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Nucleotides and the immune response to exercise

PHYSICAL AND MENTAL STRESS CAN COMPROMISE OUR IMMUNE RESPONSE, BUT CERTAIN NUTRIENTS CAN ALLEVIATE THAT RESPONSE. **DR PETER KOEPEL**, FROM PRO BIO LTD IN SWITZERLAND, EXPLORES THE SCIENCE BEHIND NUCLEOTIDE SUPPLEMENTATION AND ITS EFFECT ON AN ATHLETE'S IMMUNE SYSTEM.

Stress is a worldwide challenge to health and can come from both physical and emotional sources (1). Stress affects the hormone cortisol, which is produced by the adrenal glands. In small quantities, cortisol is helpful: it is anti-inflammatory, speeds tissue repair and controls excess immune cell production. However, continued stress raises cortisol levels beyond healthy levels and slows the production of 'good' prostaglandins. These good prostaglandins lower blood pressure, support immune function, improve nerve function, dilate blood vessels, lower blood viscosity and are anti-inflammatory. Low levels of good prostaglandin have the opposite effect,

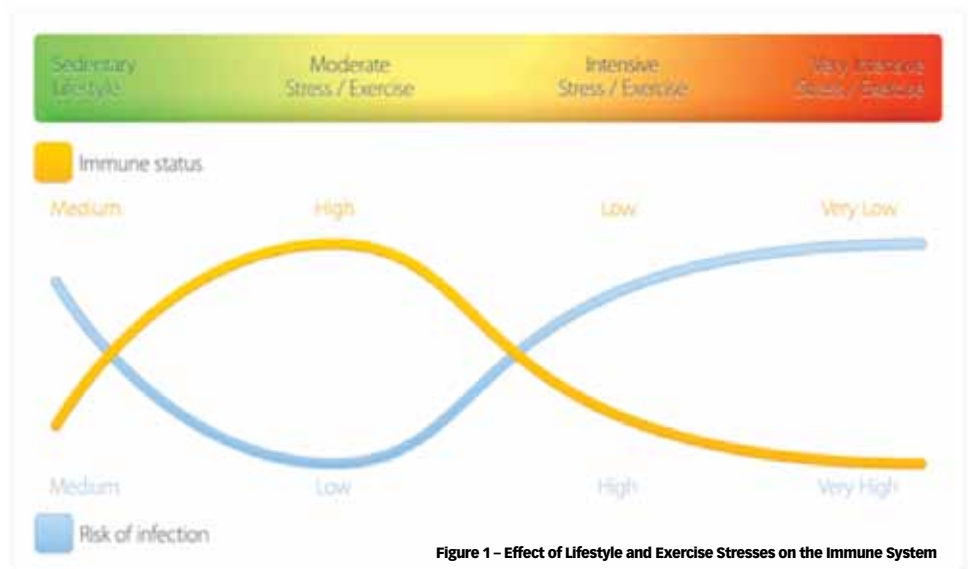


Figure 1 – Effect of Lifestyle and Exercise Stresses on the Immune System

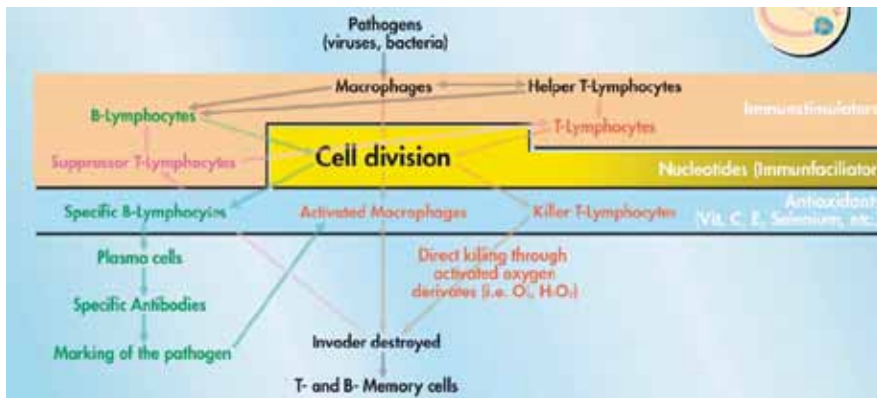


Figure 2 – Role of Nucleotides, Amino Acids and Vitamins in the Immune System

in that it causes inflammation, immune suppression, stomach acidity and irregular heart rhythms (2,3,4,5,6,7,8).

