بِسۡمِ ٱللَّهِ ٱلرَّحۡمَٰنِ ٱلرَّحِيمِ

محاضرة كيمياء حيوية 2

"Gluconeogenesis"

المستوى الثالث

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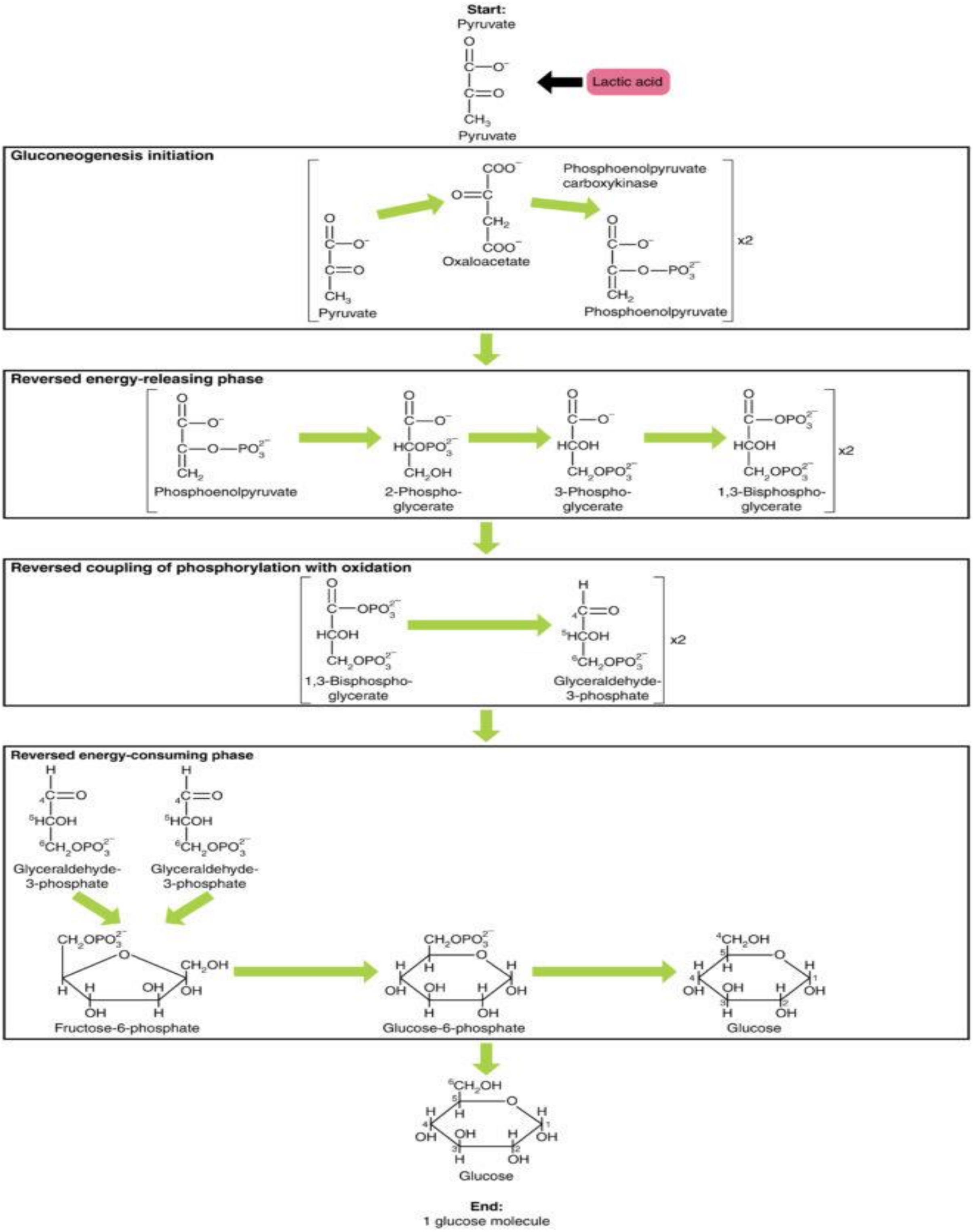
Gluconeogenesis:

Gluconeogenesis is the synthesis of new glucose molecules from pyruvate, lactate, glycerol, or the amino acids alanine or glutamine. This process takes place primarily in the liver during periods of low glucose, that is, under conditions of fasting, starvation, and low carbohydrate diets. So, the question can be raised as to why the body would create something it has just spent a fair amount of effort to break down? Certain key organs, including the brain, can use only glucose as an energy source; therefore, it is essential that the body maintain a minimum blood glucose concentration. When the blood glucose concentration falls below that certain point, new glucose is synthesized by the liver to raise the blood concentration to normal.

