

There are two Stages in this pathway. The first is the oxidative phase, in which NADPH is generated, and the second is the non-oxidative synthesis of 5-carbon sugars. Regulation by Glucose-6-phosphate dehydrogenase is the rate-controlling enzyme of this pathway. It is stimulated by NADP^+ to produce more NADPH.

PPP