Even healthy people with a balanced immune system can go through phases of sub-optimal immune function, due to situations of over-exertion, stress and exhaustion, which make them more vulnerable to infections. In Switzerland, for example, a new survey revealed that 50% of young people suffer from stress.

Excessive stress, either physical or mental, has a detrimental effect on the optimal functioning of the

immune system. During a period of stress, the immune cells nearly disappear from the blood due to raised levels of cortisol. The part of the immune system most sensitive to increased cortisol levels are the natural killer cells, a type of white blood cell that is critical to the innate immune system. A non-scientific analogy to this is the collapse of a house of cards after adding just one more card, causing it to fall down.

Figure 1 shows how lifestyle and exercise stresses influence immune status and the risk of infection.

The effect of stress on the immune system is comparable to

the effect of exercise on the muscle: an unused muscle will degenerate; a moderately or intensely-used muscle will strengthen; very intensive muscle efforts can lead to severe damage of the muscle.

Nucleotides overcome the effects of stress

Nucleotides are the base units that make up DNA, and there is a particular need for sufficiently available nucleotides in cells that divide often. This is the case for our immune cells; for the natural proliferation of the specialised cells that are an integral part of the immune system. When the body is exposed to an antigen (bacteria, virus, toxin etc), it produces an immune response. The response includes the production and proliferation of specialised white blood cells, called lymphocytes, that produce specific antibodies that recognise and react with the antigen to render them harmless. In addition to this, one of the body's biggest physical barriers to the entry of potentially harmful foreign substances is the gut lining of the intestine. The total surface area of an adult's intestine is roughly that of a tennis court – this lining has a mucous membrane (mucosa) which includes important immune cells called enterocytes. Maintaining a healthy balance of 'good' bacteria in the intestinal tract is also important to help the body maintain a healthy immune system. Although your body produces some of its own nucleotides, the proliferation of all of these cells in the immune system is aided by additional nucleotides from the diet (11,15,17,18).

"From a more holistic point of view, it is interesting that both innate and acquired immunity need rapid and unhindered cell proliferation for proper functionality. Unfortunately, cells of the immune system lack the potential to synthesise nucleotides themselves. Other cells not capable of producing sufficient amounts of nucleotides include gastrointestinal and blood cells. Importantly, nucleotides do not stimulate innate or acquired immunity, but rather provide the resource for unhindered cell proliferation, gene expression and response to special environmental and physical

Research study 1: effects of a nucleotide supplement in trained male subjects on IgA, cortisol and lactate after endurance exercise (12)

AIM: The aim of this research was to examine the effect of a nucleotide supplement on IgA and cortisol levels after endurance exercise of young, healthy males.

METHODS: At the beginning of the study, all subjects underwent a 90 min cycle ergometer test at a power that represented 60% of their VO₂max. Cortisol, IgA and lactate levels were determined pre and

post-exercise. Subjects were then randomly assigned to the placebo or NuCell® group for 60 days. At the end of the experimental phase, subjects again completed the 90 min cycle test at 60% VO₂max and had pre and post-exercise cortisol, IgA and lactate levels measured.

RESULTS: After supplementation of nucleotides, IgA was significantly (p<0.01) higher after exercise in the test subjects as compared to those taking a placebo. The pre-exercise level of cortisol was not significantly different between groups (p>0.11). However, after supplementation of nucleotides,

cortisol was significantly (p<0.0001) lower after exercise in the test subjects, as compared to the ones who took a placebo.

There was a greater difference between the pre and post-exercise changes in accumulating blood lactate in the placebo group than there was in the nucleotide supplement group (p<0.004). This suggests that athletes who ingest the supplement may be able to work at a higher level than non-supplemented athletes, or can undertake the same amount of work as previously without the same levels of blood lactate accumulating post-exercise.

The 'Changes in Lactate', shown on the y-axis, represents the increase in blood lactate levels from pre to post-exercise.

CONCLUSION: Nucleotides seem to help reduce cortisol accumulation and therefore reduce physiological stress. Additionally, nucleotide supplementation supports the formation of IgA, improving the primary immune defence of the body. Also, after exercise, the change (or build-up) in the level of lactate in the blood is diminished.