Gluconeogenesis is not simply the reverse of glycolysis. There are some important differences .Pyruvate is a common starting material for gluconeogenesis. First, the pyruvate is converted into oxaloacetate. Oxaloacetate then serves as a substrate for the enzyme phosphoenolpyruvate carboxykinase (PEPCK), which transforms oxaloacetate into phosphoenolpyruvate (PEP). From this step, gluconeogenesis is nearly the reverse of glycolysis. PEP is converted back into 2-phosphoglycerate, which is converted into 3-phosphoglycerate. Then, 3-phosphoglycerate is converted into 1,3 bisphosphoglycerate and then into glyceraldehyde-3-phosphate. Two molecules of glyceraldehyde-3-phosphate then combine to form fructose-1-6-bisphosphate, which is converted into fructose 6-phosphate and then into glucose-6-phosphate. Finally, a series of reactions generates glucose itself. In gluconeogenesis (as compared to glycolysis), the enzyme hexokinase is replaced by glucose-6-phosphatase, and the enzyme phosphofructokinase-1 is replaced by fructose-1,6-bisphosphatase. This helps the cell to regulate glycolysis and gluconeogenesis independently of each other.

As will be discussed as part of lipolysis, fats can be broken down into glycerol, which can be phosphorylated to form dihydroxyacetone phosphate or DHAP. DHAP can either enter the glycolytic pathway or be used by the liver as a substrate for gluconeogenesis.



Gluconeogenesis is the synthesis of glucose from pyruvate, lactate, glycerol, alanine, or glutamate.

Blood sugar regulation:

Blood sugar regulation is the process by which the levels of blood sugar, primarily glucose, are maintained by the body within a narrow range. This tight regulation is referred to as glucose homeostasis. Insulin, which lowers blood sugar, and glucagon, which raises it, are the most well-known of the hormones involved, but more recent discoveries of other glucoregulatory hormones have expanded the understanding of this process.

1- **Glucagon**

If the blood glucose level falls to dangerously low levels (as during very heavy exercise or lack of food for extended periods), the alpha cells of the pancreas release glucagon, a hormone which travels through the blood to the liver, where it binds to glucagon receptors on the surface of liver cells and stimulates them to break down glycogen stored inside the cells into glucose (this process is called glycogenolysis). The cells release the glucose into the bloodstream, increasing blood sugar levels. Hypoglycemia, the state of having low blood sugar, is treated by restoring the blood glucose level to normal by the ingestion or administration of dextrose or carbohydrate foods. It is often self-diagnosed and self-medicated orally by the ingestion of balanced meals. In more severe circumstances, it is treated by injection or infusion of glucagon.

2- Insulin

When levels of blood sugar rise, whether as a result of glycogen conversion, or from digestion of a meal, a different hormone is released from beta cells found in the islets of Langerhans in the pancreas. This hormone, insulin, causes the liver to convert more glucose into glycogen (this process is called glycogenesis), and to force about 2/3 of body cells (primarily muscle and fat tissue cells) to take up glucose from the blood through the GLUT4 transporter, thus decreasing blood sugar. When insulin binds to the receptors on the cell surface, vesicles containing the GLUT4 transporters come to the plasma membrane and fuse together by the process of endocytosis, thus enabling a facilitated diffusion of glucose into the cell. As soon as the glucose enters the cell, it is phosphorylated into Glucose-6-Phosphate in order to preserve the concentration gradient so glucose will continue to enter the cell.[2] Insulin also provides signals to several other body systems, and is the chief regulator of metabolic control in humans.

There are also several other causes for an increase in blood sugar levels. Among them are the 'stress' hormones such as epinephrine (also known as adrenaline), several of the steroids, infections, trauma, and of course, the ingestion of food.

Diabetes mellitus type 1 is caused by insufficient or non-existent production of insulin, while type 2 is primarily due to a decreased response to insulin in the tissues of the body (insulin resistance). Both types of diabetes, if untreated, result in too much glucose remaining in the blood (hyperglycemia) and many of the same complications. Also, too much insulin and/or exercise without enough corresponding food intake in diabetics can result in low blood sugar (hypoglycemia).