2.4.2 Metabolite Accumulation

Lactic Acid Accumulation (Lactic Acidosis)

Lactate accumulates due to production being greater than its removal. At a physiological pH, lactic acid, a strong organic acid, dissociates a proton (H^+). It is the H^+ rather than the lactate that causes pH to decrease. Although the lactate accumulation in blood is directly related to H^+ accumulation in blood, because the muscle cell membrane exports both the lactate anions and protons into the blood, in muscle the cause of acidosis is different. All the glycolytic intermediates of glycolysis are weak organic acids and dissociate protons, while the degradation of ATP also results in H^+ formation. This means that lactate accumulation is associated with acidosis for more than one reason, but it is important to recognize that it is unbuffered protons (i.e., H^+) and not lactate anions that pose difficulties for the performer. The actions mentioned above can have several negative effects. Within the muscle, the lower pH may inhibit phosphofructokinase (PFK) and ATPase and slow glycolysis. H^+ may also act to displace Ca^{2+} from troponin, thereby interfering with muscle contraction. A low pH may also trigger pain receptors (Brooks et al., 1996).

Phosphate and Diprotenated Phosphates

Phosphagen depletion during exercises results in phosphate (Pi, or HPO_4^{2-}) accumulation. Studies on isolated muscle and enzyme systems indicate that phosphate behaves much like hydrogen ion in interfering with glycolysis (PFK) and excitation-contraction coupling (Ca^{++} binding to troponin) (Brooks et al., 1996).

Calcium Ions

The accumulation of Ca^{2+} within muscle mitochondria during prolonged exercise may be more debilitating than the decrease in cytoplasmic pH from lactic acid formation. Some of the Ca^{2+} liberated in muscle from the sarcoplasmic reticulum during excitation-contraction coupling may be sequestered by mitochondria. Some increase in mitochondrial Ca^{2+} is probably beneficial, as it stimulates the dehydrogenases of the tricarboxylic acid or Krebs (TCA) cycle. However, Ca^{2+} excretion from mitochondria is energy

linked, and so, too much Ca^{2+} sequestration results in oxygen consumption and saps the mitochondrial energy potential for phosphorylating ADP to ATP (Brooks et al., 1996).

2.4.3 O_2 Depletion

The inadequacy of circulatory oxygen delivery to muscle can result in fatigue. Athletes with impaired circulatory or ventilatory function, those engaged in exercise at high altitudes, or those engaged in strenuous exercise at sea level can fall short in the balance between muscle respiratory requirement and the actual oxygen supply.

The effects of inadequate oxygen supply or utilization can be represented by increased lactate production or decreased CP levels, or both. This indicates that inadequate oxygenation of contracting muscle can result in at least two fatigue-causing effects.

The utilization of oxygen in the mitochondria is associated with the liberation of free radicals, which present a real threat to the mitochondria. Research has supplied evidence of mitochondrial damage due to free radical accumulation at the point of fatigue (Brooks et al., 1996).

2.4.4 Central and Neuromuscular Fatigue

Central Fatigue:

The CNS (central nervous system) would be indicated in fatigue if there were a reduction in the number of functioning motor units involved in the activity; or a reduction in motor unit firing frequency. There is evidence both for and against, the concept of central fatigue.

Peripheral Fatigue:

The vast majority of evidence points to the periphery as the most likely site of fatigue. Here neural, mechanical or energetic events could hamper tension

development. Fatigue due to neural factors could be associated with failure at the neuromuscular junction, the sarcolemma, or the transverse tubules.

1. Neuromuscular Junction

   The action potential appears to reach the neuromuscular junction even when fatigue occurs, suggesting that the potential "weak link" is a depletion of acetylcholine or a reduced excitability of the motor end plate. Evidence suggests that the neuromuscular junction is not the site of fatigue (Powers and Howley, 1994).

2. Sarcolemma and Transverse Tubules

   Evidence shows that stimulating the muscle at a high rate can lead to a slowing of the action potential waveform along the sarcolemma and the transverse tubules. This might be related to an accumulation of K^+, which would increase the excitation threshold of the membranes (Powers and Howley, 1994).

The primary mechanical factor that may be related to fatigue is the cross-bridge. The action of the cross-bridge depends on:

- the functional arrangement of actin and myosin
- Ca++ being available to bind with the troponin to allow the cross-bridge to bind with the active site on actin, and
- ATP, which is needed for both contraction and relaxation (Powers and Howley, 1994).

2.4.5 Psychological Fatigue

At present one can only begin to address the question of how afferent input during competition (pain, breathlessness, nausea, audience response) can influence the physiology of the CNS. A behaviorial (psychological) approach to understanding these questions may be beneficial. Through training some athletes learn to minimize the influences of distressing afferent input and therefore approach performance limits set in musculature. In order to perform optimally in an activity, the experiences of prior training and competition are

often necessary for an athlete to evaluate afferent inputs properly and to utilize them in determining the maximal rate at which physiological power can be meted out during competition (Brooks et al., 1996).

2.4.6 The Heart as Site of Fatigue

In healthy individuals there is no direct evidence that exercise, even prolonged endurance exercise, is limited by fatigue of the heart muscle. Since arterial $P0_2$ is well maintained during exercise, and the heart in effect gets the first choice at cardiac output, the heart is well oxygenated and nourished, even at maximal heart rate. Because the heart is "omnivorous" in its choice for fuels, it can be sustained by either lactic acid (which rises in short-term work) or fatty acids (which rises in long-term work). During prolonged work which leads to severe dehydration and major fluid and electrolyte shifts, changes in plasma Na^+, K^+, or Ca^{2+} can effect excitation-contraction coupling of the heart. In these cases, cardiac arrhythmias are possible, and exercise is not advised (Brooks et al., 1996).

2.5 ERGOGENIC AIDS

The premise and promise of ergogenic aid use is rooted in antiquity and is based upon superstition and ritualistic behaviour of athletes who perceive that past performances were predicted upon unique dietary constituents or dietary manipulation (Applegate and Grivetti, 1997). Coaches and athletes are continually searching for ways to gain the competitive edge and improve athletic performance. It is therefore not surprising that a variety of ergogenic substances and procedures are used routinely at almost all levels of competition. Williams (1998), estimated that approximately 89 brands of supplements exist which offer more than 300 products. Of these, 235 claim to contain unique ingredients that purportedly enhance growth and/or performance. Unfortunately, the marketing of such products depends on emotional appeal and is often loosely based on scientific evidence. Sadly, the climate generated from such tactics is one of dashed hopes and seldom-realized dreams. Overall, these disappointments only lead to a continued feeling of distrust toward the sports nutrition supplement industry as it seeks

the next blockbuster product (Earnest, 2001). Pharmacological agents are most often used by University and professional athletes, whereas nutrition supplementation and warm-up procedures are common to individuals who train for fitness and sport activities.

The term "ergogenic" relates to the application of a nutritional, physical, mechanical, psychological, or pharmacological procedure or aid to improve physical work capacity or athletic performance (McArdle et al., 1991). An ergogogenic aid, simply defined, is any substance, process, or procedure that may, or is perceived to, enhance performance through improved strength, speed, response time, or the endurance of the athlete. Another area of interest in ergogenic aids is to hasten recovery. The nature of the action of any supposed ergogenic aid may be elicited through the following:

- Direct action on muscle fibre;
- Counteraction of fatigue products;
- Fuel supply needed for muscular contraction;
- Affecting the heart and circulatory system;
- Affecting the respiratory system; and
- Counteraction of the inhibitory affects of the central nervous system on muscular contraction and other functions (Fox and Bowers, 1993).

Frequently ergogenic aids are thought of only as pharmacological agents that may be consumed to give the athlete an advantage. Pharmacological agents constitute only one of several classes of ergogenic aids. Others include nutritional (carbohydrates, proteins, vitamins, minerals, water, and electrolytes), physiological (oxygen, blood boosting, conditioning, and recovery procedures), psychological (hypnosis, suggestion, and rehearsal), and mechanical (improved body mechanics, clothing, equipment, and skill training) components.

In its broadest sense, one could call anything that can be related to an improvement in work or performance, or a delay in the onset of fatigue an

ergogenic aid. Ergogenic aids affect different people differently, as might be expected. For some, studies show a positive influence on work performance and for others, no affect whatsoever. What might prove effective with the athlete may prove inconsequential to the non-athlete and vice versa. Certain ergogenic aids may influence a person's endurance performance but may have little or no effect on activities requiring short bursts of strength and power (Fox and Bowers, 1993; Williams, 1983).

