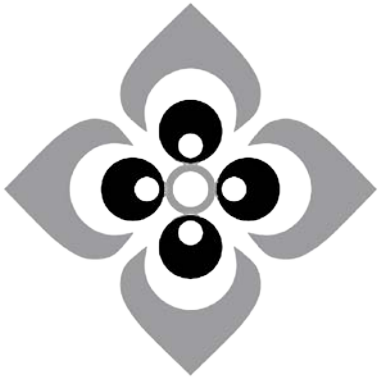

Consortium for Educational Communication

Module
on
Glycogen

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TEXT

1. INTRODUCTION

Glycogen is a readily mobilized storage form of glucose. In humans, glycogen is made and stored primarily in the cells of the liver and the muscles, hydrated with three or four parts of water. Glycogen functions as the secondary long-term energy storage, with the primary energy stores being fats held in adipose tissue. Muscle glycogen is converted into glucose by muscle cells, and liver glycogen converts to glucose for use throughout the body including the central nervous system. Glycogen is an important fuel reserve for several reasons. The controlled breakdown of glycogen and release of glucose increases the amount of glucose that is available between meals. Hence, glycogen serves as a buffer to maintain blood-glucose levels. Glycogen's role in maintaining blood-glucose levels is especially important because glucose is virtually the only fuel used by the brain, except during prolonged starvation. Moreover, the glucose from glycogen is readily mobilized and is therefore a good source of energy for sudden, strenuous activity. Unlike fatty acids, the released glucose can provide energy in the absence of oxygen and can thus supply energy for anaerobic activity.

The two major sites of glycogen storage are the liver and skeletal muscle. The concentration of glycogen is higher in the liver than in muscle (10% versus 2% by weight), but more glycogen is stored in skeletal muscle overall because of its much greater mass. Glycogen is present in the cytosol in the form of granules ranging in diameter from 10 to 40 nm (Fig 1). When glycogen is stored within muscle and liver cells, it retains water along with it (approximately 3 g of water for each gram of glycogen), so changes in glycogen content can cause quite noticeable changes in total body weight. For example, in the first few days of starvation, glycogen is used by the liver to maintain blood sugar and by muscle metabolism, and the associated water is excreted from the body in the urine, accounting for a major part of 1–2 kg loss of weight.

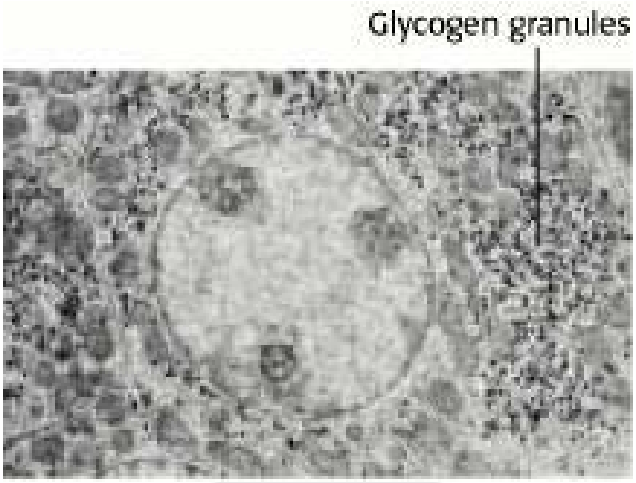

Fig. 1: Electron Micrograph of a Liver Cell

The dense particles in the cytoplasm are glycogen granules

2. STRUCTURE:

It is a very large, branched polymer of glucose residues (Fig 2) that can be broken down to yield glucose molecules when energy is needed. Most of the glucose residues in glycogen are linked by α-1,4-glycosidic bonds. Branches at about every tenth residue are created by α-1,6-glycosidic bonds. α-glycosidic linkages form open helical polymers, whereas β linkages produce nearly straight strands that form structural fibrils, as in cellulose.

