LITERATURE REVIEW

General Consideration

In relation to exercise, fatigue can be generally defined as the inability to continue to exercise at a given intensity. The degree of ability to withstand fatigue is inherited, and the basis of the fatigue pattern is in each individual's constitution. In general, the main metabolic causes of fatigue in physical activity are: 1) depletion of phosphocreatine in the muscle, 2) accumulation of lactic acid in the muscle, 3) depletion of glycogen in the muscle and 4) depletion of blood glucose (Shephard and Astrand, 1992). In contrast to fatigue, endurance is the ability of the body to undergo prolonged activity. It primarily depends on the various aspects of cardiac efficiency, which in turn affects the performance of other portions of the human organism. Many factors have influence on improving endurance performance. One of the important factors to prevent athlete from injury during activity is the diet. If the physical stresses which are imposed by strenuous training and competition are not adequately replenished by good nutrition, a proper physical restoration cannot be achieved. Thus, the coach and athletic trainer must consider nutrition education as a means toward optimal performance and injury prevention or, when injuries do occur, toward optimal healing (Arnheim, 1987).

During exercise, energy for contractile units in the muscle fiber is obtained from the hydrolysis of adenosine triphosphate (ATP). However, the amount of ATP in the muscle is limited. ATP must be regenerated from adenosine diphosphate (ADP) and phosphate; this occurs due to the oxidation of fuels. Fat and carbohydrate, or more specifically triglyceride and glycogen are the primary muscular fuels that are metabolized during prolonged exercise (Shephard and Astrand, 1992; Robergs and Robert, 1996).

The quantity of various fuel substrates utilized varies as a function of availability, physical conditioning, exercise intensity, and exercise duration. At work rates above 60% Vo_{2max} there is an almost linear relationship between exercise intensity and the rate of muscle glycogen utilization (Hermansen, *et al.*, 1967; Hultman, *et al.*, 1971; Sherman, 1995 ; Shephard and Astrand 1992; Pendergast, *et al.*, 1996). However, prolonged exercise at a moderate intensity (<50% Vo_{2max}) results in the increases of fatty acid uptake and utilization by muscles. Substrate utilization is commonly measured in terms of the respiratory exchange ratio (RER), the ratio of the volume of expired CO_2 to the volume of oxygen absorbed by the lungs per unit of time. A RER near 1.0 indicates that carbohydrate is the main substrate being consumed. When fat is the major fuel source, an RER near 0.7 is obtained. Resting muscle derives energy almost exclusively from the oxidation of fatty acids, with a minor amount of energy obtained from glucose. During exercise there is a shift from the consumption of fat to carbohydrate to meet energy needs. Accordingly, the rise of RER with exercise indicates a shift to carbohydrate

metabolism. Generally, carbohydrate is the principle source of energy during the initial onset (<2min) of exercise. As exercise continues, depending on intensity, fatty acid will be consumed in conjunction with carbohydrate to meet energy needs. Thus, RER will initially be high and fall toward 0.7 as the contribution of fatty acids increases (Wolinsky and Hickson, 1994).

Influence of Carbohydrate Diet on Endurance Exercise

During prolonged exercise, the fuel reserves of the body are mobilized to provide the energy required for muscular contraction. Carbohydrate provides the majority of energy in the diets of most people. Dietary carbohydrates have by convention been given an energy value of 4 kcal/g (17 kJ/g). Stored carbohydrate energy is located in muscle or liver in the form of glycogen, or in the blood in the form of glucose. As exercise intensity increases to levels greater than 60% of Vo_{2max}, the dependence on muscle glycogen metabolism for energy increases. Many researchers reported that during prolonged running, muscle glycogen is mainly reduced in type I, slow twitch muscle fibers, and type IIa fast contracting oxidative muscle fibers until fatigue (Hermansen, *et al.*, 1967; Gollnick, *et al.*, 1972; Costill, *et al.*, 1973; Sherman, 1995). Thus, dietary manipulations that alter pre-exercise muscle glycogen concentration, or those that reduce the rate of muscle glycogenolysis during exercise, have the positive potential to affect physical performance. It is hypothesized that a relatively high intake of dietary carbohydrate is necessary to

maintain adequate body stores of carbohydrate for preserving athletic training and performance capabilities.