For the purpose of this review three main categories of ergogenic aids are distinguished namely: pharmacological and physiological aids and nutritional aids.

2.5.1 Pharmacological and Physiological Agents

Pharmacology can be described as the study of the distribution, actions, and fate of drugs in the body. A drug is any absorbed substance that changes or enhances any physical or psychological function in the body (Liska, 1990). If our body responds in some way to a substance, either physically, biochemically or mentally, that substance can be said to have a drug effect (Mottram, 1988)

The term "doping" is often used when describing the use of a substance to enhance performance and can be defined as follows: Doping is the administration of, or the use by a competing athlete, of any substance foreign to the body or of any physiological substance taken in abnormal quantity or taken by any abnormal route or entry into the body, with the sole intention of increasing in an unfair manner his/ her performance in competition. When necessity demands medical treatment with any substance, which because of its nature, dosage, or application is able to boost the athlete's performance in competition in an artificial and unfair manner, this is to be regarded as doping (Fox and Bowers, 1993). The clinical manipulation of natural substances in the body for the same purpose is also regarded as doping. The use of so-called masking agents and methods or agents to adulterate urine in order to prevent

the detection of prohibited substances is also regarded as a doping offence (MIMS, 1996).

The International Olympic Committee (IOC) Medical Commission and the International Amateur Athletics Federation (IAAF) rules state that a doping offence is committed when:

- A prohibited substance is found to be present within an athlete's body tissue or fluids;
- An athlete uses or takes advantage of a prohibited technique, or
- An athlete admits having used or taken advantage of a prohibited substance or prohibited technique.

The practice of using various pharmacological agents and drugs has raised much controversy and presents numerous ethical, legal and clinical questions. The indiscriminate use of pharmacological agents also poses the greatest threat to the health and welfare of the athlete. Most of the contemporary controversy centres on the use of anabolic/ androgenic steroids, human growth hormone, and blood boosting abuses. Other substances of concern include amphetamines and, to a lesser degree, bicarbonates, caffeine, analgesics, stimulants like decongestants and appetite suppressants, diuretics, beta-blockers, corticosteroids, and vitamins and minerals (Fox and Bowers, 1993; MIMS, 1996).

Blood Doping/ Blood Boosting

This is one of the techniques particularly used by endurance athletes to enhance their performance. The South African Institute for Drug Free Sport regard blood doping as a prohibited method and describe the method as follows: "Blood doping : means the administration of blood, red blood cells and/or related blood products to an athlete, which may be preceded by withdrawal of blood from the athlete, who continues to train in such a blood-depleted state" (South African Institute for Drug-Free Sport, 2002).

Further the American College of Sports Medicine position stand concerning blood doping clearly condemns the practice for sport while recognizing the scientific and medical value of infusion of autologous RBC (red blood cells). As with other banned practices, blood doping is considered to be unethical and, consequently, unjustifiable in sport (Fox and Bowers, 1993).

The medical risks include the development of allergic reactions, acute haemolytic reaction with kidney damage if incorrectly typed blood is used, as well as delayed transfusion reaction resulting in fever and jaundice, transmission of infectious disease, overload of the circulation, shock, septicemia, air embolism, and thrombosis (MIMS, 1996; Fox and Bowers, 1993).

With the procedure, usually between 1 to 4 units of a person's own blood (autologos) are withdrawn, the plasma is removed and immediately reinfused, and the packed red cells are placed in frozen storage. To prevent a dramatic reduction in blood cell concentration, each unit of blood is withdrawn over a 3 to 8 week period because it generally takes this long for the person to re-establish normal red cell levels. The stored cells are re reinfused 1 to 7 days before an endurance event. As a result, the red cell count and haemoglobin level of the blood is often elevated some 8 to 20%. This hemoconcentration relates to an average increase in haemoglobin for men from a normal 15g per 100ml of blood to 19g per 100ml (or from hematocrit of 40% to 60%). These hematologic characteristics remain elevated for at least 14 days. It is theorized that the added blood volume contributes to a larger cardiac output and that the red blood cell packing increases the blood's oxygen carrying capacity and thus the quantity of oxygen available to the working muscles. This would be beneficial to the endurance athlete, especially the marathoner, for whom oxygen transport is often a limiting factor in exercise (McArdle et al., 1991).

Scientific studies of blood doping and endurance performance have produced conflicting results. Several studies have shown that blood doping increases endurance performance between 13% and 39% (measured by a treadmill run to exhaustion) and maximal oxygen consumption between 5% and 31% in

both non-athletic and highly trained endurance athletes (Belko, 1987; Ekblom et al., 1973; Ekblom et al., 1976). An equal number of studies (mostly from earlier literature), however, have found no effects of blood doping on endurance performance, maximal oxygen consumption, heart rate responses during exercise, or perceived exertion (Cunningham, 1978; Pate et al., 1979; Videman and Rytomaa, 1977). An examination of research design differences clarifies much of the conflicting evidence. Two critical factors became apparent: (1) when between 800 and 1200ml of blood, or its equivalent, is reinfused (as opposed to 450 to 500ml), aerobic capacity and endurance increases and (2) when 5 to 6 weeks elapse before reinfusion, "positive" results also are seen (Fox and Bowers, 1993). It is now clear that blood doping reduces blood lactate levels during exercise and alters the lactate turn point to higher running speeds. These effects are likely to be the more important explanations for the increased running performance after blood doping. Blood doping may also enhance heat tolerance during exercise (Noakes, 1992).

The possibility that blood doping can be detected is raised by the work of Berglund and colleagues (Berglund, 1988; Berglund and Hemmingson, 1987). They showed that the measurement of serum levels of erythropoietin, iron and bilirubin can identify 50% of boosted athletes within seven days of blood doping. An alternative technique may be to measure the distribution of red blood cell sizes, as the reinfused cells are likely to be larger than the athlete's remaining red blood cells. Thus the size distribution of the athlete's red cells will probably show an abnormal distribution of large cells. However even this technique will be unable to detect what is likely to become the new form of blood doping in the 1990's – the use of erythropoietin to naturally stimulate the overproduction of the athlete's own red blood cells (Noakes, 1992).

Erythropoietin

Endurance athletes, e.g. cyclists and marathon runners have long known that they can improve their athletic performance by increasing the flow of oxygen to their working muscles. Another technique for boosting red blood cells became apparent in the late 1980's. Erythropoietin (EPO), a hormone produced by the kidneys, stimulates the production of RBC's under conditions

of hypoxia (chronic low oxygen tension in the blood) and anemia. It travels via the circulation to the bone marrow, where it stimulates the production of red cells. The rate of formation of new red cells, is, in part determined by EPO. Whenever the kidneys senses a decrease in the circulating red cells (oxygen tension), it releases EPO into the circulation, which then stimulates the bone marrow to produce more red cells (Hopkins, 2000). Injections of EPO are very effective, athletes can expect enhancements in endurance performance of 5% or more (Sawka et al., 1996; Birkeland et al., 2000).

The benefits of this technique is similar to those achieved by blood doping. The non-therapeutic uses of EPO poses a significant health risk. The inappropriate use of EPO increases the thickness or viscosity of the blood so that the blood has difficulty passing through small blood vessels, in essence simulating the disease of erythrocythemia and polycythemia. When this increased viscosity effect is combined with the dehydration that is encountered in competitive athletics, the viscosity of the blood increases further, producing sludging of the blood in the vessels. At hematocrit above 55%, the blood viscosity increases exponentially, thereby substantially increasing the risk of a coronary artery occlusion or a cerebral artery occlusion. Similarly, occlusions can occur in other blood vessels producing other complications. With this in mind, it has been speculated that EPO may have contributed to the unusually high number of deaths that have occurred in competitive cyclists from the Netherlands and Belgium (MIMS, 1996; Fox and Bowers, 1993; McArdle et al., 1991; Noakes, 1992).

Unfortunately there has been no dependable and fair test for EPO abuse. The International Cycling Union (UCI) now tests for the thicker blood by measuring the proportion of the red cells (the hematocrit or packed cell volume) in a blood sample. By itself, this test is not a good indicator of EPO abuse, because a few athletes have a naturally high hematocrit, while others can get a high proportion from altitude training. A cyclist exceeding the upper limit is therefore not banned for EPO abuse, but is simply not permitted to compete because of the health risk. In any case, cyclists can cheat the test. When told they are to be tested, apparently they have 10 minutes to report to

the medical team. A cynical informant claims that is long enough for an athlete to run 500ml of saline into a vein. By diluting the blood, the saline immediately brings the hematocrit down by a few percent. The normal hematocrit for "clean" elite cyclists is around 44% (Schumacher et al., 2000).

