METABOLISM

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ARKAN ACADEMY

Gluconeogenesis

- The production of glucose from non-carbohydrate sources (reverse of glycolysis)
- It starts initially at the fasting state (90% in the liver, 10% kidney)
  - During prolonged fast kidney becomes a major glucose-producing organ (kidney 40%, liver 60%)
- Gluconeogenesis precursors:
  - *TAGs (fats):* Fatty acids are broken down by beta oxidation, and glycerol enters gluconeogenesis
  - *Glucogenic amino acids* such as alanine, oxaloacetate, …
  - *Lactate*
- Most of these precursors such as lactate and alanine are converted into pyruvate which is converted into OAA then completes the process
  - Some glucogenic amino acids (such as aspartate) are converted directly to OAA
  - Glycerol is converted into triose-phosphates
- Gluconeogenesis which are the reverse of the glycolysis with the same enzymes, except for the 3 irreversible steps which are done by different enzymes

Pyruvate → phosphoenolpyruvate

- It occurs in 2 compartments (***mitochondria***, ***cytosol***)
- In the mitochondria, *pyruvate* is converted into *oxaloacetate* by carboxylase which requires ***ATP and biotin*** (which carries the CO_2), the OAA is converted into *malate* which can be transported into the cytosol by a specific transporter
- In the cytosol, malate is converted into *OAA* which is converted into *PEP* by ***PEP carboxykinase***
  - It requires ***GTP*** hydrolysis to provide energy and a phosphate group
- It is activated by acetyl CoA

Fructose 1,6-bisphosphate → Fructose 6-phosphate

- Done by the enzyme ***Fructose 1,-bisphosphate phosphatase*** which is opposite to PFK-1
  - Occurs in the ***cytosol***
  - It is inhibited by *AMP* and *fructose 2,6-bisphosphate*

Glucose 6-phosphate → glucose

- It is done by ***glucose 6-phosphatase*** in the ***ER*** of liver and kidney
- Glucose is then transported into the cytosol by ***GLUT7***
- The net results of gluconeogenesis for the production of 1 glucose:
  - *Consumed 4 ATP and 2 GTP*

- Gluconeogenesis is activated by:
  - ***Glucagon:*** Activates gluconeogenesis by activating fructose 1,6-bisphosphatase and increase the gene expression of PEP-carboxykinase
  - ***Availability*** gluconeogenic substrates

- Sources of Blood Glucose:
  - Diet (Starch, mono- and disaccharides, glucose)
    - ✓ Sporadic consumption depends on diet
  - Glycogen (storage form of glucose)
    - ✓ Rapid response and limited amount
    - ✓ Important energy source for exercising muscle
  - Gluconeogenesis (sustained synthesis)
    - ✓ Slow in responding to falling blood glucose level

Brain requires 120 g/day of glucose

Past Papers

1. One of the following is not a precursor for gluconeogenesis:
   A. Alanine
   B. Glucogenic amino acids
   C. Glycerol
   D. Acetyl CoA
   E. Lactate

2. Which enzyme is involved in both glycolysis and gluconeogenesis?
   A. Pyruvate carboxylase
   B. Fructose-1,6-Bisphosphotase
   C. Glucose-6-phosphotase
   D. Phosphoglycerate Kinase

3. Which of the following hormones stimulates Gluconeogenesis?
   A. Insulin
   B. Glucagon
   C. Acetylcholine

4. During an overnight fast, Gluconeogenesis occurs mainly in:
   A. Liver
   B. Kidney
   C. Muscles

5. Gazan woman was stuck under a building for two days; Which organ plays a role in compensating for the lack of dietary glucose:

