Unit 3 Lecture 11

METABOLISM

Anabolism is defined as the chemical reactions that combine simple substances into more complex molecules (requires energy). Examples of anabolism include glycogenesis (conversion of glucose to glycogen in the liver and skeletal muscles), gluconeogenesis (conversion of protein or triglyceride molecules into glucose), and lipogenesis (conversion of glucose or amino acids into lipids).

Catabolism is defined as the chemical reactions that breaks down complex molecules into simpler ones (releases energy). Examples include glycolysis (breakdown of glucose into two molecules of pyruvic acid), glycogenolysis (glycogen is broken down to glucose and released from the liver), and lipolysis (breakdown of lipids into glycerol and fatty acids).

Metabolism is defined as all of the chemical reactions of the cell. The purpose of metabolism is to produce energy in the form of ATP. Glucose contributes to 1% of the total energy requirements of the body, and its reserves (in the form of glycogen) can last for roughly a day. Fatty acids contribute to 77% of the total energy produced and can last for up to two months depending on the individual. Amino acids stored as proteins are not usually used to create energy but can account for 22% of the body's fuel requirements if absolutely necessary.

There are three primary chemical reactions that take place within the cell to produce energy from the breakdown of food molecules. The first, called glycolysis (or the glycolytic pathway), is a series of reactions that occurs in the cytoplasm. It does not require oxygen and is therefore considered an anaerobic reaction. Glycolysis can produce two molecules of ATP very quickly from one molecule of glucose. The second series of reactions is called the citric acid cycle (CAC, or Krebs cycle). This reaction, which takes place inside the mitochondria, requires the presence of oxygen and therefore is an aerobic reaction. It can produce two molecules of ATP per molecule of glucose.

The third series of reactions is closely linked to the citric acid cycle and is called oxidative phosphorylation (also known as the electron transport chain). This reaction can produce 34 molecules of ATP from one molecule of glucose. It also occurs in the mitochondria of the cell and also requires oxygen. All of these equations are linked together through various intermediate steps. Each of the food molecules can enter one or more of these reactions to make energy (ATP). For example, glucose (as well as its storage form glycogen) can enter glycolysis at the beginning of this reaction. Amino acids (AA) can be converted to pyruvate to enter glycolysis or can be converted to acetyl coenzyme A (acetyl CoA) to enter the citric acid cycle

(CAC) to produce ATP. Fats (triglycerides) can be broken down to glycerol and free fatty acids. The glycerol molecules can enter glycolysis, and the fatty acids can be converted to acetyl CoA to enter the CAC.

The Metabolism of Glucose

Glucose is a monosaccharide, and is stored as glycogen in most cells of the body. Most glycogen stores can be found in the liver and skeletal muscle. Glucose is a common fuel source for all the cells in the body. However, it is one of the only fuel sources for the brain, unlike most other cells in the body. Other cells can use fats and amino acids as well as glucose. Because the brain cells cannot store any glucose, the liver stores glucose for the brain.

In glycolysis, G-6-P will undergo a series of reactions that will result in the production of ATP and the end product of pyruvate. The pyruvate can then undergo two possible reactions; it can either enter the citric acid cycle (CAC) and produce lots of ATP (with the help of oxidative phosphorylation) or it can enter another shorter reaction to produce a small amount of ATP and the by-product lactate (also called lactic acid).

Which reaction will pyruvate take? That depends on whether oxygen is present or not. If there is sufficient oxygen (O2), then most of the pyruvate will enter the CAC. Since it is an aerobic pathway, it requires O_2. If there is not enough O2 present, then the CAC will not be running at full capacity and the pyruvate will be converted to lactic acid.

The Metabolism of Glucose via Lactic Acid

During strenuous exercise, your cardiovascular system may not be able to supply sufficient oxygen to your working muscle cells to produce ATP via the citric acid cycle (CAC). However, since glycolysis is anaerobic, this reaction can continue without oxygen to produce ATP and the end product pyruvate. With insufficient oxygen, the CAC will not work at full capacity and pyruvate will start to accumulate. If too much pyruvate accumulates, then even glycolysis will be slowed. In order to keep glycolysis working so it can produce ATP for the muscles, the pyruvate will be converted to lactic acid. The accumulation of lactic acid causes the "burning" sensation in the muscle and is believed to interfere with the contractile proteins causing fatigue. You should recall that the accumulation of lactic acid will cause the blood vessels to dilate and the decreasing pH will unload more oxygen from hemoglobin. These mechanisms will help to increase blood flow and increase oxygen delivery to this working tissue to reduce the buildup of lactic acid. It is very important to note that most of the reactions we have seen so far are reversible—that is, they can work in both directions. For example, if oxygen is restored, lactic acid can be converted back to pyruvate to enter the citric acid cycle. Also, pyruvate can be turned back into glycogen, through G-6-P, and stored for later use.

