

Fondazione Paolo Sorbini
per la scienza nell'alimentazione



Milan 5th-6th May 2017

Science in Nutrition
4th International Congress

Positive Nutrition

THE LATEST DISCOVERIES ON THE POWER OF NUTRITION
RELATED TO HEALTH & SLIMMING,
ANTI-INFLAMMATORY DIET AND SPORTS PERFORMANCE.

Milano, 5-6 Maggio 2017
Hotel Principe di Savoia | Piazza della Repubblica, 17

CONGRESS PROCEEDINGS

“ If we want to advance we must carry out research.
This is especially true in nutrition.
Research must be continuous. ”

Paolo Sorbini

SCIENCE IN NUTRITION 4th INTERNATIONAL CONGRESS POSITIVE NUTRITION

5th MAY 2017

Welcome

Maurizia Sorbini

Presidente Fondazione Paolo Sorbini

1ST SESSION

POSITIVE NUTRITION FOR HEALTH & SLIMMING

Chairman: **Barry Sears**

A Balanced Omega-6 to Omega-3 Ratio for Health

Artemis Simopoulos

New Treatments for Diabetes

Camillo Ricordi

Functional Nutrition: the Key of Life

Sara Farnetti

Nutritional Management of Insulin Resistance

Carol Johnston

Round Table

Positive Nutrition: the Pillars of Longevity

2ND SESSION

POSITIVE NUTRITION FOR ANTI-INFLAMMATORY DIET

Chairmen: **Benvenuto Cestaro - Giovanni Scapagnini**

The Role of Anti-inflammatory Nutrition in the Treatment of Chronic Disease

Barry Sears

Positive Nutrition and Nutraceutical Interventions for Improving Healthspan and Longevity

Giovanni Scapagnini

Biochemical Mechanism and Nutritional Treatment to Prevent Inflammation, Oxidative Stress, Aging and Chronic Disease

Benvenuto Cestaro

The Role of Omega-3 Fatty Acids in the Management of Chronic Disease

Jing Kang

Prevention of Metabolic Complications in Pregnant Women

Enrico Ferrazzi

SCIENCE IN NUTRITION 4th INTERNATIONAL CONGRESS POSITIVE NUTRITION

6th MAY 2017

3rd Session POSITIVE NUTRITION FOR SPORTS PERFORMANCE

Chairman: **Rodolfo Tavana**

Remembering Enrico Arcelli

Nutraceuticals Role in Sports Nutrition

Fabrizio Angelini

Sports Nutrition of the Future

Asker Jeukendrup

The Role of Betaine on Body Composition and Performance

Gregory Paul

Hydration Management for Training and Competitions: New Perspectives

Luca Mondazzi

Cocoa Flavanols and Endothelial Function: what Perspectives in Sports

Davide Grassi

Anti-inflammatory Diet and Injury Risks in Sportsmen

Stefano Righetti - Elena Casiraghi - Francesco Chiappero - Serena Martegani

Maurizia Sorbini

President of Paolo Sorbini Foundation

WELCOME

I am full of emotion and I am very proud to open the 4th International Congress Science in Nutrition 2017, titled Positive Nutrition. It is a real pleasure to welcome you all.

The first edition of the congress organized in 2008 under the auspices of the Paolo Sorbini Foundation for Science in Nutrition in 2008 (which had been established by my brothers Pino, Alberto and myself) was a real challenge. It was the continuation of a journey started by our father, Paolo Sorbini, aimed at promoting scientific research and disseminating the results of new studies on nutrition in a quest for a healthier life. In his farsightedness and profound intuition, our father was able to rely on the outstanding support of Enrico Arcelli, who accompanied him in this journey towards new frontiers. I feel deeply moved in remembering him today. In fact, the third session, on sports, is dedicated to him. I would also like to remember with great affection Fulvio Marzatico, a very good researcher who was one of the speaker in the previous conference.

Glycemic index and glycemic load were the main topic of the 2008 Congress, and this paved the way to an improvement in quality of life. This year, in the three sessions of the Congress, we would like to shed light on Positive Nutrition. Light means knowledge, light means research. I am referring to an ongoing research effort that encourages permanent updating of knowledge in the field of human nutrition. This has always been Doctor Sorbini's message.