Oxygen

How important is oxygen to the healthy body? Many experts conclude that the lack of oxygen in human cells and tissue is linked to a vast variety of health problems and disease, and that supplemental oxygen therapies have remarkable physiological benefits. A diversity of beneficial oxygen therapies is being utilized today. What is oxygen therapy? Oxygen therapy is any supplemental process that safely increases the available dissolved oxygen content in the body. Therapies may also include the processes that enhance the body's ability use or promote oxygen absorption. Most treatments are generally expensive and should be administered or supervised by a licensed medical professional. Here are brief descriptions of some accepted oxygen therapies (Nu Science Corporation, 2001d):

- Bottled Oxygen: is often prescribed as inhalation therapy for serious bronchial and other respiratory problems.
- Hydrogen Peroxide Therapy (H_20_2): hydrogen peroxide is manufactured in the bloodstream to help fight bacteria, viruses, yeast, fungi and other invading pathogens. The ingestion of H_20_2 is extremely controversial because it can cause an adverse reaction in the digestive tract: excess hydrogen causes an unbalanced pH, as well as possibly produce dangerous free radicals. H_20_2 therapy should only be utilized under the direct supervision of a licensed health care professional

Studies have been conducted regarding the ergogenic effects of breathing oxygen (1) prior to exercise, (2) during exercise, and (3) during recovery from exercise (Fox and Bowers, 1993). It is common to observe athletes breathing oxygen-enriched or hyperoxic gas mixtures during times out, at half time, or following strenuous exercise. The belief is that this procedure significantly enhances the blood's oxygen carrying capacity and thus facilitates oxygen

transport to the exercising muscles. The fact is however, that when healthy people breathe ambient air at sea level, the haemoglobin in arterial blood leaving the lungs is about 95 to 98% saturated with oxygen. Thus, breathing high concentrations of oxygen could increase oxygen transport by haemoglobin to only a small extent, i.e., about 1 ml of extra oxygen for every 100ml of whole blood. The oxygen dissolved in plasma when breathing a hyperoxic mixture would also increase slightly from its normal quantity of 0.3ml to about 0.7ml per 100ml of blood. Thus, the blood's oxygen-carrying capacity under hyperoxic conditions would be increased potentially by about 1.4ml of oxygen for every 100ml of blood, with 1.0ml extra attached to hemoglobin and 0.4ml extra dissolved in plasma (McArdle et al., 1996). There is some evidence that breathing oxygen immediately prior to exercise has some beneficial effects on performance, provided that the exercise is performed while holding the breath. Studies in which oxygen was breathed prior to a non-breath-holding type of exercise show very little if any effect on performance (Fox and Bowers, 1993).

There is a rather large body of information indicating that breathing oxygen-enriched air (33 to 100% oxygen) has a beneficial effect on exercise performance (Allen and Pandolf, 1977; Hughes et al., 1968; Miller, 1952). Oxygen breathing during both light and heavy exercise has resulted in reduced blood lactic acid levels, heart rates, ventilation volumes, and a significant increase in maximal oxygen consumption. Since available evidence does not indicate that hyperoxic gas mixtures increase cardiac output, the increase in maximal oxygen consumption must be due to an expanded a-$v0_2$ difference. This may be partially explained by the fact that even a small increase in haemoglobin saturation during hyperoxia, as well as additional oxygen dissolved in the plasma, increases total oxygen availability during strenuous exercise where the total blood volume is circulated 4 to 7 times each minute. The increase in partial pressure of oxygen in solution breathing hyperoxic gas also facilitates its diffusion across the tissue-capillary membrane to the mitochondria. This may account for its more rapid rate of utilization in the beginning phase of exercise. When considering the increase in arterial oxygen content when breathing hyperoxic gas that is reported in the literature,

however, it appears that the maximum increase does not exceed 10% (Eiken and Tesch, 1984). In terms of exercise performance, the reduction in pulmonary ventilation commonly observed breathing hyperoxic gas would reduce the oxygen cost of breathing and theoretically liberate significant oxygen for the use by the working muscles. Evidence also suggests that hyperoxia increases local muscular performance in static and dynamic movements in which the central circulation does not appear to be a limiting factor. The proposed mechanism for this ergogenic benefit is that the local high oxygen pressure enhances the rate of energy release in the active muscle. Although the breathing of hyperoxic mixtures appears to offer positive ergogenic benefits during endurance performance, its practical application in sports seems limited. Even if an appropriate breathing system could be devised, its legality during actual competition is unlikely (Fox and Bowers, 1993; McArdle et al., 1991).

Although there is not a great deal of research on the practice of administering oxygen during recovery, any beneficial effects, either on the recovery process itself or on performance of a subsequent work-bout, are inconsequential. Research indicated that oxygen inhalation did not preferentially alter lactate removal. Although there may be a psychological effect, there is no physiological basis for use of oxygen during recovery (Fox and Bowers, 1993; McArdle et al., 1996).

$HB0_2$

In recent years, professional and university teams have started using hyperbaric oxygen therapy to treat sports injuries. From muscle contusions and ankle sprains to delayed-onset muscle soreness (Borromeo et al., 1997). Because of the importance of oxygen in the aerobic energy system, many athletes and researchers have also investigated the possible ergogenic effects of hyperbaric oxygen (Delaney and Montgomery, 2001).

Normally, 97% of the oxygen delivered to the body tissues is bound to hemoglobin, while only 3% is dissolved in the plasma. At sea level, barometric pressure is 1 ATA, or 760 mmHg, and the partial pressure of

oxygen in arterial blood ($Pa0_2$) is approximately 100 mmHg. At rest, the tissues of the body consume about 5ml of oxygen per 100 ml of blood. During hyperbaric oxygen treatments, barometric pressure is usually limited to 3 ATA or lower. The oxygen content of inspired air in the chamber is typically 95% to 100%. The combination of increased pressure (3 ATA) and increased oxygen concentration (100%) dissolves enough oxygen in the plasma alone to sustain life in a resting state. Under hyperbaric conditions, oxygen content in the plasma is increased from 0.3 to 6.6 ml per 100 ml of blood with no change in oxygen transport via hemoglobin. $HB0_2$ at 3.0 ATA increases oxygen delivery to the tissues from 20.0 to 26.7 ml of 0_2 per 100 ml of blood (Delaney and Montgomery, 2001).

Professional athletes have reportedly received hyperbaric oxygen before sports participation, believing that performance would improve. Contradictory findings have been reported regarding the effect of a single hyperbaric oxygen treatment on aerobic performance. A Yugoslavian study (Staples and Clement, 1996), demonstrated that hyperbaric oxygen prior to treadmill running to volitional exhaustion increased peak running velocity and maximal oxygen consumption when measured 30 minutes and 3 hours post treatment. $HB0_2$ was administered for 60 minutes at 2.8 ATA. Enhanced performance and $V0_2$ max were attributed to additional oxygen storage in skeletal muscle. However to their knowledge, this link has yet to be definitely established (Delaney and Montgomery, 2001). In contrast, two recent studies (James et al., 1993; Potera, 1995), reported no change in submaximal and maximal exercise performance following hyperbaric oxygen therapy. It is difficult to rationalize how prior hyperbaric oxygen could enhance performance. Tissue retention of oxygen following treatment is unlikely since tissue autoregulation reduces oxygen levels upon return to a normobaric, normoxic environment (Delaney and Montgomery, 2001). Only two human studies (Staples et al., 1999; Potera, 1995) have examined hyperbaric oxygen to alleviate exercise-induced fatigue. These research studies indicated that recovery from exercise-induced fatigue was not enhanced following a single hyperbaric oxygen treatment (Delaney and Montgomery, 2001). Hyperbaric oxygen treatments are not without risks.

Its side effects can be divided into two categories: pressure effects and oxygen toxicity

2.5.2 Nutritional Aids

There are three basic rules regarding nutrition. Firstly, the body requires essential nutrients: carbohydrates, proteins and fats (energy supplying nutrients) and the vitamins, minerals, trace elements and water that are necessary for the utilization of that energy. Second, these nutrients are contained in four basic food groups: (i) the meat, fish and meat substitute group; (ii) the fruit and vegetable group; (iii) the milk and diary produce group; and (iv) the bread and cereal group. Third, these four basic food groups should be eaten in specific portions each day (Noakes, 1992). The manipulation of the following is the most common usage of nutritional substances as ergogenic aids: carbohydrates, water and electrolytes and vitamin and mineral supplements.