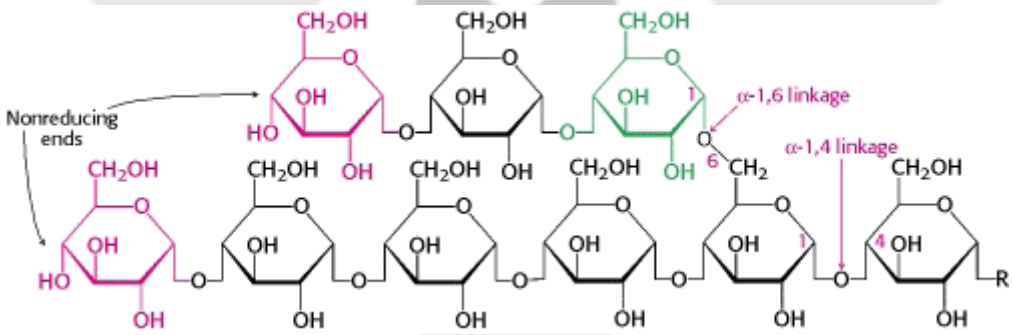

Fig. 2: Glycogen Structure

3. GLYCOGEN METABOLISM:

Glycogen degradation and synthesis are relatively simple biochemical processes. Glycogen degradation consists of three steps: (1) the release of glucose 1-phosphate from glycogen, (2) the remodeling of the glycogen substrate to permit further degradation, and (3) the conversion of glucose 1-phosphate into glucose 6-phosphate for further metabolism. The glucose 6-phosphate derived from the breakdown of glycogen has three fates (Fig 3): (1) It is the initial substrate for glycolysis, (2) it can be processed by the pentose phosphate pathway to yield NADPH and ribose derivatives; and (3) it can be converted into free glucose for release into the bloodstream. This conversion takes place mainly in the liver and to a lesser extent in the intestines and kidneys. Glycogen synthesis requires an activated form of glucose, uridine diphosphate glucose (UDP-glucose), which is formed by the reaction of UTP and glucose 1-phosphate. UDP-glucose is added to the nonreducing end of glycogen molecules. As is the case for glycogen degradation, the glycogen molecule must be remodeled for continued synthesis.

The regulation of these processes is quite complex. Several enzymes taking part in glycogen metabolism allosterically respond to metabolites that signal the energy needs of the cell. These allosteric responses allow the adjustment of enzyme activity to meet the needs of the cell in which the enzymes are expressed. Glycogen metabolism is also regulated by hormonally stimulated cascades that lead to the reversible phosphorylation of enzymes, which alters their kinetic properties. Regulation by hormones allows glycogen metabolism to adjust to the needs of the entire organism. By both these mechanisms, glycogen degradation is integrated with glycogen synthesis.

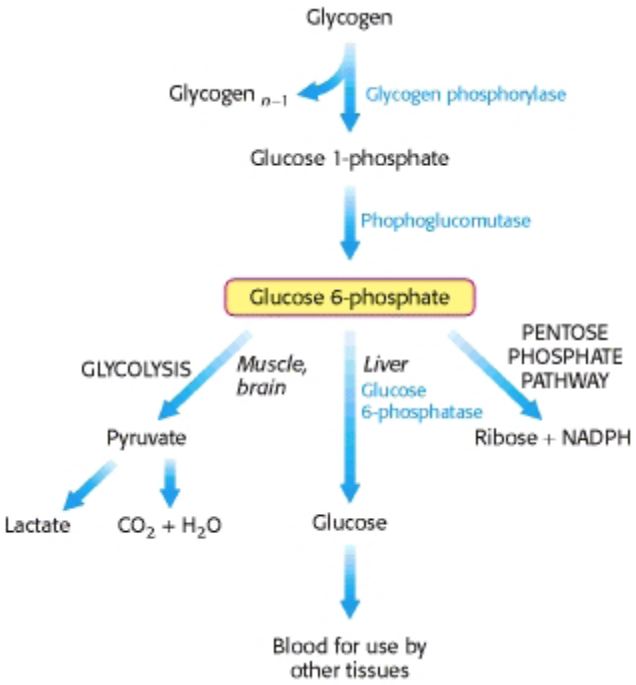

Fig. 3: Glycogen metabolism

4. GLYCOGEN DISORDERS:

The most common disease in which glycogen metabolism becomes abnormal is diabetes, in which, because of abnormal amounts of insulin, liver glycogen can be abnormally accumulated or depleted. Restoration of normal glucose metabolism usually normalizes glycogen metabolism, as well. In hypoglycemia caused by excessive insulin, liver glycogen levels are high, but the high insulin levels prevent the glycogenolysis necessary to maintain normal blood sugar levels. Glucagon is a common treatment for this type of hypoglycemia.

