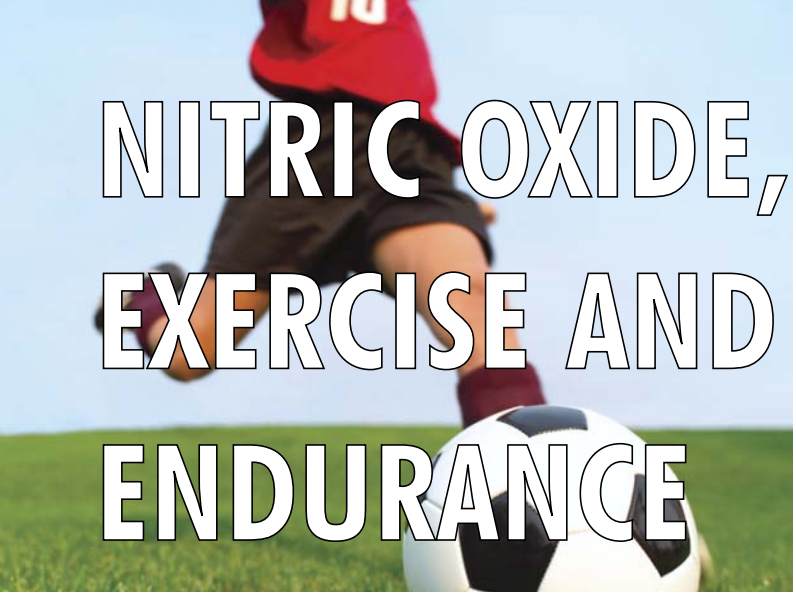

NITRIC OXIDE, EXERCISE AND ENDURANCE

It is widely recognized that exercise improves a plethora of cardiovascular symptoms including cholesterol, blood pressure, risk of stroke, vascular inflammation, and many others. Furthermore, researchers in the field of Applied Physiology and Sports Medicine have found that exercise also improves the function of the heart, accelerates cardiac rehabilitation, controls congestive heart failure (a condition where the heart is unable to pump the blood efficiently) and prevents intermittent leg pains caused by poor blood flow due to blockage and hardening of the arteries.

Recent research seems to suggest strongly that the benefits of exercise on cardiovascular health are in large part due to raised NO levels. Exercise increases the production of NO by the endothelial cells. Since NO is a potent vasodilator and increased production of this molecule causes blood vessels to become relaxed and widened, thereby allowing more blood flow and increased oxygen delivery to the body's tissues. Lack of exercise, improper diet and lifestyle and ageing will all eventually lead to reduced NO generation at the tissue level, and particularly in the blood vessels, resulting in a consequent worsening of cardiovascular symptoms.

Although it is acknowledged that exercise positively influences NO levels one wonders if the reverse is also true. Namely can higher NO levels improve exercise capacity?

Again researchers at University of Exeter in the UK and the Karolinska Institute in Sweden have looked into this phenomenon in great detail and have independently come up with some surprising findings! Essentially these researchers have found that raising NO levels can indeed have a positive impact on exercise capacity and endurance!

For example, Lundberg and Weitzberg's group in Sweden conducted a small human randomized double-blind-placebo-controlled study, where healthy male athletes were given a dose of 7 millimoles of inorganic nitrate for three days prior to an episode of low-intensity exercise on a cycle. This dose of the nitrate corresponded to the amount of nitrate that would be found in a plate of salad.

The researchers showed that supplementing with even this low dose of nitrate significantly improved the performance of the athletes as measured by amount of oxygen being consumed (Vox). In other words, consumption of nitrates reduced the body's demand for oxygen during exercise. Furthermore, in addition to reducing the body's oxygen requirement, or "oxygen cost", the researchers also noticed that the time taken to reach exhaustion was also increased. This suggests that consuming nitrates prior to exercise can actually reduce and/or prevent exercise fatigue! In a follow-up study by the same research group showed that nitrates acted in the same positive way when athletes performed high intensity exercise as well!

These findings were further supported by the British researchers at Exeter University. Led by Dr. Nigel Benjamin, one of the pioneers of the nitrate/nitrite/NO research, this group used beetroot juice instead of sodium nitrate. The effect of beetroot juice was evident as quickly as 1 hour after consumption, and reached maximum effect after three hours. The studies using beetroot juice confirmed the findings that nitrates reduce oxygen consumption and fatigue during exercise. A second study by the same British group showed a similar effect when beetroot juice was taken for a longer time period of 15 days. In other words, the positive effects were still evident when nitrates were being consumed on a longer term basis. This was not solely an acute phenomenon!

Interestingly, both the British and Swedish studies noted that there was no increase in production of lactic acid in the athletes consuming nitrates! Lactic acid production normally occurs following exercise and is one reason why athletes become fatigued. As oxygen becomes rate limiting, and tissues start becoming starved of oxygen, the body resorts to an alternative, less efficient mechanism of energy production that produces lactic acid as a by-product. However, these studies demonstrated that in the presence of NO, energy production in the muscles remains efficient, which in turn improves the body's ability to tolerate high intensity exercise for longer time periods. It has been shown that nitrate supplementation prevents the depletion of a key muscle protein called phosphocreatine; phosphocreatine measurements are an indicator of energy usage in the form of ATP. Research results have suggested that nitrates cause muscle contractions to use less energy.

