Brain Oxidation Ketone Bodies Spare Protein in Long Starvation

The accompanying graph shows the amount of urea excreated per day in subjects first maintained for a short period of time on glucose as the only "food" source (Glucose 700 grams/day), and then fasted for various periods of time (Fasting 12 hours, Starvation 3 days, Starvation 5-6 weeks). Urea excretion increased after a short (12 hour) fast, but then declined. Why?

If the pattern of fuel utilization that occurs during a brief fasting were to persist for an extended period, the body's protein would be quite rapidly consumed to the point where critical functions would be compromised. However, metabolic changes occur during prolonged fasting that conserve (spare) muscle protein. The figure shows the main features of metabolism during prolonged fasting (starvation). After 4 or 5 days of fasting, when the body enters the starved state, muscle decreases its use of ketone bodies and depends mainly on fatty acids for its fuel. The liver, however, continues to convert fatty acids to ketone bodies. The result is that the concentration of ketone bodies raises in the blood. The brain begins to take up these ketone bodies form the blood and to oxidize them for energy. Therefore, the brain needs less glucose than it did after an overnight fast. Glucose is still required, however, as a energy source for red blood cells, and the brain continues to use a limited amount of glucose, which it oxidizes for energy and utilizes as a source of carbon for the synthesis of neurotransmitters. Overall, however, glucose is "spared" (conserved). Less glucose is used by the body, and therefore, the liver needs to produce less glucose during prolonged fasting than during shorter periods of fasting.

Because the stores of glycogen in the liver are depleted by about 30 hours of fasting, gluconeogenesis is the only process by which the liver can supply glucose to the blood if fasting continues. Amino acids, produced by the breakdown of muscle protein, continue to serve as a major source of carbon for gluconeogenesis. However, as a result of the decreased rate of gluconeogenesis during prolonged fasting, muscle protein is "spared", i.e., not as much muscle protein is degraded to supply amino acids for gluconeogenesis.

During the conversion of amino acid carbon to glucose by the process of gluconeogenesis, the nitrogen of the amino acids is converted to urea. Consequently, because of decreased production of glucose, the production of urea also decreases during prolonged fasting compared to its production early in a fast.