Carbohydrates

Carbohydrates serve the primary function of supplying energy for cellular work. They are the only stored nutrient that can generate ATP anaerobically and aerobically depending on the availability of oxygen. Carbohydrates supply approximately half of the body's energy requirements during light and moderate exercise. Another important fact concerning carbohydrates is that they must continually be degraded via the "carbohydrate flame" so that lipid nutrient can be processed during activities such as marathon running which is prolonged and of high intensity (Meyer en Meij, 1996)

The breakdown of glucose is complex and involves three pathways:

1. glycolysis/ Embden- Meyerhoff pathway (within the cytoplasm of cell)
2. the Krebs cycle (occurs in the mitochondria of the cell)
3. electron transport chain (occurs within the mitochondria of the cell) (McArdle et al., 1991)

A simplified equation to represent the complete breakdown of glucose:

$C_6H_{12}O_6 \rightarrow 6\ H_2O + 6\ CO_2 + 38\ ATP + Heat$

The Krebs Cycle (Citric acid/ tricarboxylic cycle)

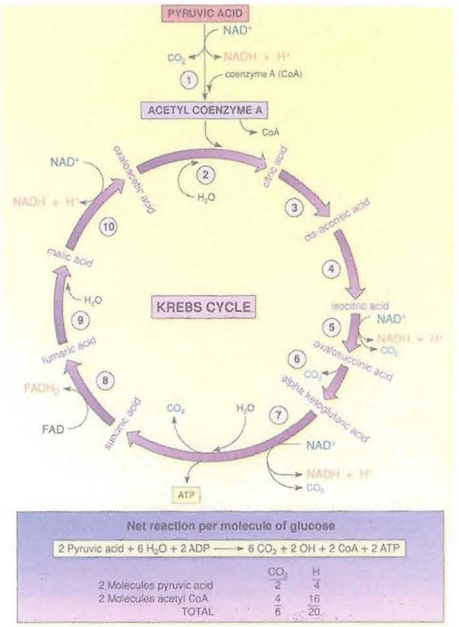

Figure 2.6: A flow sheet for release of hydrogen and carbon dioxide during the degradation of one molecule of pyruvic acid in the mitochondrion (McArdle et al., 1991).

Although the glycolytic pathway is exclusive to carbohydrate oxidation, breakdown products of carbohydrates, fats and proteins can be oxidized in the Krebs cycle reactions. Fatty acids destined to be oxidized for energy metabolism can be freed directly into the cycle as Acetyl-CoA. In the same way Acytel-CoA can be used to synthesize fatty acids. For this reason fat and glucose metabolism is closely interwoven. Amino acids to be used for ATP synthesis are deaminated and converted to keto acids, which enter the citric acid cycle. In reverse, keto acids can be converted to non- essential amino acids as needed. Therefore in addition to serving as the final common metabolic pathway for the oxidation of food fuels, it is also a source of building materials for anabolic reactions (De Vries, 1986).

Pyruvic acid is converted to Acetyl-CoA, before it enters the Krebs cycle. Three important events play a role to enable this to take place:

1. Decarboxylation

2. Oxidation
3. Acetic acids combine with co-enzyme A to form Acetyl- CoA

Pyruvic acid + NAD^+ + CoA → acetyl – CoA + NADH + H^+ (Seeley et al., 1992).

The citric acid cycle begins with the production of citric acid (6- carbon molecule) from the combination of acetyl–CoA (2 carbon molecules) and a four-carbon molecule called oxaloacetic acid. A series of reactions occur, resulting in the formation of another oxaloacetic acid, which can start the cycle again by combining with another acetyl-CoA. During the reactions of the citric acid cycle three important events occur (Marieb, 1995; Fox and Bowers, 1993):

1. ATP production: For each molecule of citric acid, one molecule of ATP is offered.
2. NAD + FADH: For each citric acid molecule, three NAD+ molecules are converted to NADH+H^+ molecules, and one FAD molecule is converted to $FADH_2$. The NADH +H^+ and $FADH_2$ molecules act as electron carriers that enter the electron transport chain to produce more ATP.
3. Carbon dioxide production: Each of the 6-carbon citric acid molecules that are found at the start of the cycle is changed to a 4-carbon oxaloactic acid molecule at the end of the cycle. Two of the carbon atoms found from the citric acid molecule are used to form two carbon dioxide molecules. For each glucose molecule that starts aerobic respiration, two pyruvic acid molecules are produced in the process of glycolysis. Each of these pyruvic acid molecules is converted into Acetyl-CoA molecules that enter the citric acid cycle. This means to be able to determine the number of molecules produced from glucose by the citric acid cycle, “two turnovers” of the cycle must be counted. The result from this would be 2 ATP, 6 NADH + H^+, 2$FADH_2$ and 4 carbon dioxide molecules (Marieb, 1995).

The Electron Transport Chain and Oxidative Phosphorylation

Similar to the glycolysis, none of the reactions in during the Krebs cycle makes direct use of oxygen. This is the exclusive function of the electron transport chain. However because the reduced coenzymes produced during the Krebs cycle are the substrates of the electron transport chain "mill", these pathways are coupled and both phases are considered to be aerobic (Martini, 1995). The hydrogen removed during the oxidation of food fuels are finally combined with molecular oxygen in the electron transport chain and the energy released during those reactions is harnessed to attach inorganic phosphate groups to ADP. This type of phosphoralytion is known as oxidative phosphoralytion (Marieb, 1995).

Most components of the electron transport chain are proteins bound to metal atoms (cofactors). Most of these proteins are a brightly coloured iron containing pigments called cytochromes. Neighbouring carriers are clustered together to form three major respiratory enzyme complexes that are alternatively reduced and oxidized by picking up electrons and then passing them on to the next complex in the sequence. The first of these complexes accepts hydrogen atoms from NADH+ H^+ oxidizing it to NAD^+. $FADH_2$ transfers its hydrogen baggage slightly further along the chain. The hydrogen delivered to the electron transport chain by reduced coenzymes is quickly split into protons and electrons.

The protons escape into the watery matrix and the electrons are shuttled along the membrane from one receptor to the next. Ultimately hydrogen is delivered to molecular oxygen to form water. The transfer from NADH+ H^+ to oxygen, release large amounts of energy. If hydrogen combined directly with molecular oxygen the energy would be released in one big burst and most of it would be lost to the environment as heat. Instead energy is released in many small steps as the electrons move from one electron receptor to the next. Each successive carrier has greater affinity for electrons than those preceding it. Thus the electrons cascades "downhill" from NADH + H^+ to lower energy levels until they are finally delivered to oxygen, which has the greatest affinity of all for the electrons. The electron transport chain uses the stepwise release

of electronic energy to pump protons from the fluid matrix into the inter-membrane space. Since the membrane is nearly impermeable to H^+, this chemiosmotic process creates an electro-chemical proton gradient across the inner membrane that temporarily stores the potential energy that will be utilized in the synthesis of ATP (Seeley et al., 1992).

This proton gradient has two important functions:

1. It creates a pH gradient, with the hydrogen concentration in the matrix much lower than that in the inter-membrane space.
2. It generates a voltage across the membrane that is negative on the matrix side and positive in the mitochondrial membranes. This results in the strong attraction of the protons back into the matrix. The only areas of the membranes that are freely permeable to H^+ are large enzyme protein complexes called ATP synthase. As the protons take this route they create an electrical current, and ATP synthase harnesses this electrical energy to catalyse the attachment of a phosphate group to ADP to form ATP, thereby ensuring the completion of oxidative phosphoralytion (Marieb, 1995).