   A. Liver and kidney
   B. Skeletal muscles
   C. Heart
   D. Brain

6. The main role of the glucose produced by gluconcogenesis in the liver is:

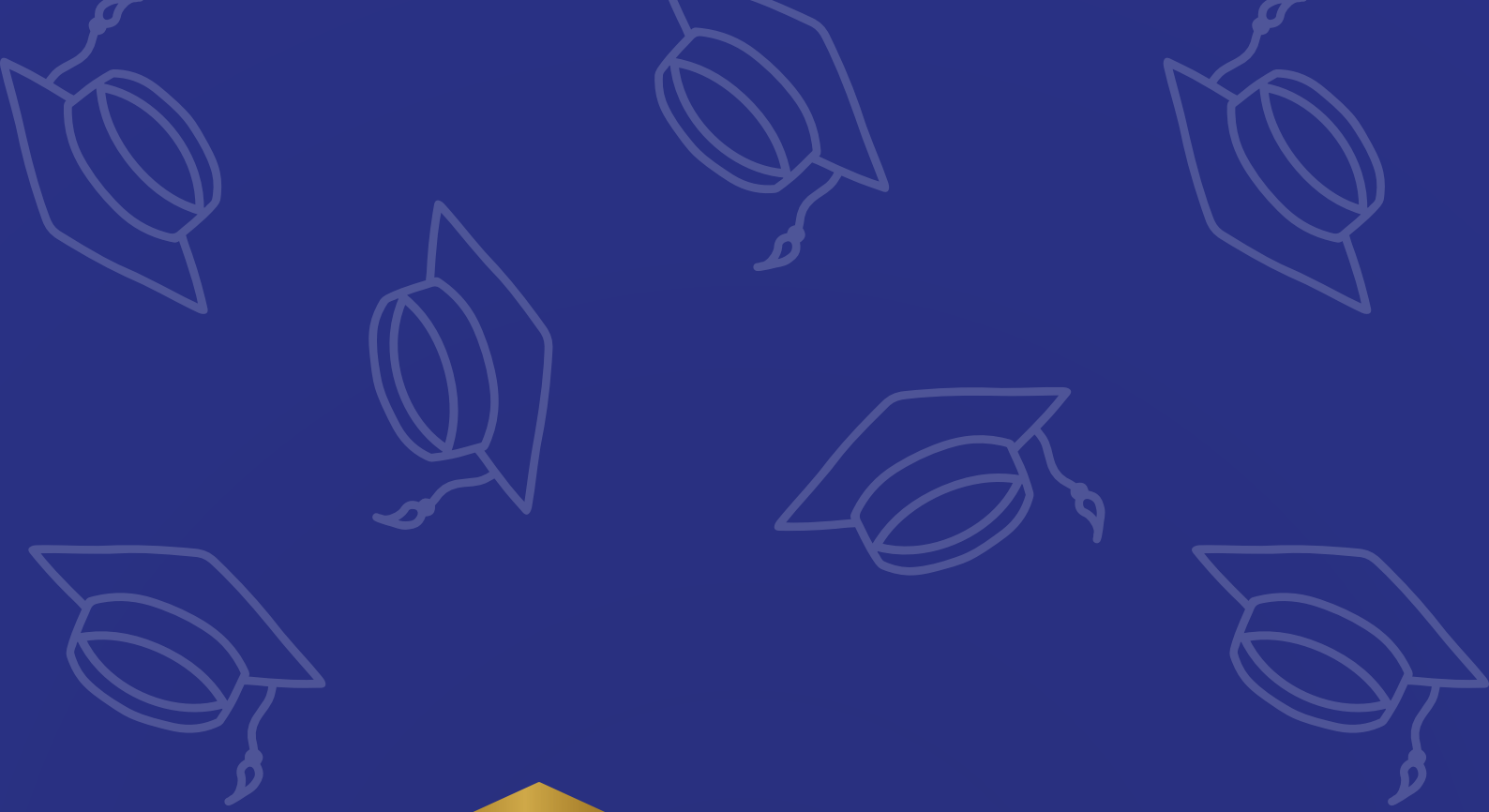
   A. To maintain blood glucose levels
   B. To supply muscles with glucose to be metabolized for energy production
   C. To be used for lactose production
   D. To be used for the synthesis of sugar moiety of glycoproteins, glycolipids and protcoglycans
   E. To be used for glycogen synthesis and storage

7. The cofactor required by the enzyme that produces of oxaloacetate from pyruvate is

   A. Coenzyme A
   B. Pantothenic Acid
   C. Biotin
   D. NADH
   E. Lipoic Acid

8. A newborn with organomegaly in several organs due to glycogen storage in lysosomes was diagnosed with pompe's disease. The biochemical deficiency in this patient is:

   A. Glycogenin primer deficiency
   B. Lysosomal α-1,6 glycosidase deficiency
   C. Glucose-6-phosphate deficiency
   D. Glycogen phosphorylase deficiency
   E. Lysosomal α-1,4 glucosidase deficiency



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