A student experiment

Carbohydrate is stored as glycogen in both muscles and the liver. It is liver glycogen that is the first line of defense when blood glucose concentration falls. That large glycogen reserve in our muscles cannot be released to the circulation. Hepatic gluconeogenesis takes over after some hours, using lactate and amino acids to form glucose. It should be emphasized that the level of blood glucose will be maintained within narrow limits <u>as long as a source of amino acids is available</u>. The only real question is ”will these come from me or my food"? The body's proteins are its largest "glucose reserve". Without an adequate blood sugar level, (<u>> 2.5-3 mmol/l)</u> brain activity is impaired. Interestingly. it is the transport of glucose into the brain that becomes rate-limiting at low blood glucose levels, not the initial phosphorylation og glucose by hexokinase.

The question addressed in this student exercise is "does the choice of diet after a fast alter the liver's ability to replace glycogen used to replace blood glucose”? All of the rats used in this exercise were fasted overnight. Three of these were then offered bread (a carbohydrate-rich diet), dried fish (a high-protein diet) or margarine (a fat-rich diet) and allowed to eat for one day. Their livers were then removed and glycogen was extracted. This stored carbohydrate represented the glucose these animals obtained from the diets <u>that was in excess of their immediate energy needs</u>.

Our students analyze the glycogen content of the liver extracts and usually get the following results:

Diet	Liver glycogen mg/gram liver
24 hour fast	7.8
fast + 24 h. bread	66.8
fast + 24 h. dry fish	21.3
fast + 24 h. margarine	7.1

How do we explain these results?

- **Fast**: As shown in the figure above, ingested carbohydrates are rapidly used in rats (and humans). Liver glycogen becomes the major source of circulating glucose within 2-4 hours after a meal; the so-called postpranial period. The very low levels of liver glycogen seen after a day's fast follow the extensive use of this material to stabilize blood glucose. Since the fasting period was so long (a day is a long time for a rat), the animal had to produce blood sugar from amino acids taken from its own proteins.
- **High Carbohydrate Diet:** Bread is an excellent source of starch and is a carbohydrate supply limited only by appetite. This rat ate extremely well, literally making a cave in the bread and living in this delicious tunnel of food. Starch is absorbed as glucose and is rapidly stored as glycogen in both muscles and the liver. It is interesting to note that the level reached following refeeding after a fast exceeds that normally seen. It would seem that the body learns of experience, guarding itself against another fast. This effect lasts for two days or more in humans and is seen in both liver and muscle. The "overshoot phenomena" of glycogen levels is well-known in athletic circles and is used by many to build up an energy reserve before sports competitions.
- **High Protein Diet:** The fish product used in this experiment was prepared from cod, a lean fish. This animal received almost only protein as an energy source in its diet. Never the less, we see that this animal managed to increase its liver glycogen level markedly, indicating that it was able to produce glucose from the fish protein. Furthermore, there was a good bit in excess of that was used as an energy source and this was saved as glycogen. That works in rats, but not for you and me. Rats have a proportionally larger liver than humans. This allows a much higher rate of gluconeogenesis and ureogenesis than that seen in humans. People who try to survive on high-protein low-fat diets experience weakness, fatigue, intestinal distress and weight loss. This has been called "rabbit starvation" and is discussed here. The mechanism lying back of the liver's limited ability to convert amino acids to glucose and glycogen is also taken up.
- **High Fat Diet:** Margarine is essentially a pure fat product, consisting almost entirely of triglycerides. The rat fed margarine had a very low liver glycogen level. It essentially experienced a two-day carbohydrate fast. Glucose cannot be synthesized from the fatty acids resulting from the breakdown of triglycerides. This results from the fact that fatty acid

oxidation produces solely 2-carbon fragments. These are further metabolized in the citric acid cycle. Here, two molecules of CO_2 are lost from the cycle for each 2-carbon fragment that enters. Therefore, no net synthesis of the precursors of glucose can take place. The fat-fed rat could not obtain glucose from the diet and. presumably, had to use its endogenous proteins to support the level of blood glucose.

- **High Protein-High-Fat Diet:** We have not experimented with this kind of diet here but a few comments are required. Diets comprised of 20-30% protein and with little or no carbohydrate have been known for hundreds of years. Such a diet can function well as a source of energy for humans. We do not need to eat carbohydrates at all; we **can** produce all the glucose we need from dietary proteins. The catch is that we can only get something like 1000-1500 kilocalories daily from glucose made from amino acids. We must cover at least half of our caloric requirements from fat in addition to proteins. This is the makeup of pemmican, the meat and fat mixture used by Indians, Eskimos and Lapps for thousands of years. This is discussed in the references cited earlier (click here and here).
- The enormous population increase that has followed the development of agriculture has made it quite impossible for **all of us** to survive on such diets. There is simply not enough animal protein available to support the world's population.