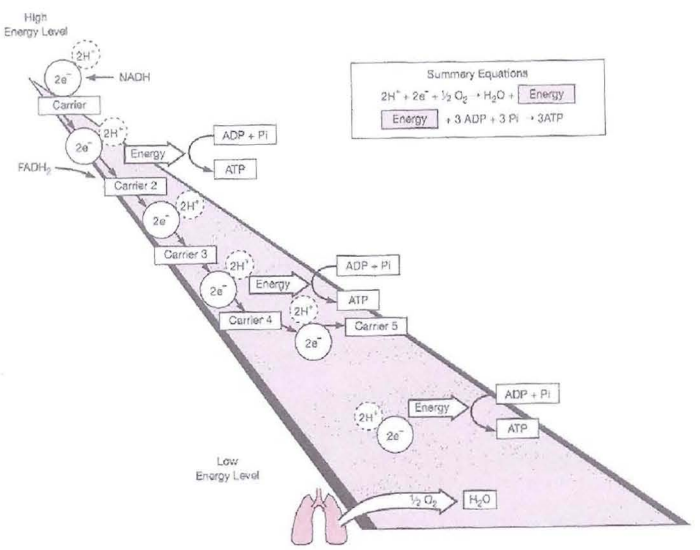

Figure 2.7: The electron transport system (Fox and Bowers, 1993).

Total energy transfer from Glucose metabolism

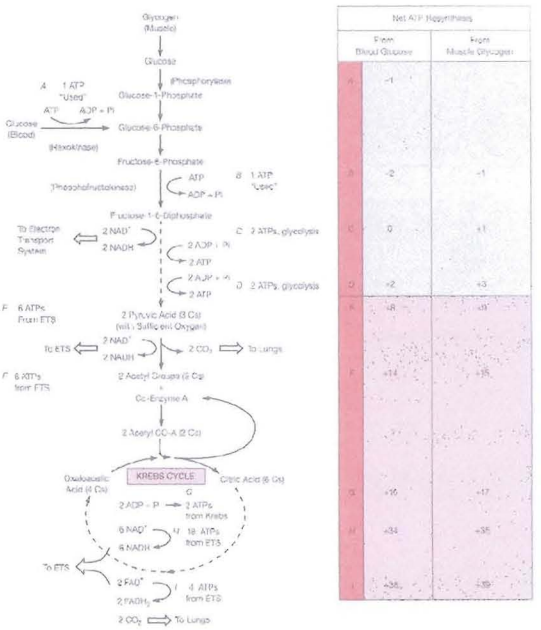

Figure 2.8: Sources of ATP resynthesis from the complete oxidation of carbohydrate in the form of either blood glucose or muscle glycogen (Fox and Bowers, 1993).

Carbohydrate as an ergogenic aid has its beginnings strongly rooted in science. Early in the 20th century it was apparent that during very heavy, intense exercise, the primary fuel source was carbohydrate (Horstman, 1972). Carbohydrate (CHO) loading is one of the more popular methods of nutritional modification used by endurance athletes to improve performance. It is also one of the most studied ergogenic aids for athletic performance (Walberg-Rankin, 1995). Although the judicious adherence to this dietary technique can significantly improve specific performances, there are also some negative aspects that could prove detrimental (McArdle et al., 1993). Reduction of body stores of carbohydrate and blood glucose is related to the perception of fatigue and the inability to maintain high-quality performance. This has been clearly shown with aerobic, endurance events of moderate intensity of over 90 minutes duration. Carbohydrate intake may also have relevance for athletes involved in short, high-intensity events, especially if body weight control is an issue (Walberg-Rankin, 1995). The process of glycogen loading (carbohydrate loading) may be incorporated to elevate muscle glycogen stores above their normal resting levels prior to endurance

competition (Fox and Bowers, 1993). Generally glycogen super-compensation is applicable where the athlete is continuously in motion for more than an hour at a time. Super-compensation may have value for events with an anaerobic component to the extent that lowered levels of glycogen can have adverse effects on lactate production (anaerobic power) (Fox and Bowers, 1993). Some recent studies further confirm that consumption of a high-carbohydrate diet for 2 or more days prior to an endurance event enhances performance relative to a low carbohydrate diet. For example, O'Keefe et al. (1989) found that 1 week on a 72% carbohydrate diet allowed cyclists to exercise at 80% of $V0_2$ max for 113 minutes, whereas they could only cycle 60 minutes when they consumed a 13% carbohydrate diet for the same period (Walberg-Rankin, 1995). Under circumstances where an athlete must perform multiple events in one day, super-compensation is appropriate. For these purposes one can simply increase the dietary intake of carbohydrates for 48 to 72 hours prior to competition. The practice of ingesting glucose 30 to 45 minutes before competition is not recommended. It can lead to a rapid fall in blood glucose levels with the onset of exercise and increase the rate of glycogen utilization. One other point of consideration is that with the storage of one gram of glucose about 2.7 grams of water will be taken into storage. Thus, with a storage of 700 gm of glucose an additional storage of about 1.9 kg of water will occur. So the athlete should not be surprised to have a precompetition weight gain. This can be an advantage or disadvantage depending on the event.

One aspect that has not received a lot of thought until now is that there are differences between the genders in the metabolic response to exercise. Recently research has demonstrated that females oxidize proportionally more lipid and less carbohydrate during endurance exercise as compared to males (Horton et al., 1998; Friedlander et al., 1998). These gender differences are partially mediated by higher estrogen concentrations in females. Specific areas where there are gender differences in nutritional/ supplement recommendations include carbohydrate nutrition, protein requirements and creatine supplementation. The research indicate that females do not carbohydrate load in response to an increase in dietary carbohydrate when

expressed as a percentage of total energy intake (i.e., 55-75%), however if they consume >8g CHO/ kg^{-1}/ d^{-1} they show similar increases compared to males (Tarnopolsky, 2000). In a study using treadmill running, Tarnopolsky et al., (1991), found that females have significantly less glycogen depletion in the vastus lateralis following 15.5 km of treadmill running, as compared to males. The hypothesis explaining this phenomenon is that the glycogen sparing was due to an enhanced oxidation of lipid by the muscles. The mechanism behind the potential glycogen sparing effect is likely the female sex hormone, 17-β-estradiol. Two studies have demonstrated that the administration of 17-β-estradiol to male (Rooney et al., 1993) and female oophorectomized (Kendrick et al., 1987) rats resulted in significant muscle glycogen sparing during exercise.

Water and Electrolytes

Competing in ultra-endurance events lasting longer than 2-3 hours probably puts more demand on the fluid and energy balance of the body than any other from of exercise (Brendon and Hopkins, 2000). Of all the physiological perturbations that can cause early fatigue during exercise, dehydration is arguably the most important, if only because the consequences of dehydration are potentially life threatening. The rise in body temperature that normally accompanies exercise stimulates an increase in blood flow to the skin and the onset of sweating (Murray, 1995). Water loss in amounts as low as 2 to 3 % of body weight can impair performance through the disruption of circulatory and thermoregulatory functions (Fox and Bowers, 1993). Normal hydration is protective of these thermoregulatory responses, whereas even a slight amount of dehydration results in measurable declines in cardiovascular and thermoregulatory function. Mild to severe dehydration commonly occurs among athletes, even when fluid is readily available. This voluntary dehydration compromises physiological function, impairs exercise performance, and increases the risk of heat illness. Recent research illustrates that maintaining normal hydration (or close to it) during exercise maintains cardiovascular and thermoregulatory responses and improves exercise performance. Consequently, it is in the athlete's best interest to adopt fluid-

replacement practises that promote fluid intake in proportion to sweat loss (Murray, 1995). For an acclimatized person, water loss by sweating may reach a peak of about 3 litres per hour during severe work and average nearly 12 litres on a daily basis. Furthermore, several hours of intense sweating can cause sweat-gland fatigue that ultimately leads to the inability to regulate core temperature. Elite marathon runners frequently experience fluid losses in excess of 5 litres during competition (McArdle et al., 1991). The daily intake of fluid is usually closely balanced with the volume of fluid that is lost in urine, faeces, sweat and respiration and via insensible water loss through the skin so that, at rest in thermo neutral conditions, body fluid balance is maintained at more or less 0.2% of total body weight. This balance requires the constant integration of input from hypothalamic osmoreceptors and vascular baroreceptors so that drinking behaviour closely approximates fluid loss, a minimum of about 2 l/day (Murray, 1995). Noakes (1992), feels that the rates of fluid ingestion are probably acceptable in most runners, with the increasing probability that the fluid intakes of runners competing in very long races will be greater than required. It would seem that the only runners whose fluid intakes may be inadequate, are those who run the fastest in races of between 10 to 42km. At these high exercise intensities, rates of gastric emptying and possibly intestinal absorption are likely to be impaired. In addition, their high rates of ventilation make the actual process of drinking both difficult and uncomfortable. Of course the fast running speeds of these elite athletes ensure high metabolic rates and therefore also high sweat rates. Thus it is precisely these runners, who also have the greatest difficulty in replacing their fluid loss during exercise.