In these two days of debate, extremely relevant scientific themes will be analyzed by authoritative speakers coming from renowned foreign Universities (including Harvard, Arizona, Washington, St Louis, Miami, Loughborough and Leicester) as well as Italian ones (Milan, Pavia, Insubria, Parma, L'Aquila, Molise). Researchers will illustrate their investigations and experiences and allow us to take stock of the current knowledge on correct nutritional approaches and propose guidelines for a healthy lifespan in a longer-lived population. In particular, I would like to thank the Presidents of the three sessions, Benvenuto Cestaro, Giovanni Scapagnini and Barry Sears, for their scientific contribution to the Congress and all of you who have come who numerous.

It is an honour and pleasure to thank the Lombardy Region for their patronage of the Congress, which acknowledges the importance of the topics discussed here.

I would also like to extend my gratitude to the companies that have made Science in Nutrition 2017 possible: DuPont, Enervit, Epax, Gandola, Inflammation Research Foundation. In giving the floor to Professor Giovanni Scapagnini for an introduction to the Congress, I wish you two very fruitful working days.

First Session

POSITIVE NUTRITION FOR HEALTH AND SLIMMING

Chairman: Barry Sears

A BALANCED OMEGA-6 TO OMEGA-3 RATIO FOR HEALTH

Artemis P. Simopoulos

President of World Council on Nutrition, Fitness and Health – WCNFH and Center for Genetics, Nutrition and Health- Washington D.C. USA

Founding member and past president of the International Society for the Study of Fatty Acids and Lipids (ISSFAL)

Human beings evolved on a diet that had equal amounts of ω -6 and ω -3 fatty acids. This balanced ratio of ω -6 to ω -3 is critical to human development during pregnancy and lactation, in the prevention of chronic diseases and in their management. The ω -6 and ω -3 fatty acids are metabolically and functionally distinct. The typical Western diet now provides an ω -6 to ω -3 ratio of around 16:1. High dietary intake of ω -6 fatty acids as occurs today leads to increases in white adipose tissue and chronic inflammation, which are the 'hallmarks of obesity'. ω -6 and ω -3 fatty acids specifically metabolise to prostaglandins, thromboxane and leukotrienes. Prostaglandin E_2 from AA leads to differentiation and proliferation of adipose tissue and prostaglandin $F_{2\alpha}$ also from AA prevents the browning of white adipose tissue, which is the good fat tissue as it increases thermogenesis, burning fat through the release of heat. ω -3 fatty acids decrease adipose tissue development and lead to weight loss. A high intake of LA from vegetable oils leads to a disproportionate increase in AA in individuals with haplotype D (genetic variants in fatty acid desaturase (FADS)1 and FADS2), which increases the risk of obesity. ω -3 fatty acids (EPA and DHA) decrease adipose tissue and produce lipid mediators-resolvins, protectins and maresins, which are neuroprotective and lead to resolution of inflammation. Furthermore ω -3 fatty acids lead to increased fatty acid oxidation and mitochondrial biogenesis. A high ω -6 to ω -3 ratio in current Western diets coupled with an increased synthesis of proinflammatory cytokine interleukin 6 (IL-6) from the adipose tissue of an already overweight and obese population propagates obesity by increasing or maintaining chronic inflammation. It is therefore essential to return to a balanced dietary ω -6 to ω -3 ratio. By decreasing ω -6 and increasing ω -3 in the diet, the proadipogenic pathway can be inhibited. The preferred ratio of ω -6 to ω -3 for optimal health is 1:2/1, which is consistent with the evolutionary aspects of diet.