Experimentally, the subjects could tolerate the 75% work rate for 115 min after a normal mixed diet giving an initial glycogen content of about 100 mmol/kg wet muscle. In addition, when the glycogen concentration was reduced after the subject spent 3 days on an extreme fat and protein diet, the exercise time to exhaustion was only about 60 min. In contrast, after 3 days on a carbohydrate rich diet, the subject's glycogen content became higher, and the time on 75% work rate could then be prolonged to about 170 min on the average. Bergstrom, *et al.* (1967) demonstrated that at a work rate of about 75% Vo_{2max}, the larger the initial muscle glycogen stores, the longer the subject could continue to exercise at this load. It was further observed that the most pronounced effect was obtained if the glycogen depots were first emptied by heavy prolonged exercise and then maintained low by giving the subject a diet low carbohydrates, following by a few days with a diet rich in carbohydrates.

Hermansen, *et al.* (1967) demonstrated that reduction in muscle glycogen during bicycle exercise was linearly related to Vo_{2max}. and the subjects were unable to continue pedaling when the muscle glycogen content was practically zero. Also, Neufer, *et al.* (1987) observed that subjects fed a solid carbohydrate supplement 5 min before the beginning of exercise had significant improvement in performance in a ride to exhaustion. Furthermore, Brewer, *et al.* (1988) demonstrated that

endurance capacity during treadmill running could be improved by supplementing normal mixed diets with either complex or simple carbohydrates. The complex carbohydrate group improved their running times by 26%, and the simple carbohydrate group improved by 23%. Based on these findings, it may be implied that the capacity for prolonged strenuous work is limited by muscle glycogen.

In prolonged athletic events in which the work rate exceeds about 75% Vo_{2max}, not only endurance but also speed, are affected by the initial muscle glycogen content. Williams, *et al.* (1992) reported that dietary carbohydrate loading improved endurance performance during 30 km treadmill running. Although there was no overall improvement in performance time for carbohydrate group, but this group ran faster during the last 10 km of the simulated race. Furthermore, eight of nine runners in the carbohydrate group had faster times for 30 km than during their first attempt, and had better times than the control group. Conclusively, the pre-exercise carbohydrate feeding delays fatigue and improves work output by maintaining carbohydrate availability. An increased carbohydrate availability presumably allows maintenance of the rate of carbohydrate oxidation at a level sufficient to maintain a high rate of energy expenditure especially during the later stage of exercise (Sherman, 1995; Wright, *et al.*, 1991). Also, it has been demonstrated that carbohydrate feeding improved performance by facilitating glycogen synthesis in type II muscle fibers during exercise (Sherman, 1995).

Although depletion of muscle glycogen stores is associated with exhaustion, it has been suggested that the development of hypoglycemia may also be an important factor. The amount of energy derived from blood glucose increases as a function of intensity/duration of exercise. The mechanisms responsible for the enhanced uptake of glucose by muscle during exercises remain uncertain. There is evidence that muscle contraction induces an increased uptake of glucose (Wallberg-Henriksson and Holloszy, 1984). The available blood glucose is derived from hepatic glycogenolysis and gluconeogenesis. The shift to blood glucose utilization results in an increased rate of glycogen breakdown by the liver. During prolonged exercise at high intensity, hepatic glycogen stores will be depleted. Consequently, hepatic glucose production is less than peripheral utilization and hypoglycemia results. Fatigue occurs when blood glucose declines to hypoglycemic concentrations. Although the muscle may well be involved, it appears that fatigue in such events can also be related with the brain. The brain interprets the decrease in blood glucose level as a danger signal and steps are taken to decrease power output (Shephard and Astrand,1992). Pruett, (1970) observed that subjects who exercised to exhaustion at 70% Vo_{2max} had blood glucose level 37.5% lower than pre-exercise levels. Several studies have shown that during exercise there is a fall in blood glucose from the beginning of exercise; however blood glucose concentrations are almost significantly higher after carbohydrate diets than after the mixed diet (Bergstrom, *et al.*, 1967; Coyle, *et al.*, 1986; Wright, *et al.*, 1991). There is also a report that high carbohydrate diet is apparently sufficient to maintain normal blood