Slower runners, especially during ultra marathon races, have less difficulty in drinking adequately and some may even have too much of a good thing. By drinking (for example) 1000ml instead of 500ml each hour during an ultra marathon, some runners have developed potentially fatal water intoxication or hyponatraemia (low blood sodium concentrations). Typically runners who are affected are not elite, competitive runners but those who are completing these ultra marathons in between 9 and 11 hours. Their slow running speeds allow them ample time to drink fluid from the vast number of feeding stations

available during these races. But, more importantly, their slow running speeds and resultant slow metabolic rates cause them to sweat at much slower rates than those calculated by previous workers, who studied only elite marathoners. It is clear that sweat rate calculations based on elite runners are erroneous if applied to the average runner of the same body mass, who runs much more slowly. For example, researchers originally believed that if a 50kg runner loses 5,5 l of sweat during a 05:30:00 ultra marathon, then that runner should obviously drink a litre of fluid every hour to maintain a water balance. This calculation ignores the water lost from glycogen, which may not have to be replaced. Thus the general (but incorrect) rule was devised that a 50kg person should drink a litre of fluid for every hour of running, and that those who are heavier should drink a little more. But now it is known that this advice is safe only if the runner is able to finish the race in 05:30:00. A less competitive 50kg runner who religiously followed that advice but took 10:00:00 to complete the race would finish the race with a fluid credit of 4l , enough to cause water intoxication if the runner is predisposed to the condition.

The finding that the incidence of hyponaetremia is on the increase among slower ultra marathon runners suggests that this is happening more frequently. The question would be why this extra fluid causes the runner to develop this condition. One possibility is that it is not so much the absorbed fluid that is the problem, but rather the unabsorbed fluid in the intestine. Thus one theory is that most of the fluid ingested by these athletes is not absorbed, but remains in the intestine. This causes sodium in particular to move from the body into that undigested fluid. Whenever fluid that does not contain sodium is ingested, sodium moves into the fluid before it is absorbed. In other words, sodium is needed for water to be absorbed into the intestine. Sodium moves out of the cells lining the gut into the digested water. The loss of this sodium then causes all the bodily changes that produce this disturbing condition. But whatever the mechanism, this condition does show that drinking too much during exercise can be detrimental to the health of some predisposed individuals (Noakes, 1992)

The content of fluid replacement drinks is very important. The diet normally contains sufficient electrolytes to compensate for any acute losses experienced through activity. Exception is noted where very high sweat rates over a period of days may occur. A concerted effort will be needed to insure added electrolyte intake, especially as it relates to potassium (Fox and Bowers, 1993). Obviously one possible aim of fluid ingestion would be to match the the electrolyte losses in sweat (Noakes, 1992). The minerals sodium, potassium, and chlorine are collectively termed electrolytes because they are dissolved in the body as electrically charged particles called ions. Sodium and chlorine are the chief minerals in blood plasma and extracellular fluid. A major function of these electrolytes is to modulate fluid exchange within the body's various fluid compartments. This allows for a constant, well regulated exchange of nutrients and waste-products between the cell and its external fluid environment. Potassium is the chief intracellular mineral. Perhaps the most important function of the mineral electrolytes sodium and potassium is their role in establishing the proper electrical gradients across cell membranes. This electrical difference between the interior and exterior of the cell is required for the transmission of nerve impulses, for the stimulation and contraction of muscle, and for the proper functioning of glands. The electrolytes are also important in maintaining the permeability of the cell membranes and controlling the balance between the acid and base qualities of the body fluids, especially the blood (McArdle et al., 1991).

Vitamins and Minerals

In addition to protein and carbohydrate, athletes have been interested in vitamin supplementation since the 1930's after the discovery and isolation of these compounds. By 1939, leading Tour de France cyclists reportedly performed better after taking vitamin supplements (Applegate and Grivetti, 1997). In spite of widespread usage, there appears to be little compelling evidence for supplemental intake of various vitamins with the exception of iron and vitamin C. Most vitamins, when taken in excess, are merely excreted in urine. There is no justification for the consumption of megadoses of vitamins. None of the known vitamins, when taken in excess of their recommended daily allowance, produces an ergogenic effect. One

consideration for recommending vitamin supplementation to athletes relates to those who restrict caloric intake to "make weight" (wrestlers, boxers or jockeys, among others) or to keep body weight to a minimum for cosmetic and other reasons (gymnasts, dancers, and figure skaters, among others). Because vitamin intake is closely related to caloric intake it would not be inappropriate to take a multivitamin/ mineral pill on a regular basis for those who restrict caloric intake (Fox and Bowers, 1993).

Recent studies have provided the scientific basis for the use by athletes of some micronutrients, such as antioxidants (Barrarre et al., 1993, Clarkson, 1995, Nieman et al., 1989). This has led to the development of commercial products to enhance antioxidant intake and to prevent antioxidant damage due to endurance and high intensity exercise.

Caffeine

Caffeine is one of the best researched substances in food supply. The overwhelming scientific evidence suggests that, in moderation, it has no adverse health effects. According to the International Food Information Council, moderation refers to 1 to 2 mugs of brewed coffee per day (Clark, 1997). Caffeine is the most widely ingested psychoactive drug in the world. Because caffeine enhances performance in many individuals, it has been banned by the International Olympic Committee. But ironically, the level at which caffeine is banned far exceeds the amount needed to enhance performance. Higher, illegal levels are generally attained with caffeine supplements, since a 68kg-athlete would need to drink 3 to 4 large cups of coffee within an hour before activity to reach the upper acceptable limit. Just 1.5 to 3 milligrams of caffeine per 0.454 kg of body weight (225 to 450 milligrams for a 68kg man) is enough for an energy-enhancing effect. That's as little as one 283.5 gram cup of coffee. Habitual caffeine consumers experience less ergogenic effect than people who consume it rarely. Caffeine affects each person's performance differently (Clark, 1997).

As many know, chronic use of caffeine leads to dependence, tolerance, drug craving, and upon abrupt cessation unpleasant withdrawal symptoms. Thus,

caffeine fulfils pharmacological criteria by which agents are classified as drugs of abuse. Nevertheless, its use is legal and only at high, but readily attainable, levels is it banned from sport. Its use is widespread by athletes as young as 11 years of age who are seeking athletic advantage over fellow competitors. It is likely that its use will not decline soon because it is inexpensive, readily available, medically quite safe, socially acceptable, and by most measures legal. However, at levels allowed in sport, caffeine through its wide-ranging physiological and psychological effects increases endurance in well-trained athletes (Sinclair and Geiger, 2000). The IOC has set a standard of greater than 12mcg/ml in the urine as doping. This is the equivalent of six to eight cups of coffee consumed in one sitting and then being tested within 2 to 3 hours following consumption (Fox and Bowers, 1993).

Results of studies reported over the last five years strongly indicate that caffeine effectively increases athletic performances in endurance events; less clear however is whether caffeine affords benefit in short burst-type events (Graham et.al., 1994; Doherty, 1998). In reviewing the primary literature on effects of caffeine on performance in endurance events, one is struck by the variability of results reported. Two principal reasons help explain the variable results. First, care was not taken to use only well-trained athletes. Second, test subjects were included in whom prior use of caffeine was not carefully controlled. These variables, likely prevented researchers from finding statistically significant differences between control and test subjects (Sinclair and Geiger, 2000).

If a metabolic ergogenic effect of caffeine does exist, it is probably related to its role in aiding the mobilization of free fatty acids (FFA). Fats are the bodies most concentrated source of energy. The energy yield from the breakdown of fats is approximately twice that gained from either proteins or glucose. Most products of fat digestion are transported in lymph in the form of fatty protein droplets called chylomicrons. Eventually, the lipid in the chylomicrons are hydrolysed by plasma enzymes, and the resulting fatty acids and glycerol

(three fatty acids and one glycerol = triglycerol), are taken up by the body cells where they are processed in various ways (lipolysis) (Marieb, 1995).