NEW TREATMENTS FOR DIABETES

Camillo Ricordi

Director Diabetes Research Institute and Cell Transplant Program, Stacy Joy Goodman Professor of Surgery and Medicine. Professor of Biomedical Engineering, and Microbiology and Immunology, University of Miami, Florida, USA

Strategies for restoration of beta cell mass will fall under either “replacement” (transplantation of insulin producing cells), “differentiation/reprogramming” (generation of insulin producing cells from native non-insulin-producing cells), “regeneration” or “expansion” of residual beta cell mass (e.g., from endogenous precursors/stem cells or by beta cell expansion in micro-secretors). A multicenter Phase III trial of transplantation of adult pancreatic islet has been recently completed and is moving towards a Biological License Application (BLA) in the USA, while novel technologies to engineer an intra-abdominal mini-endocrine pancreas are currently being tested in pilot clinical trials. Novel immunotherapy technologies will be explored for restoration of self-tolerance or to block the alloimmune destruction of the new insulin producing cells, independently from the technology used for restoration of beta cell mass, such as regeneration, reprogramming or replacement (e.g., transplantation of pancreatic islets or stem cell derived insulin producing cells). Abrogation of autoimmunity and alloimmunity, or their effects, could be achieved by either tolerance induction strategies or immune protection (e.g., engineered microenvironment or selective permeability physical barriers like those introduced by micro-, conformal- or nano-encapsulation). Any future therapeutic technology considered must avoid side effects such as those associated with life-long immunosuppression, currently limiting the indications of adult islet transplantation to the most severe cases of T1DM. There is a broad consensus on the idea that stem cells will eventually replace adult pancreatic islets in the future. However, the jury is still out regarding the candidate cell type/s and approach that will ultimately succeed. Differentiation technologies for generation of insulin-producing cell from adult stem cells will be further developed, spanning from signal-driven approaches, to genetic manipulation and even strategies of in-vivo maturation after systemic administration. The more suitable alternatives between replacement, reprogramming and regeneration strategies will be further developed in pre-clinical model systems and tested in pilot clinical trials, while carefully assessing safety, efficacy, cost-effectiveness and the relative potential for scale up, to offer a realistic therapeutic option for most patients affected by diabetes.

FUNCTIONAL NUTRITION: THE KEY OF LIFE

Sara Farnetti

Internal Medicine Specialist

Ph.D.in Pathophysiology of Metabolism and Nutrition

Associate Professor Diabetes Research Institute, University of Miami Miller School of Medicine

The interaction “Food - Organic Functions” regulates, with its code, the balance between health, maximum performance and risk of disease. Awareness of the impact of the food we eat and knowledge of food dynamics and kinetics allow us to achieve better health by preventing, treating and healing widespread disorders and pathologies. If we exploit the fine mechanisms that link “food - hormones - metabolism” we can be in shape for longer, preserve the genes of longevity, and reduce the incidence of cancer, diabetes, cardiovascular and central nervous system degenerative diseases. These are the main killers of our time and are related to the Metabolic Syndrome. This condition identifies a number of risk factors, in particular the increase in waist circumference, a true index of the presence of the killer instigator, i.e. visceral fat. This fat may be located in the abdomen around vital organs and in hepatocytes, myocytes, and at epicardial level. Adopting a functional nutrition strategy in every meal has a clear preventive and therapeutic impact since “every meal is a hormonal project”. Combining foods is essential, keeping in mind not only the balance of nutrients but also the ability of food to promote the release of hormones and neurotransmitters and to regulate the ratio between essential fatty acids. These molecules are crucial for the distribution of adipose tissue at the abdominal or subcutaneous level, in the trunk or thighs.

They affect mood, sleep-wake rhythm, improve muscle tone, have a pro- or anti inflammatory and antioxidant action and they alter the equilibrium of the gut microbiota. These effects are independent of the calories of ingested food and are, however, closely related to its functional action. The nutritional composition of foods, in fact, is not the main determinant. The way to prepare, cook, and associate food with other foods may have indications and contraindications and have a direct effect on organ function. Foods used in a functional way contain the code of life.

NUTRITIONAL MANAGEMENT OF INSULIN RESISTANCE

Carol S. Johnston

Professor and Associate Director of the Nutrition Program in the School of Nutrition and Health Promotion at Arizona State University, USA

Insulin is a pancreatic hormone that enables cells, particularly muscle cells, to remove glucose from the blood stream. Insulin resistance, the best predictor of risk for type 2 diabetes, is characterized by the decreased ability of insulin to exert its metabolic actions on target cells. The degree of insulin resistance is commonly evaluated using the Homeostasis Model Assessment (or HOMA-IR) equation: $(\text{fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mmol/L)}) / 22.5$. Values $\rightarrow 1.85$ in men and $\rightarrow 2.07$ in women aged 50 years old are suggested to indicate high cardio metabolic risk. The mechanisms of insulin resistance are complex, and involve dysfunctions in the intracellular signaling cascade that takes place following the attachment of insulin to its receptor. Increased inflammation appears to be associated with this dysfunction, specifically the presence of intracellular reactive oxygen species (ROS). Raised muscle diacylglycerol (DAG) concentrations have also been implicated in insulin resistance.