Apart from this, glycogen storage disorders are a group of inherited diseases that result from a lack of, or abnormal functioning of, one of the proteins (enzymes) involved in the conversion of glucose to glycogen or the breakdown of glycogen back into glucose. Because there are a number of different enzymes involved in glycogen production and breakdown, there are a number of different glycogen storage disorders. In fact, there are over 12 types of glycogen storage disorder. Each disorder has a different enzyme lack or malfunction. If the enzyme problem is with one of the enzymes involved in glycogen production (synthesis), this causes reduced amounts of normal glycogen to be produced and sometimes abnormal glycogen being produced. If the enzyme problem is with one of the enzymes involved in glycogen breakdown back into glucose,

this can lead to:

- Low levels of glucose in the body (a condition known as hypoglycaemia).
- A build-up of glycogen in the muscles and liver.

Because glycogen storage disorders are inherited and can affect energy production and metabolism within the body, they are also known as inborn errors of metabolism.

5. **FUNCTIONS OF GLYCOGEN:**

There are important differences between the major functions of liver and muscle glycogen. The main role of liver glycogen is to provide a reserve supply of glucose in order that blood glucose concentration can be kept at an adequate level to supply the brain (which does not use other fuels) during periods of fasting, or when glucose use is increased during physical work and exercise. Thus, after meals, some of the carbohydrate consumed is stored as liver glycogen, and during fasting, this glycogen is broken down and the glucose is released into the blood. In a healthy adult, the liver glycogen store is usually between 50 and 100 g, containing enough glucose to satisfy the brain's requirements for up to 24 hours.

The main role of muscle glycogen is to provide fuel for the muscle's own contraction during exercise. In fact, muscle glycogen cannot be broken down to glucose and so cannot be used to raise blood glucose concentration directly. However, in some circumstances, when their metabolism is partly anaerobic, skeletal muscles produce lactic acid from glycogen. When this lactic acid passes into the blood it is taken up by the liver, where it is converted into glucose; thus it can be used indirectly to raise blood glucose. The major stimulus causing the breakdown of muscle glycogen is contraction of the muscles. Thus, the onset of exercise is accompanied by the initiation of glycogen breakdown. The extent to which the muscles continue to use their glycogen store depends on the intensity of the exercise. With low intensity exercise (such as slow walking, cycling, or swimming) the muscles do not use much glycogen as they are able to take up fat from the blood as a source of energy for contraction. However, with higher intensity exercise (jogging, brisk uphill walking, running) the muscles need to use glycogen or glucose from the blood to support the higher rate of energy expenditure. A well-nourished person will have enough glycogen in their muscle to

enable them to exercise for 1–2 hours at approximately two-thirds of their maximum capacity for aerobic exercise. However if people consume a very high carbohydrate diet, especially for at least three days after first depleting their muscle glycogen levels, it is possible to double this normal glycogen content, ensuring that a longer period of exercise can be sustained before it is used up. This is known as *carbohydrate loading*, or glycogen supercompensation, and is often used by distance especially, marathon runners before important running events.

6. GLYCOGEN AND MUSCLE TISSUE:

Glycogen occurs as granules in the muscle cells as insoluble components of the cell. It is the most important source of carbohydrate energy. In red muscles and in muscles that are not working extremely hard, it is likely that most of the energy is supplied via the tricarboxylic acid cycle and the mitochondrial electron transport chain (aerobic respiration). This system provides a large quantity of ATP molecules per molecule of substrate utilized and allows for the complete conversion of substrate to carbon dioxide and water. The mitochondrial system, however, requires oxygen and in some instances, when the muscle is under heavy stress, oxygen is not available in sufficient amounts to maintain mitochondrial function. The anaerobic glycolytic system then becomes predominant. This is especially likely in white muscles, which are generally involved in sporadic bursts of activity requiring very large amounts of energy. During anaerobic glycolysis, glycogen is converted through a series of phosphorylated six-carbon and three-carbon intermediates to pyruvate, which is then reduced to lactate. This system requires the cofactor NAD+, and it continually regenerates the NAD+ required. The terminal enzyme of the sequence, lactate dehydrogenase, is principally responsible for regeneration of NAD+. In anaerobic glycolysis, ATP production is much less efficient than it is in aerobic respiration. For example, anaerobic glycolysis yields only 2 or 3 moles ATP per mole of glucose, whereas aerobic respiration yields 36 or 37 moles ATP. Also, anaerobic glycolysis results in incomplete oxidation of substrates and accumulation of lactate. Lactate can penetrate the cell membrane, and much of it is removed to the blood, where it goes to the liver and is used in the resynthesis of glucose. The glucose is then carried back to the muscle, where glycogen is eventually produced.