Oxidation of Glycerol and Fatty Acids

The only fats that are routinely oxidized for energy are neutral fats. Catabolism of these fats involves the breakdown of their two building blocks namely glycerol and fatty acids (Marieb, 1995). Glycerol is accepted into the anaerobic reactions of glycolysis as 3- phosphoglyceraldehyde, a glycolysis intermediate which then flows into the Krebs cycle. ATP energy harvest from the complete oxidation of this compound is approximately half of that of glucose (18 – 19 ATP/ glycerol). The gluconeogenic role of glycerol is important when carbohydrates are restricted in diet or during long duration activities. The process of fatty acid catabolism takes place within the mitochondria of the cell. This process is known as beta-oxidation. Each fatty acid molecule is split/ cleaved into two carbon acetyl fragments. ATP is used to phosphorylate the reactions, water is added, hydrogen is passed to NAD^+ and FAD, and the acetyl fragments joins with the coenzyme A to form an acetyl-CoA. This enters the Krebs cycle. The process of beta-oxidation cannot take place unless oxygen is able to accept hydrogen. The term beta-oxidation reflects the fact that the carbon in beta (3^{rd}) position is oxidized during the process. The splitting step occurs between the second (alpha) and third (beta) carbon atoms in each case (Marieb, 1995).

Total Energy Transfer from Lipid Catabolism

For each 18-carbon fatty acid molecule, 147 molecules of ADP are phosphorylated to ATP during beta-oxidation and the Krebs cycle metabolism. Since there are three fatty acid molecules in each triglyceride molecule, 441 ATP molecules are formed from the fatty acid component. The fact that 19 molecules of ATP are formed during glycerol metabolism, a total of 460 molecules of ATP is generated for each neutral fat catabolized. The efficiency of energy conservation is about 40% (Fox and Bowers, 1993).

The caffeine may have a glycogen-sparing effect in that it enables more fat to be used as fuel, with less usage of glycogen. Glycogen-sparing is known to

reduce muscular fatigue (Fox and Bowers, 1993). Caffeine also appears to cross the membranes of all tissues in the body, making pure investigations of mechanism in the exercising human impossible. For example, because caffeine enters both the nervous system and skeletal muscle, it is not possible to separate central and peripheral effects. It also seems likely that different mechanisms could be responsible for performance enhancement in different types of exercise. There are three major theories for the ergogenic effect during exercise. The first theory involves a direct effect on some portion of the central nervous system that affects the perception of the effort and/ or affects the propagation of neural signals somewhere between the brain and the neuromuscular junction. The second theory proposes a direct effect of caffeine or one of its by-products on skeletal muscle. Possibilities include handling of irons, inhibition of phosphodiesterase (PDE) leading to an elevation in adenosine 3', 5'- cyclic monophosphate (cyclic AMP), and direct effects on key regulatory enzymes such as phosphorylase (PHOS). The third theory involves an increase in fat oxidation and decrease in carbohydrate oxidation. Caffeine or a caffeine metabolite may mobilize free fatty acids (FFA) from adipose and/ or intramuscular stores indirectly by increasing circulating epinephrine (EPI) or directly by antagonizing adenosine receptors that normally inhibit FFA mobilization. The greater FFA availability increases muscle fat oxidation and decreases CHO oxidation, presumably improving performance in exercise situations where CHO availability limits performance (Spriet, 1995).

Many of the potential side effects of caffeine ingestion are well known: anxiety, jitters, inability to focus, gastrointestinal discomfort, insomnia, irritability and, with higher doses, heart arrhythmias and hallucinations. While the side effects associated with doses below 9ml/kg body weight do not appear to be dangerous, they can be disconcerting if present prior to a competition. It appears that complaints about side effects are reduced when 6 vs. 9ml/kg doses are administered. There is a great variability in almost all performance and metabolic responses to caffeine. This appears to be true for all groups studied, including mild and heavy caffeine users, users who abstained from caffeine for varying lengths of time, and non-users. The variability of muscle

glycogen sparing following caffeine ingestion is greater in samples of untrained males than in trained males (Chesley et al., 1994).

Caffeine also has a diuretic effect, that is, it enhances urine formation, often causing a need to urinate within an hour after consumption. Yet two studies with subjects who took caffeine before they exercised showed no detrimental effects on hydration during exercise (Falk et al., 1990; Gordon et al., 1982). Thus it appears that caffeine does not increase urine production during exercise. The extra adrenaline the body secretes during exercise may block caffeine's effect on the kidneys. After exercise, caffeine is a poor choice for fluid replacement. The best approach is to use non-caffeineated beverages just after activity (Clark, 1997).

Cellfood®

Cellfood® is a proprietary super energized complex concentrate held in colloidal suspension. It is ingested orally in the form of fluid droplets added to water. It contains 78 trace elements and minerals, combined with 34 enzymes, 17 amino acids, dissolved and nascent oxygen, suspended in a solution of deteurium sulphate (D_2SO_4). Cellfood® is unique due to its ability to create nascent oxygen or "newly born" oxygen (Latin- Nascere). In biochemical terms nascent oxygen refers to this newly born single oxygen (elemental oxygen) that has not yet entered into biochemical reaction. Nascent oxygen is negatively charged (O^-). Free radicals on the other hand are positively charged ions of single oxygen (O^+). The opposite charge of these ions cause them to attract each other, forming a single pure oxygen molecule (O_2). Nascent oxygen "seeks out" and neutralizes dangerous free radicals, combining to form pure oxygen in the process.

{O^- [nascent oxygen] and O^+ [free radical ions] = O_2 [stable oxygen]}

According to the manufacturer the main conceivable benefits of Cellfood® with regards to aerobic metabolism include the following (Storey, 1982):

- Increase in cellular respiration: When Cellfood® is mixed into water, an exothermic reaction takes place providing oxygen and hydrogen to the individual cells of the body. The steady flow of oxygen and hydrogen to all parts of the body allow for simultaneous oxygenation and reduction within the cells.
- Metabolic efficiency catalyst: Cellfood® enhances nutrient absorption and increases metabolism. It promotes greater availability of vitamins, minerals, herbs, and other nutrients.
- Energy boosting properties: Cellfood® allows the body to function cleanly and efficiently, resulting in an increased energy level over time.
- Colloidal minerals: The minerals contained in Cellfood® are in a special colloidal suspension for easier absorption and utilization by the body.

The development background to Cellfood® is thus, according to the product literature (Oxygen for Life, 1999), the genius and inventor behind Cellfood® is Everet Storey, twice Nobel Laureate, who worked on the American "Manhattan Project". This project was top-secret, and to this day, not much has been revealed about it. Albert Einstein credited Storey with the "water splitting technology" that he patented; and from his research, the hydrogen bomb was developed. Because of exposure to extreme radiation, the people on the project began to die. Everett Storey himself was affected and, by the early 1950's he had lost 30kg in weight.

So, Storey worked on saving his own life and giving mankind something useful. In 1956 he invented a deuterium-based product, which he called "Cell Food" or "Liquid Life". In the development of "Cell Food", Storey used work of Dr. Harold Urey, who in 1932 had discovered deuterium (the only non-radioactive isotope of hydrogen), which had subsequently been kept secret because of its role in the hydrogen bomb and as the principal fuel for space exploration. Storey spent most of his life researching deuterium's incredible

health benefits, which kept him alive until his death at the age of 74 in 1984 (Oxygen for Life, 2000).

In January 1978, Everett Storey applied for Food and Drug Administration (FDA) registration of "Cell Food" (also known as Deutrosulfazyme). On the Pharmaceutical Composite Form he described it as: "Champagne colour to amber colour with passage of time, but instead of a loss in potency, there is actually a small increase each year."

Under the section "Therapeutic effects: he stated:

- Aids materially in the digestive process;
- Assists in the cleansing of upper intestine and lower intestine, and restores normal bowel function;
- Enables the blood stream to deliver directly to each body cell a minimum of 78 assimilable elements for complete, direct and quick nutrition; and
- Provides a steady flow of both oxygen and hydrogen to all parts of the body, thus effecting the hitherto "impossible" achievement of simultaneous oxidation and reduction within a given cell".

In 1985 the American Government passed the "Deuterium freedom act of 1985" in which recognition was given to the work of Everett Storey and his product. The ACT, section 2(b) line 15 states: " Deuterium can and does form all other elements, and stands at the very core of the Universe. The ashes of hydrogen constitute water. Heavy hydrogen combined with water becomes 'heavy water' (deteurium oxide). Line 25 states: Because of deteurium's facility to speed up the digestive process, it will aid in patients getting more mileage out of the food they consume; and, at the same time, reduce the toxicity in the blood stream. Deutrosulfazyme is a systemic normalizer. In 1995, with the change in American legislation, Cellfood® was classified as a nutritional supplement and not as a drug or patented medicine. Until then, over $2 million had been spent on clinical tests, and Cellfood® had only been available for experimental purposes. After 1995, it was made available to the public.