Significant reductions in insulin resistance can be achieved by antioxidant supplementation which helps to reduce intracellular ROS. For example, 8-week supplementation with CoQ10 (100 mg/d), selenium (200 $\mu\text{g/d}$), vitamins E (400 IU/d), or vitamin C (1000 mg/d) has been shown in separate randomized, placebo-controlled trials to reduce insulin resistance by around 20%.

Increased fatty acid delivery to cells in situations of excess calorie ingestion or high-fat diets, increases cell content of bioactive lipid species such as DAG. DAG has inhibitory effects on the insulin receptor mediated signaling cascade. Calorie restriction reduces DAG concentrations in cells and raises levels of mitochondrial fat oxidation, concurrent with reductions in insulin resistance.

Muscle mass is a robust predictor of insulin sensitivity; however, calorie restriction associated weight loss reduces muscle mass in most incidences. We hypothesized that high protein meals coupled with calorie restriction may spare lean mass and accentuate weight loss-induced improvements in insulin sensitivity. Utilizing a single-blinded, randomized controlled study design, we demonstrated that novel high-protein foods (providing ~ 20 g protein/serving) consumed throughout the day at meals was equally effective at reducing body weight as an isocaloric control diet composed of foods with standard protein content; however, fat-free mass was increased for the high-protein group in comparison to losses noted for the control group ($+1.5 \pm 3.8$ kg vs. -0.5 ± 1.5 kg respectively; $p=0.018$). Furthermore, the high-protein group displayed greater reductions in insulin resistance in comparison to the control group in the face of similar losses in total mass (-1.7 ± 1.4 vs -0.7 ± 0.7 respectively; $p=0.020$).

Several nutrition intervention strategies have proven highly successful at reducing insulin resistance in high risk populations, particularly antioxidant supplementation and calorie restricted meal plans that include high-protein foods. These nutritional strategies for reducing insulin resistance are safe and simple to implement at any age, an important consideration since insulin resistance can progress to type 2 diabetes.

ROUND TABLE

POSITIVE NUTRITION: THE PILLARS OF LONGEVITY

Nutrition and superfood are the key pillars of positive nutrition. The Zona diet is an example of an effective, balanced nutritional strategy. Aside from being based on restricting calorie intake, it also requires the use of anti-inflammatory superfood and supplements, such as omega-3 fatty acids and polyphenols. Food becomes a source of beneficial substances for one's health, and has a specific impact on the body and the functioning of each cell. For such pillars to be even more solid, they require robust foundations: physical exercise, anti-stress practices - especially yoga - breathing and meditation. These are true allies in the daily battle against inflammation. These topics were the focus of the round table debate, moderated by Linus and underpinned by top-class global exponents of scientific research into nutrition. The first three names on this list are the Congress chairs: Benvenuto Cestaro (University of Milan), Giovanni Scapagnini (University of Molise) and Barry Sears (Inflammation Research Foundation of Boston, USA); alongside them, Silvia Brambilla (Milan), Elena Casiraghi (Milan), Sara Farnetti (University of Miami, USA), Asker Jeukendrup (University of Loughborough, UK), Jing Kang (University of Harvard - Boston, USA), Camillo Ricordi (University of Miami, USA), and Artemis Simopoulos (President of the World Council on Nutrition, Fitness and Health - WCNFH - Washington D.C. - USA).

Every expert showed how longevity depends on a correct lifestyle. Ageing is not merely a physiological condition, as one must age well and in good health. The tools to do this exist. Physicians tell us as much; positive nutrition shows us as much.

Simply living longer is not sufficient. Longevity is one consideration; the duration of one's good health - or healthspan, to use the American term - is another, focusing on the years without illness. Lengthening one's life in good health requires fighting inflammation through eating.