glucose throughout the exercise (Simomsen, *et al.*, 1991). It is most likely that the high rate of carbohydrate oxidation during exercise is due to the greater availability and utilization of blood glucose. Therefore, dietary manipulations that elevate the pre-exercise concentration of liver and/or muscle glycogen or that provide a source of blood glucose during exercise have the potential to favorably influence athletic training and performance capabilities. However, a high carbohydrate diet has the potential to enhance insulin action. Consequently, a rapid decrease in blood glucose and a diminution in lipolysis are not only possible but also a greater carbohydrate utilization may occur during early stages of sustained exercise. This metabolic response to high carbohydrate ingestion may rapidly deplete the body's carbohydrate storage and contribute to premature fatigue (Okano, *et al.*, 1996). Experimentally, carbohydrate loading prior to exercise does not result in a sparing of endogenous carbohydrate stores during exercise but only "spares fat" (Bosch, *et al.*, 1993). Carbohydrate ingestion during exercise only slows the rate of liver glycogen breakdown (Bosch, *et al.*, 1993; Bosch, *et al.*, 1994; Coyle, *et al.*, 1984). Additionally, carbohydrate appears to influence blood lactate concentration (Kelman, *et al.*, 1975). Blood lactate is higher after the high carbohydrate diet than on the normal diet. It has long been suspected that lactate accumulation plays a role in the development of fatigue (Bergstrom, *et al.*,1967; Hultman, *et al.*, 1967; Asmussen, *et al.*, 1974). An increase of lactic acid in the muscle may impair the function of the muscle cells. Furthermore, the increased blood lactate concentration may inhibit the mobilization of free fatty acids (FFA) which in turn

suppresses fat metabolism by limiting the supply of FFA substrate to the muscle cell (Holloszy and Coyle, 1984; Astrand and Rodahl,1986). Additionally, some researchers reported that carbohydrate loading was of no benefit to performance during prolonged exercise (Sherman, *et al.*, 1981; Devlin, *et al.*, 1993).

Influence of Fat Diet on Endurance Exercise

Fat serves several physiologic functions in the body. It is the most concentrated source of energy, supplying twice as much calories (9 kcal/g) as either carbohydrate or protein. Fats and carbohydrates are composed of the same elements: carbon, hydrogen, and oxygen. Glycerides, the most common form of fat, compose of one, two, or three fatty acid molecules which attach to a molecule of glycerol. The majority of glycerides found in food and in the body is triglyceride, which molecule consists of three fatty acids and one glycerol, and is stored in adipose tissues, liver, and skeletal muscles.

Shifts in substrate utilization from carbohydrate to fat, during prolonged low intensity (Hambleton, *et al.*, 1980; Hintz, *et al.*, 1987), moderate (Oldham, *et al.*, 1990), or high intensity exercise (Duren, *et al.*, 1987; Harkins, *et al.*, 1992) have been suggested. This implies that not only muscle glycogen but also muscle triglyceride are of importance for the energy metabolism in man during exercise (Forgberg, *et al.*, 1971). Dietary and pharmacological studies have shown that increasing

availability and oxidation of fatty acid during exercise reduces the degree of glycogen depletion (Rinnies, *et al.*, 1976; Hickson, *et al.*, 1977). This suggests that there is potential for exogenous fat to reduce carbohydrate oxidation and consequently delay fatigue during endurance exercise (Costill, *et al.*, 1977; Hickson, *et al.*, 1977). Rinnies, *et al.* (1976) reported that increasing concentration of fatty acids leads to an increased fatty acid oxidation accounting for the slower glycogen depletion during prolonged exercise. Consequently, there was a small decrease in blood glucose as well as a smaller rise in blood lactate concentration in the animals with increased plasma FFA than in the control group. This was consistent with the work of Terblanche, *et al.* (1981) who demonstrated that carbohydrate feeding before exercise was ineffective in protecting against depletion of glycogen, probably because the elevation of plasma glucose stimulated insulin secretion, resulting in the inhibition of lipolysis and of FFA release from adipose tissue. On the other hand, an elevation of plasma FFA has been shown to spare muscle and liver glycogen, protecting against hypoglycemia and increasing endurance for prolonged strenuous exercise (Hickson, *et al.*, 1977). However, Okano, *et al.* (1996) suggested that a single high carbohydrate meal or high fat meal given 4 hours before exercise influenced fuel utilization in the initial stage of prolonged exercise while it had little effect on endurance capacity, heart rate, and the rating of perceived exertion. Accordingly, chronic exposure to a high fat diet increases the capacity of the muscle to oxidize fat has been proposed (Jansson and Kaijser, 1982; Schrauwen, *et al.*, 1997). Experimentally, following long term use of high fat diet, the muscle fibers

undergo a shift of energy substrate from carbohydrate to fat, which spares muscle glycogen during physical exercise (Miller, *et al.*, 1984; Simi, *et al.*, 1991). This is consistent with the reports that fat combustion during exercise is higher after a fat rich diet than after a carbohydrate rich diet (Simi, *et al.*, 1991) or a normal diet (Miller, *et al.*, 1984). Likewise, Muoio, *et al.* (1994) suggested that the muscle cells had an ability to oxidize more fat during exercise, provided that the carbohydrate supply was low during the days before exercise.