In 1997, Cellfood® was unanimously voted by the Inventors Clubs of America for the 1997 Advanced Technology Award which was presented by the International Hall of Fame in Atlanta, U.S.A. Cellfood® received this award because of: 1) it's unique ability to produce both nascent oxygen and hydrogen inside the body, resulting in the simultaneous cleansing and building of body cells and tissues; and 2) it's unique ability to hold 78 elements, trace minerals and minerals in liquid colloidal suspension.

All the substances in Cellfood® are natural substances. Cellfood® has no alcohol, no glucose, and no substances that are on the banned list of substances regarding international, professional and amateur athletic associations. Cellfood® is made from the finest natural substances which are cryogenically, not chemically, extracted and are totally non-toxic. The nutrients in Cellfood® are in colloidal form. Colloidal particles are minute (4-7 nanometres in diameter), and because of the Brownian Movement Phenomenon, they take on a negative charge, and remain suspended in liquid. Because most bodily fluids (like blood and lymph) are colloidal and negatively charged, the body perceives Cellfood® as a normal healthy body fluid, and allows the nutrients in Cellfood® to pass immediately through the sensitive membranes of the mouth, throat and oesophagus, directly into the blood stream.

The vast majority of living organisms rely on oxygen to generate oxidative power. The actual mechanism is not a direct chemical reaction, rather a series of electron transfers through a number of intermediate compounds that readily accept and release electrons alternating between an oxidized and reduced form. This route is called the electron transport chain and is similar in all organisms. As the strongest oxidizing agent of the chain, oxygen is the final electron accepter. Oxygen's vital role in living organisms is essentially as a substance on which to "dump" electrons. Many micro organisms are anaerobic and do not require oxygen for survival. These organisms are able to utilize sulphur and other compounds as oxidizing agents. All organisms generate reducing power through the reversible biochemical reactions of nicotinamide-

adenine dinucleotide (NAD), flavins, cytochromes, and other substances while existing in an oxidized or reduced form. By participating in the electron transport chain, the reduced form is continually regenerating from the oxidized form (Nu Science Corporation, 2001b). The Krebs cycle can be compared to machine designed to remove hydrogens from food; the hydrogens are sent to the Electron Transport System (ETS). Each molecule of the hydrogen carrier in the NAD delivers two electrons and one proton of a hydrogen molecule to the ETS. The energy produced by the ETS is used to form the chemical bond between Adenosine Diphosphate (ADP) and inorganic phosphate to form ATP. This highly effective delivery system enables over 95% of the nutrients in Cellfood® to be absorbed and utilized at cellular level. This percentage is high compared to the low absorption rates of tablets (15%) and gel caps (25%). Furthermore, because Cellfood® is colloidal, the similarity between it and other bodily fluids increases the bioavailability of nutrients (Nu Science Corporation, 2001a).

Many oxygen products tend to flood the body with oxygen, often creating harmful oxygen free radicals. The release of these reactive oxygen species results in oxidative injury to biologic systems such as lipids found in cell membranes, and proteins found in blood vessels and myocardial tissues. Cellfood® is different in the sense that it scavenges and bonds with dangerous oxygen free radicals, supplying the body with usable oxygen in a controlled and time-released manner, at cellular level, only where it is needed. Cellfood® therefore, in no way creates free radicals. It causes free radical singlet atoms of oxygen to be neutralised. Another defence mechanism against free radicals is the enzyme catalase. Catalase breaks down hydrogen peroxide, a metabolic waste product in the body, and liberates oxygen for the body to use. Cellfood® contains the enzyme catalase. If people use other products, such as ozone and stabilised oxygenated water, they should use antioxidants to minimise the free radical effect that can be caused by the flooding effect of too much oxygen too quickly in the body (Oxygen for Life, 1999).

Hydrogen is mainly used for reduction purposes. Hydrogenation (also called reduction) is the addition of hydrogen to a molecule. Most body processes

require hydrogen while playing a vital role in the electron transport chain. Fed by fusion and fission, hydrogen is the most common element in the universe (Nu Science Corporation, 2001c). The nascent hydrogen atoms that are produced by Cellfood® are used by the body for many functions, such as irrigating, building and strengthening cells and organs; preventing inflammation, promoting osmosis; moistening lung surfaces for gas diffusion; and regulating body temperature. Hydrogen is essential for the processes of digestion, assimilation and elimination; and for transporting nutrients through the arteries to the brain and all body tissues. A person who weighs 80kg has about 7kg of hydrogen in his body. The body normally obtains hydrogen from water, other liquids, fruits and vegetables. Lack of hydrogen leads to dehydration from inside and outside the cells; and extreme dryness and abnormal nerve heat are generated in the body.

Cellfood® is a liquid concentrate, taken by mixing a number of drops in a quarter of a glass of distilled or filtered water. How much Cellfood® one takes depends upon the individuals needs. Each person has unique needs, and because Cellfood® is a nutritional supplement, everyone responds in a unique manner. Most people take about 12 drops first thing in the morning. One cannot overdose on Cellfood®. Because it is a nutritional supplement made from natural substances, the body only uses what it needs, and eliminates the rest through the normal channels of elimination. Cellfood® can be taken at any time. Most people take it first thing in the morning before brushing their teeth or eating.

Switch™

Switch™ contains all of the above mentioned ingredients of Cellfood® with two added substances. The first substance being Citrin K and the second being L-Carnitine. Citrin-K contributes 25% to the total Switch™ make up. L-Carnitine contributes 20% to the total Switch™ make up. A 100ml bottle of Switch™ contains about two months supply at 20 drops per serving. Each of these servings contains: 250mg Cellfood® proprietary blend; 110mg Citrin K; and 90mg L- Carnitine.

Citrin K

Hydroxy Citric Acid (HCA) is a natural compound extracted from the rind of the fruit Garcinia cambogia. HCA supplementation acts as an appetite suppressant, and it has shown the ability to inhibit the actions of ATP-citrate lyase in the liver. This enzyme is partially responsible for the conversion of dietary carbohydrates to fat. This may make it extremely effective for low fat diets. HCA has also been shown to increase glycogen storage, which may actually act to curb hunger and increase athletic performance (Phillips, 1997).

L- Carnitine

Carnitine is a quaternary amine whose physiologically active form is beta-hydroxy-gamma-trimethylammonium butyrate. This is found in meats and diary products and is synthesized in the human liver and kidneys from two essential amino acids, lysine and methionine (Armsey and Green, 1997). Carnitine plays a number of important roles in exercise metabolism (Hawley and Burke, 1998).

Firstly, this nonessential amino acid is a very popular "fat-burning" supplement in the sport nutrition market (Philips, 1997). It is well-known as a transport molecule for taking fatty acids inside the mitochondria of muscle cells where they are oxidised. It also plays a role in regulating the balance between key chemicals in other metabolic processes and is known to act as a buffer for pyruvate, thus reducing muscle lactate accumulation associated with fatigue (Armsey and Green, 1997).

It has been reported that after a period of carnitine supplementation, well-trained subjects increased their maximal oxygen consumption. The key claim of this supplement is that it can enhance fat metabolism by increasing the transport of fat to its site of oxidation. Long-chain fatty acid oxidation in all tissues is carnitine dependent; therefore, hereditary and acquired carnitine deficiencies cause triglyceride to accumulate in the skeletal muscles, impair fatty acid utilization, and reduce exercise capacity. Carnitine supplementation can usually reverse these changes (Hawley, 1998). Thus it is often an

ingredient in fat loss supplements, as well as making claim to increase exercise capacity (Hawley and Burke, 1998).

The possible mechanisms by which carnitine could have a positive effect include enhancing oxidation of fatty acids, a critical energy compound during exercise; preserving muscle glycogen during exercise, a factor potentially related to fatigue resistance; shifting fuel use towards glucose, thereby decreasing the oxygen requirement of exercise; improving resistance to muscle fatigue; and increasing the oxidative capacity of skeletal muscle (Philips, 1997)

More recent studies have found flaws in some of these claims, and have failed to replicate the findings of improved performance in athletes. Muscle biopsy studies have failed to find evidence that heavy training reduces muscle carnitine levels, or that these levels are increased by carnitine supplementation of up to one month. A change in muscle content after supplementation is a prerequisite if any benefits are to take place. Clinical studies investigating carnitine and its effects on exercise performance or metabolism during exercise have usually involved a small number of test subjects, but this background has provided sufficient foundation to encourage further studies (Hawley and Burke, 1998).