"Inflammation can be a double-edged sword," Barry Sears explained. "It allows us to defend ourselves against microbial invasion and allows our injuries to heal. Yet, on the other hand, if the inflammatory response is not sufficiently resolved, the resulting chronic low-level inflammation can attack our organs, accelerating the early development of chronic disease. Maintaining inflammation in a zone that is not too low, but not too high is one of the key factors of positive nutrition, as it makes it possible to keep hormones in check, especially insulin, and to reduce the early onset of chronic diseases. Cells need to be trained to be healthy, adopting a suitable nutrition programme."

"Insulin is an essential hormone for life," clarified Camillo Ricordi. "Without it, in reality, cells cannot use glucose as an energy source. Stabilising insulin is a fundamental part of an anti-inflammatory diet. It is necessary to eliminate negative nutritional combinations that stimulate the silent inflammation caused by the perfect nutritional storm. Limiting refined carbohydrates and sugars, which rapidly increase insulin levels, increases the positive factors. This re-establishes the hormonal and genetic balance. Anti-inflammation nutrition with low calorie intake must be seen as a way of reducing the signals from genes, especially those that stimulate forms of silent inflammation."

"An anti-inflammatory diet requires a reduction in pro-inflammatory foods," added Benvenuto Cestaro, "such as hydrogenated fatty acids (oven products, confectionery, fast food, margarine etc.), saturated fatty acids (red meat, milk, butter and cheese), omega-6 fatty acids (containing arachidonic acid comes). The focus should be on mono-unsaturated fatty acids (e.g. olive oil) and, above all, omega-3 polyunsaturated

fatty acids. The ideal ratio between omega-6/omega-3 in a diet is roughly 1:2. A further recommendation: reduce calorie intake, without causing oneself to feel tired or hungry, which in turn cause most of us to give up weight-loss diets.”

“In the history of man,” explained Artemis Simopoulos, “our parents maintained a balance between omega-6 and omega-3 fatty acids, leading to the development of the body and the brain. A balanced ratio between omega-6 and omega-3 is vital for human development during pregnancy and breastfeeding, and for preventing and managing chronic diseases. Omega-3 fatty acids are essential, but in the food we eat every day, there are only small quantities of such acids. This is at the basis of the inflammation processes that might explain the increase in chronic-degenerative diseases. Today, the western diet is based on a ratio between omega-6 and omega-3 often exceeding 20:1, which is too high. Too many omega-6 fatty acids lead to an increase in white fatty tissue and chronic inflammation. This leads to the production of pro-inflammation substances in fatty tissue in people who are already overweight or obese, resulting in an increase in obesity and inflammation. Positive nutrition is designed to return the balance in a diet between omega-6 and omega-3 to the ideal 1:2 ratio, although 1:1 is better, like our forefathers.”

“Positive nutrition is based on the premise that every type of food can have specific, positive functions for our body,” highlighted Sara Farnetti. “We need to learn to see every meal as a hormone strategy that directly influences what each of our organs does and has an impact on our DNA. Functional nutrition helps us understand the workings of food that could be a tool in preventing, treating and even healing. Indeed, food can activate the longevity gene by directly influencing our genes.”

“We are used thinking about a diet as privation,” stated Giovanni Scapagnini. “In other words, we see it as the need to remove or eliminate the consumption of specific types of foods, if we have health issues like high cholesterol or diabetes. Yet, food can be a source of beneficial substances for one’s health - genuine medication - that act in very precise ways on the body and the functioning of each individual cell. Positive nutrition is also based on positive biology. Research is not into diseases or sick people, but the positive aspects of healthy people or populations that live far longer than average. Okinawa and Sardinia are two of the famous ‘Blue Zones’.”

“Inhabitants of these Blue Zones,” continued Scapagnini, “all have, above all, one thing in common: a low-calorie diet. They also all have diets with low glycaemic index carbohydrates, mainly from sources like fruit and vegetables, with little use of refined sugars and starches. Fish (or seaweed, for Okinawa) provides significant amounts of omega-3 polyunsaturated fatty acids. They also eat plenty of fruit and vegetables with lots of polyphenols. Omega-3 and polyphenols are seen as superfoods because it has been found that they are ever present in those populations that live the longest. They are like trainers for our cells because they can trigger gene transcription. In practice, they teach cells to maintain control of oxidative stress, inflammation and metabolism.”