Glycogen is depleted by several stress conditions, and in general, it is desirable to minimize these conditions as much as possible. Stress conditions include exercise, fasting, hot and cold temperatures, and fear. Increased glycogenolysis and lipolysis generally accompany stress, but not all animals react in the same way or to the same degree to any one of these stresses. Within a given species, the response to stress may vary among breeds or between sexes. Heat stress affects the quality of chicken breast muscle. Heat-stressed birds exhibit lower ultimate pH values and are tougher than unstressed birds, and they have lower water-holding properties. It is now widely recognized that stressed animals are likely to have a subnormal content of glycogen in their muscles, whereby, post-mortem, the pH of their flesh fails to attain acidic values and the attributes of eating quality in the meat will be adversely affected. The “ultimate” or final pH that a muscle tissue attains is also important. A low ultimate pH in beef provides resistance to the growth of microorganisms and a normal color. Sometimes a high ultimate pH occurs. Long-term stress before slaughter or starvation uses up the glycogen so that less lactic acid is formed after slaughter resulting in an abnormal muscle condition in which it remains dark purplish-red on exposure to air instead of a bright red colour. This is termed dark, firm and dry (DFD) in the case of pigs and “dark cutting” in beef. The condition is rarer in lambs. Such meat and products made with it have a pH above 6.0 and spoil quickly since the low acidity favours rapid bacterial growth.

If animals are stressed immediately prior to slaughter as when they are roughly handled or fight one another the muscle glycogen is released into the blood stream and, after slaughter, is rapidly broken down to lactic acid while the carcass is still warm. This high level of acidity causes a partial breakdown of muscle structure which results in pale, soft and exudative meat (termed PSE) - a condition mostly occurring in pigs. The meat losses some of its water-binding capacity which is so important in certain types of meat processing.

PSE and DFD meat are perfectly safe to eat but limited in their processing capacity. PSE meat has higher drip and cooking losses due to the reduced water-binding capacity (WBC). As well as the pale colour the meat has less flavour than usual. DFD meat has normal or increased WBC and so is suitable for scalded/boiled sausages and other cooked products but it has poor meat flavour. While there is no remedy for these defects in the meat, DFD and PSE meats can be blended with normal meat for

the preparation of products of good quality.

After slaughter as the glycogen in the tissues is exhausted rigor mortis sets in and the whole carcass become stiff. This is due to the contraction of the muscle fibres when the actin filaments of the muscle fibres slide inwards between the myosin filaments so shortening the myofibrils.

As far as meat quality is concerned, perhaps the most important manifestation of the post-mortem denaturation of the muscle proteins is their loss of water-holding capacity, because in practice it is a more universal phenomenon than discoloration. The point of minimum water-holding capacity of the principal proteins in muscle (i.e. the isoelectric point) is 5.4–5.5. Since, the production of lactic acid from glycogen, at any given temperature and rate, will generally cause the pH to reach 5.5, normal meat will lose some fluid ('weep'). This will, obviously, be less if the ultimate pH is high, however. The post-mortem pH of meat will be determined by the amount of lactic acid produced from glycogen during anaerobic glycolysis, and this will be curtailed if glycogen is depleted by fatigue or fear in the animal before slaughter. Since pH is an important determinant of microbial growth, it will be obvious that the ultimate pH of meat is significant for its resistance to spoilage. Most bacteria grow optimally at about pH 7 and not well below pH 4 or above pH 9, but the pH of maximal growth is determined by the simultaneous operation of variables other than the degree of acidity or alkalinity itself. Some of the bacteriological enzymes which cause spoilage may have different optima from that of the organism itself. Thus, whereas bacterial proteolytic enzymes operate best near neutrality, the enzymes which attack carbohydrates tend to have optima below 6; and organisms such as lactic acid bacteria, of which the predominant activity is carbohydrate breakdown, have optima between pH 5.5 and 6. In fresh meat, the encouragement given to bacteria by a high ultimate pH, especially in the deeper areas of the carcass which are slow to cool, causes 'bone taint'. Muscle which has a high ultimate pH because of a deficiency of glycogen at death, also lacks the glucose which is produced by amylolysis postmortem, albeit in much smaller quantity than lactic acid by glycolysis. In the absence of a readily available carbohydrate substrate, micro-organisms attack amino acids immediately, causing early spoilage, including off-odours. Proper resting before slaughter, or the feeding of sugar, builds up muscle glycogen, giving a lower ultimate pH and increasing storage life.