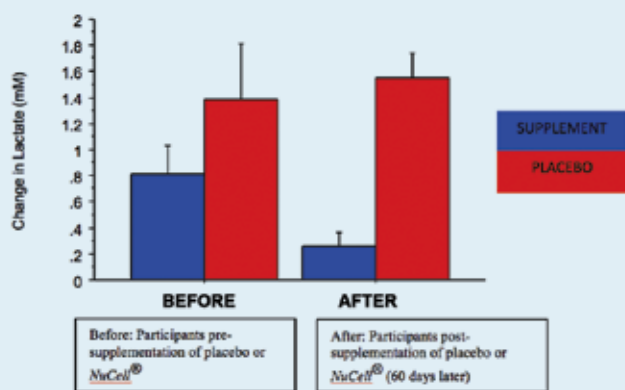


Figure 3 – differences in lactate post-nucleotide supplementation (NuCell®) and placebo

► challenges. Their universal use, fundamental functionality and efficacy in every living organism, make nucleotides a valuable management tool for many stress and health-related conditions.” – *FSN magazine: Nucleotides – the building blocks of life, Dr P Koepfel, July/Aug 2011.*

Figure 2 demonstrates the cell division that is required to progress the immune response from the innate to the adaptive immune systems. The role of nucleotides and antioxidants (present in Pro Bio’s NuCell® supplement) are illustrated.

It has been found that the application of a nucleotide-free diet significantly suppresses cellular immunity (10). In several studies, nucleotide supplementation has been shown to reverse the immunosuppression caused by malnutrition and starvation. A trial with race horses, for instance, revealed that cortisol levels after an anaerobic exercise test was significantly lower in horses fed on a diet supplemented with nucleotides, compared to horses fed the non-supplemented diet, while immunity parameters simultaneously improved. In the same trial, a significant increase of the liver enzymes was found in the horses supplemented with nucleotides (9).

Until recently, there has been limited available data on nucleotide supplementation on the immunologic effects and on stress parameters in humans. This is an area of research that Swiss company Pro Bio Ltd, along with Nucleotide Nutrition Ltd, have been pioneering. Pro Bio’s exclusive formulation of purified nucleotides has been shown to lower the formation of cortisol and therefore prevent the decline of the immune system in endurance athletes (12,13,16). Refer to Research study 1.

Research study 2: nucleotides effects on oxidative stress (24).

INTRODUCTION: Oxidative stress, induced by high doses of Polyunsaturated Fatty Acids (PUFAs), was quantified at the beginning and end of 21 days of supplementation of PUFAs by the ‘Comet-test’, which measures the damage to the DNA of white blood cells. During the comet-test, the DNA becomes isolated and exposed to electrophoresis (19): an intact, non-damaged DNA will stay at the point of application. However, DNA that is exposed to oxygen radicals

becomes cracked into smaller parts. These smaller DNA parts can migrate in the electric field and form a tail; the more damage that occurs in the DNA, the longer the tail.

Control
PUFAs
PUFAs + nucleotides



Figure 3 – Free Radical Damage to DNA by PUFAs and Protection by Nucleotides

RESULTS: In the control group, 4% of the lymphocytes showed damaged DNA. In the group with PUFAs alone, 15% of the lymphocytes had damaged DNA. If nucleotides were applied together

with the PUFAs, the amount of lymphocytes with damaged DNA was again, only 4%.

CONCLUSION: These results show that the application of nucleotides can reverse the damage of the DNA caused by oxidative stress. Nucleotides are therefore a very important food supplement to sustain the repair mechanisms in the body, with primary importance to the efficient function of the immune system. Nucleotides support the protection of the body against the damaging effects of oxygen radicals and help to lower the negative effect of stress.

Effects of a nucleotide supplement on oxidative stress

Oxidative stress is known to induce genotoxic effects upon immune cells. Increased production of free radicals has been attributed to cigarette smoking, high UV radiation, excessive mental or physical stress and exposure to heavy metals. They are also detected in athletes after excessive training, due to high oxygen turnover (20,21,22,23). Because free radicals also occur naturally in a healthy metabolism, the organism protects itself by virtue of antioxidants and cell repair mechanisms (14).

Since nucleotides play a role as immunomodulatory nutrients, their role in the prevention of effects of oxidative stress formation could be of interest. The aim of Research study 2 was therefore to evaluate the effect of nucleotide supplementation on oxidative stress, induced by a high proportion of dietary Polyunsaturated Fatty Acids (PUFAs).

Nucleotides in the sports world

The NuCell® nucleotide product already mentioned, now has a new sister product, called NuCell®IM, which is designed for sportspeople. The research behind NuCell®IM has been conducted to show that a specialised combination of vitamins, amino acids and nucleotides can enable generally healthy sports men and women to support their immune (shown in Figure 2) and hormonal responses during times of heavy demand (12,13,25).