“These precious nutrients,” explained Scapagnini, “can be obtained by choosing food carefully or, when necessary, using a supplement. Unfortunately, it is simply not true that healthy eating is sufficient to get all the nutrients we need, both because food has become nutritionally less rich and because the quantities we manage to eat are insufficient for getting these beneficial nutrients. This does not necessarily

mean one has to take a pill, as a health bar or chocolate might be what is needed - the key is that it contains the required active ingredients.”

“Positive nutrition also extends to movement,” noted Elena Casiraghi. “Everyone now knows that regular physical exercise is good for one’s health. The body needs to be trained through moderate physical exercise. This is also how cells are trained. One could start with 100 minutes a week, in three sessions: a 40-minute low aerobic intensity session at the weekend and a further two 30 minute sessions during the week, with rest days in-between. The best times are early in the morning, before eating, or in the evening using interval training. It is also a good idea to introduce 1 or 2 bodyweight sessions a week.”

“Nutrition and physical exercise,” noted Asker Jeukendrup, “are fundamental aspects for a sports person to perform. The future of sports nutrition is based on two points of view. The main areas of development are focused on periodised nutrition and personalised nutrition, which set out short and long-term planning for nutrition and supplements in accordance with the training plans and habits of each individual.”

“To lose weight and live longer,” said Silvia Brambilla, “anti-stress techniques are necessary, starting with yoga. Authoritative research has shown that yoga reduces cortisol, the stress hormone. Deep, slow breathing encourages oxygen exchange, helps slow the heart rate and stabilise pressure. Doing such activities constantly is mindfulness, which draws out the wisdom in each of us, stimulates the perception of one’s own individual strength and balance. It leads to a different, positive perception of ourselves that leads to a natural change in lifestyle, where choices are pondered better and more sustainable. From nutrition to physical exercise.”

These issues are explored in a book entitled “Positive Nutrition: The Pillars of Longevity” - published by Sperling & Kupfer - that was also the source of the name for this round-table discussion, a true statement for well-being in the future. Because it teaches cells how to learn to live better and longer, starting from restricting calorie intake.

Second Session

POSITIVE NUTRITION FOR ANTI-INFLAMMATORY DIET

Chairmen: **Benvenuto Cestaro, Giovanni Scapagnini**

THE ROLE OF ANTI-INFLAMMATORY NUTRITION IN THE TREATMENT OF CHRONIC DISEASE

Barry Sears

President, Inflammation Research Foundation, Peabody, MA USA

The underlying cause of many chronic diseases is chronic low-level inflammation at the cellular level. This is termed as cellular inflammation. Anti-inflammatory nutrition is a comprehensive dietary program to lower such inflammation in the blood, brain, and the gut. The primary dietary interventions used to treat cellular inflammation are the Zone Diet, high-dose omega-3 fatty acids, and high-dose polyphenols. The Zone Diet is a calorie-restricted, balanced macronutrient dietary program rich in prebiotics shown to alter hormonal responses in the blood and to reduce cellular inflammation. High-dose omega-3 fatty acids are instrumental in the resolution of existing cellular inflammation, especially in the brain. Finally, high-dose polyphenols are useful in maintaining gut health, the integrity of the barrier between the microbiota in the gut and the blood, as well as activating specific gene transcription factors if they enter into the blood.

The clinical markers in the blood that determine that success of such each of the factors that compose anti-inflammatory nutrition include the following:

1. the ratio of arachidonic acid (AA) to eicosapentaenoic acid (EPA) as a marker of systemic cellular inflammation;
2. the ratio of triglycerides to HDL cholesterol as a marker for insulin resistance;
3. the levels of glycosylated hemoglobin as a marker for long-term glycemic control.

The use of anti-inflammatory nutrition provides the potential not only to alter the expression of inflammatory genes, but also to resolve existing inflammation in many chronic disease conditions.