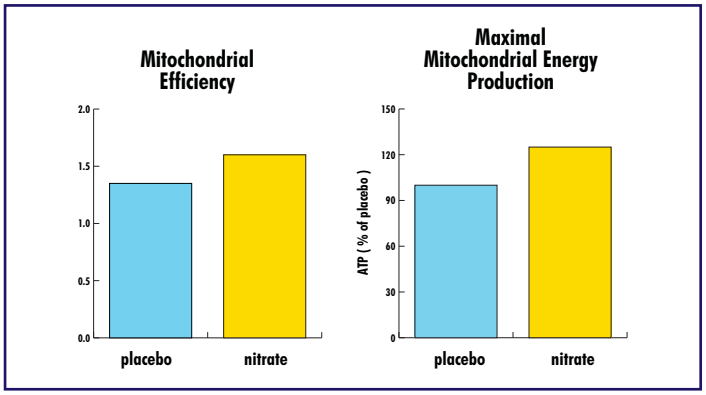

Figure 9. Graph showing improvements to mitochondrial function associated with an increased intake of dietary nitrate. Higher nitrate levels were shown to improve two key measures of mitochondrial function: the efficiency of energy (ATP) production (as measured by oxidative phosphorylation ratio) and also the maximal energy (ATP) production. This means that increasing dietary nitrates enables mitochondria to produce more energy more efficiently!

Nitrite has also been shown to interact directly with the mitochondria; the cellular powerhouses or energy generating factories of the cells. Mitochondria produce energy in the form of ATP, which is the energy currency that all cell processes require to function. Dr. Sruti Shiva at the University of Pittsburg School of Medicine has studied the complex actions and interactions of NO at the mitochondrial level and proposes that the unique exercise enhancing effects of inorganic nitrates and vegetables rich in nitrates may well be due to their specific interactions with various enzymes involved in energy production in the mitochondria. These interactions not only explain the exercise enhancing and oxygen sparing effects of NO but also help to explain its cell protective effects. At the cellular level, NO acts to reduce the generation of reactive oxygen species, which prevents cellular and DNA damage and also helps to prevent apoptosis or cell death.

In terms of athletic performance, the potential benefits of inorganic nitrates are enormous. For athletes, this small, but important molecule may open the door for improved performance without the negative health and legal implications associated with other sport enhancing drugs!

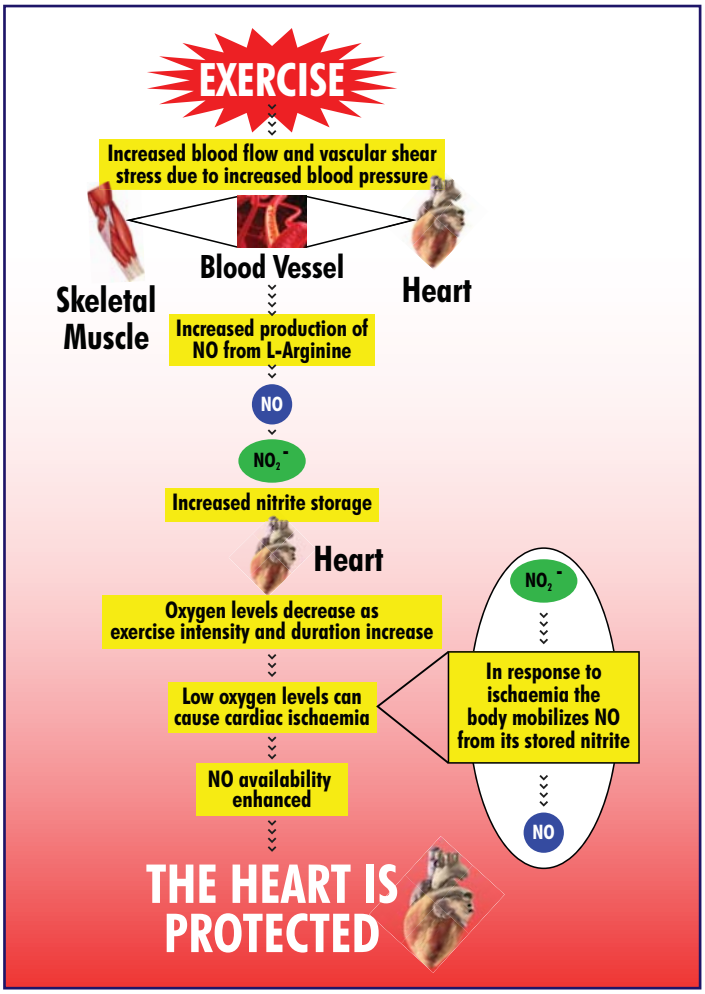

Figure 10. Diagram showing the stress imposed by exercise on tissues like the heart and how nitrate/nitrite can increase NO availability and protect the heart tissue when oxygen is limited

However, the significance of all of these findings extends far beyond the field of exercise physiology. For instance nitrates could be of great benefit to individuals suffering from reduced motility or exercise capacity. The ability of NO to reduce muscle energy use and extend the time to fatigue could be highly beneficial to ambulatory convalescing patients, seniors and heart patients who have a reduced exercise capacity and require assistance in recovery times from their illness.