The vitamins and nutrients contained in NuCell®IM also have a role in the process of cell division and regeneration, protecting cells from oxidative stress and contributing to iron absorption and normal red blood cell formation. In recognition of the need for sports men and women to be able to choose sports supplements that are free from prohibited substances, NuCell®IM is registered and tested through the HFL Sports Science *Informed-Sport* prohibited substances testing programme. *FSN*



About the author
Dr Peter Koepfel has a

PhD in biochemistry and immunology. He was trained in biochemistry, with a special interest in clinical immunology at the Institute of Virology at the University of Zürich. He then worked as a researcher in osteoarthritis and osteoporosis in a pharmaceutical company in Basel. Since 1989 he has been involved in producing special additives for human nutrition for Pro Bio Ltd, laterally becoming the managing director of this company in year 2000.

REFERENCES

- Seyle H (1975). The stress of life New York, McGraw-Hill.
- Biondi M (2001). Effects of stress on Immune function: an overview. In Ader R et al. *Psychoneuroimmunology*. San Diego (CA): Academic press.
- Avitsur R et al (2001). Social stress induces glucocorticoid resistance in subordinate animals. *Horm Behav*. 39.
- Avitsur R et al (2009). Social Interactions, Stress, and Immunity. *Immunol Allergy Clin N Am*. 29.
- Miller GE et al (2002). Chronic psychological stress and the regulation of pro-inflammatory cytokines. *Health Psychol*. 21.
- Dantzer R & Kelley KW (1989). Stress and immunity: an integrated view of relationships between the brain and the immune system. *Life Sci*. 44.
- Schedloski M & Schmidt RE (1994). Stress and the immune system. *Naturwissenschaften*. 83.
- Avitsur R (2006). Social Interactions, Stress and Immunity. *Neurologic Clinics*. 24.
- Art T et al (1994). Cardio-respiratory, haematological and biochemical parameter adjustments to exercise: effect of a probiotic in horses during training. *Vet Res*. 25.
- Vasquez-Garibay E et al (2004). Nutritional support with nucleotides addition favors Immune response in severely malnourished infants. *Arch Med Res*. 35.
- Van Buren C & Rudolph F (1994). Dietary nucleotides: A conditional requirement. *Nutrition*. 13.
- McNaughton L et al (2006). The effect of a nucleotide supplement on salivary IgA and cortisol after moderate endurance exercise. *J Sports Med & Phys Fit*. 46:84-89. <http://nucleotides4health.org/immunity.html>
- McNaughton L et al (2007). The effects of a nucleotide supplement on the immune response to short term, high intensity exercise performance in trained male subjects. *J Sports Med & Phys Fit*. 47(1):112-119. <http://nucleotides4health.org/immunity.html>
- Rezar V et al (2003). Wheat and oat bran effectively reduce oxidative stress induced by high fat diets in pigs. *Annals of Nutrition and Metabolism*. 47:78-84.
- Yu IT et al (2002). Role of glutamine and nucleotides in combination on growth, immune response and FMD antibody titres of weaned pigs. *Animal Science*. 75:379-385.
- McCowan KC & Bistrain BR (2003). Immunonutrition: problematic or problem solving? *Am J Clin Nutr*. 77:764-770.
- Carver JD (1994). Dietary nucleotides: cellular immune, intestinal and hepatic system effects. *J Nutr*. 124(1 Suppl):144S-148S.
- Carver JD (1999). Dietary nucleotides: effects on the immune and gastrointestinal systems. *Acta Paediatr Suppl*. 88(430):83-88.
- Olive PL et al (1992). Factors influencing DNA migration from individual cells subjected to gel-electrophoresis. *Exp Cell Res*. 198:259-267.
- Alessio HM (1993). Exercise-induced oxidative stress. *Med Sci Sports Exerc*. 25(2):218-224.
- Alessio HM et al (2000). Generation of reactive oxygen species after exhaustive aerobic and isometric exercise. *Med Sci Sports Exerc*. 32(9):1576-1581.
- Niess AM et al (1999). Free radicals and oxidative stress in exercise-immunological aspects. *Exerc Immunol Rev*. 5:22-56.
- Kim JD et al (1996). Influence of age, exercise, and dietary restriction on oxidative stress in rats. *Aging*. 8(2):123-129.
- Salobir J et al (2005). Effect of nucleotide supplementation on lymphocyte DNA damage induced by dietary oxidative stress in pigs. *British society of Animal Science*. 81:135-140.
- Hess JR & Greenberg NA (2012). The role of nucleotides in the immune and gastrointestinal systems: potential clinical applications. *Nutr Clin Pract*. 27(2):281-294.