From the view point that muscle glycogen is spared by elevation of plasma fatty acid during exercise leads to an interesting question whether chronic exposure to high fat diets influences exercise performance. Phinney, *et al.* (1983) reported that endurance was not reduced in subjects who were allowed to adapt to a high fat diet for 4 weeks in spite of having lower muscle glycogen than normal. Early studies demonstrated that despite these large differences in substrates and hormone concentrations in plasma between high fat diet and high carbohydrate diets there were no differences in performance on the time trial (Whitley, *et al.*, 1998). However, Miller, *et al.* (1984) found that rats exposed to a prolonged high fat diets had increased activity of mitochondrial enzyme responsible for β-oxidation and were able to endure a high intensity work bout longer than ad libitum fed animals. This is in agreement with the report that high fat diet substantially improve maximal oxygen consumption (Vo_{2max}) The mechanism behind the increase in Vo_{2max} is not obvious. It can be suppressed that part of the difference in Vo_{2max} could be explained either by the greater oxygen

consumption in relation to energy yield for fat compared with carbohydrate oxidation or by the increased levels of nor-epinephrine and epinephrine has been observed after a fat diet (Simi, *et al.*, 1991; Boyadjiev, 1996). Additionally, Lambert, *et al.* (1994) suggested that 2 weeks of high fat diet were sufficient to alter endogenous carbohydrate stores and relative rates of substrate oxidation in the absence of marked ketosis. From this view point, the major metabolic consequences of the adaptations of muscle to endurance exercise are a slower utilization of muscle glycogen and blood glucose with a greater reliance on fat oxidation, it has been inferred that animals and humans adapt to high fat diet in much the same way as they do to endurance training (Phinney, *et al.*, 1983; Muoio, *et al.*, 1994; Lambert, *et al.*, 1996; Miller, *et al.*, 1984; Simi, *et al.*, 1991). The ability to utilize fat as a fuel is a function of the oxygen transport capacity, and the choice of fat utilization for the exercising muscle depends on the work rate in relation to the individual's maximal oxygen uptake. The greater Vo_{2max} attained, the greater the percentage contribution of fat to energy metabolism at a given work rate. Since physical training increases Vo_{2max}, it also increases the facility for utilizing fat as a source of muscular energy during certain types of activity (Costill, *et al.*, 1990). In addition, a lower RQ (respiratory quotient) in trained as compared to untrained subjects indicates a relatively larger fat combustion in trained subjects (Hermansen, *et al.*, 1967). Issekultz, *et al.* (1965) showed that at the same work rate on the treadmill, the utilization of FFA rose or declined in trained and untrained dogs, respectively. One reason for this difference was that training enhanced

the O_2 supply to the active muscle cells, so that the exercise, in the case of the trained dog, might be performed to a greater extent aerobically. Consequently, less lactic acid was formed in the trained dog. The increase of lactic acid production in untrained dogs inhibited the FFA release from the adipose tissue. A resulting decrease of plasma FFA results in the decreased turnover rate or decreased rate of utilization of FFA.

In 1991, Simi, *et al.* demonstrated that the enzymatic adaptation in rat skeletal muscle observed after intensive endurance training could be enhanced by superimposition of high fat diet. This was supported by the work of Boyadjiev (1996) who demonstrated that a high fat diet improved the submaximal running endurance and if combined with submaximal training increased its effect several fold. In addition, high fat diet increased Vo_{2max}, and training made it even greater, but the effect on Vo_{2max} was the greatest when the two were used in combination. Also, under the influence of high fat diet the activities of the key enzymes for the carbohydrate and fat metabolism as expression of an adaptation process in the aerobic systems of muscles increased and the muscle fibers underwent a shift of the energy substrate from carbohydrate to fat, both in fast and slow oxidative muscular fibers which spares muscle glycogen during physical exercise. Although the potential effects of high fat diets on the aerobic working capacity of muscles have been well documented. One of the drawbacks in promoting dietary fat as an ergogenic aid is the strong relationship between dietary fat and fat body deposition. (Miller, *et al.*, 1984; Oscai, *et al.*, 1987). Thus, whether or not

the combination of high fat and carbohydrate loading in the endurance trained individual will optimize the endurance performance is of current interest.