The Metabolism of Glucose via the Citric Acid Cycle

If there is a sufficient supply of oxygen, then the citric acid cycle (CAC) can function at full capacity. The pyruvate from glycolysis is converted to acetyl coenzyme A (acetyl CoA), which then enters the CAC. As mentioned earlier, the CAC in conjunction with oxidative phosphorylation together produce a total of 36 molecules of ATP from one molecule of glucose (2 ATP from CAC and 34 from oxidative phosphorylation). They also produce the by-products CO_2 and H_2O. The CO_2 will diffuse into the blood and leaves the body at the lungs.

The Fed and Fasted State

Food molecules can be either stored or metabolized to produce ATP. The fed state (also called the absorptive state) is the condition the body is in after a meal; when the levels of nutrients in the blood are quite high. During this period, the body's primary goal is to store all this new fuel (amino acids, fats, and glucose) for later use. Between meals, particularly in the morning before breakfast, the nutrient levels in the blood are very low. This is the fasted state (or post absorptive state), and the body's goal is to maintain blood glucose levels. In order to do this, the body will be utilizing its stored nutrients, including fats and glycogen.

The Absorptive (Fed) State

Once your body has eaten, it is time to store all the nutrients (fatty acids, amino acids, and glucose). This is the fed state of metabolism. Glucose will be stored in the muscle and liver as glycogen. Any excess amounts of glucose are converted to fatty acids by the liver. These fatty acids are released into the circulation and taken up by adipose (fat) tissue and stored as triglycerides for later use. Amino acids from the digestion of protein are taken up by cells in the body for protein synthesis. This could include the building of muscle proteins or for use in making new protein carriers. Any excess amino acids are converted to fatty acids.

The Postabsorptive (Fasted) State

It is 4:00 PM and you are hungry. You have not eaten since breakfast, so your body is in the fasted state. How can you possibly continue without food? You will recall that your glycogen stores in your cells last less than a day. Your fat stores, on the other hand, can last up to two months. The important point to remember is that most of the cells in the body can use different nutrient molecules to make energy. The brain, which can normally only use glucose, is an exception. Therefore, it is very important to keep the glucose concentrations in the blood from dropping too low. In order to maintain circulating glucose levels, the liver will produce and release glucose into the blood from its own glycogen stores. In addition, the liver can make new molecules of glucose from glycerol, amino acids, pyruvate, and lactate in a process called gluconeogenesis. Muscle cells cannot produce glucose from their stores of glycogen. Instead, the muscle cells will produce pyruvate or lactate from glycolysis and release these molecules into the blood. They will then be converted to glucose by the liver for use by the brain.

Regulation of Metabolism

Regulation of metabolism is important since the body must be able to switch from the fed state to the fasted state when necessary. This regulation of metabolism is performed by the pancreatic hormones insulin and glucagon. These hormones are secreted by the endocrine portion of the pancreas and work through feedback mechanisms.

Regulation by Insulin

Insulin is the hormone of the fed state. It is secreted from cells in the pancreas called beta cells in response to high levels of glucose in the blood. It has an effect on most cells in the body (with the exception of the brain and red blood cells), but its major target site is muscle, liver, and adipose (fat) tissue. Insulin's primary effect is to promote the storage of food nutrients (glucose, amino acids, and free fatty acids) while at the same time inhibiting their release from storage in muscle, liver, and adipose tissue. When insulin is released from the pancreatic beta cells, it will cause the following:

- Increased glucose uptake and utilization by cells
- Increased glycogen formation (glucose storage) which causes decreased blood glucose levels
- Increased triglyceride formation (fat storage) decreases blood fatty acid levels
- Increased protein synthesis (protein storage) decreases amino acid levels in the blood

A certain level of glucose is always in the blood. After a meal these levels will increase dramatically and will cause the release of insulin. This, in turn, will result in the storage of the nutrients. As the blood glucose levels begin to drop back to normal circulating levels, insulin secretion from the pancreas decreases as well.

Diabetes mellitus is a disease of the pancreas where the beta cells of Islets are destroyed. People with this disease are therefore unable to produce insulin; consequently, their cells are unable to take up nutrients from the blood. The level of glucose in the blood reaches very high levels and is excreted in the urine. Without daily injections of insulin people with diabetes mellitus would eventually die.

Regulation by Glucagon

Glucagon is the hormone of the fasted state. It is secreted by cells in the pancreas called alpha cells. Essentially, its effects are completely opposite to those of insulin. Glucagon is released when glucose levels in the blood drop below the normal circulating level. It stimulates cells to release their fuel stores into the blood. Its main target sites are the liver and adipose tissue. Glucagon will cause the following:

- Increased glycogenolysis (breakdown of glycogen stores)
- Increased gluconeogenesis (formation of new glucose molecules in the liver)
- Increased lipolysis (breakdown of fat stores); all of which result in:

- Increased blood glucose levels
- Increased levels of fatty acids in the blood
- As the levels of blood glucose increase, glucagon levels will drop.

NUTRITION

Since the world of nutrition changed recently, I'd like you to go to the following site (www.mypyramid.gov) by clicking on the link. Look at Tour the Pyramid and Inside the Pyramid.

Vitamins are organic nutrients that maintain growth and normal metabolism. Many function in enzyme systems. Minerals are inorganic substances that help regulate body processes.