POSITIVE NUTRITION AND NUTRACEUTICAL INTERVENTIONS FOR IMPROVING HEALTHSPAN AND LONGEVITY

Giovanni Scapagnini

Professor of Clinical Biochemistry at Department of Medicine and Health Science, University of Molise, Campobasso, Italy

Proper nutrition is a direct factor affecting well-being and health. Beyond the nutritional value, nutraceuticals and functional foods contain health-promoting components with specific beneficial effects on ageing. Diet-regulated genes play a crucial role in the onset and progression of several chronic disorders and dietary interventions can be used to mitigate these diseases but also to maintain health. The nutrient regulation of key genes involved in ageing may prevent oxidation and inflammation, reducing cellular damages to proteins, membranes, and mitochondria. In recent years, there has been a growing interest, supported by a large number of experimental and epidemiological studies, about the beneficial effects of some commonly used food-derived phytochemicals. In particular, spices, herbs and fruits contain polyphenols endowed with potent antioxidative and chemopreventive properties. Although the exact mechanisms by which polyphenols promote healthspan remain to be elucidated, it is now well demonstrated that these compounds act on a number of different molecular targets, impinging on several signaling pathways, and showing pleiotropic activity on cells and tissues. A possible general mechanism of polyphenols healing activity, relate to their ability to overexpress highly protective inducible genes, involved in the cellular stress response, and by these modulating oxi-inflammation at both cellular and organism level. We have previously demonstrated that curcumin, the yellow pigment of curry, strongly induces antioxidant genes expression in different cells via the activation of heterodimers of NF-E2-related factors 2 (Nrf2)/antioxidant responsive element (ARE) pathway. We have recently demonstrated the *in vivo* ability of berries anthocyanins and cocoa flavanols to improve oxidative status (Oxidized-LDL and F2-isoprostanes) in healthy adults, and protect cellular and blood lipids from oxidative damages. Furthermore, we have shown their ability to downregulate pro-inflammatory cytokines and their downstream biochemical pathways, and to modulate mitochondrial biogenesis and glucose metabolism via the activation of AMP kinase. Despite the translational gap between basic and clinical research, the current understanding of the molecular interactions between polyphenols and oxy/inflammatory response could help in designing effective nutritional strategies to delay the onset of chronic diseases and improve healthy aging.

BIOCHEMICAL MECHANISM AND NUTRITIONAL TREATMENT TO PREVENT INFLAMMATION, OXIDATIVE STRESS, AGING, AND CHRONIC DISEASE

Benvenuto Cestaro

Professor of Biological Chemistry and Biochemistry of Nutrition University of Milan
Medical Faculty - Italy

In the past 20 years evidence has been accumulated suggesting that inflammation-induced oxidative stress and damage to cellular components play an integral role in the age-related deterioration of biochemical and physiologic processes and in the incidence of age-related disease. Mitochondria are the primary site for ROS generation as a by product of aerobic metabolism and the accumulation of mitochondrial oxidative damage over time diminishes the cellular efficiency in energy production (ATP). Moreover, oxidative stress contributes to functional and structural alterations of tissues and blood vessels that decrease the supply of oxygen and nutrients to the various organs and body systems, thus further reducing energy production. The deficiency of ATP decreases the bioavailability of all the molecules whose biosynthesis requires the intervention of ATP itself and slows down the process of repair and replacement of the various lipid or glycoprotein molecules, which make up the bilayer structural organization of the cell membrane. Current evidence suggests that the processes at the cell surface seem to be of comparable importance for the life of an individual as the nucleus for the preservation of the species. Inflammation-induced oxidative stress leads to progressive structural alteration of membranes manifested by a progressive reduction of membrane fluidity that causes a secondary metabolic damage to the cells. The membrane hardening, in fact, limits the capacity of membrane proteins to collide with their ligands, thus reducing the activity of enzymes, receptors for hormone or neurotransmitter, ion channels and the trans-membrane carriers for amino acids and glucose. There is thus a spiral of structural and functional damage to cells and tissues, starting with the reduced efficiency in ATP synthesis which is further amplified by the decreased rate of synthesis of membrane macromolecules and lipids, the increase in intracellular calcium and potassium, and the increase in inflammation and ROS-induced peroxidation processes. How the onset of this spiral could be kept under control with either an adequate diet or a supply of appropriate functional food will be the main issue of this presentation.

THE ROLE OF OMEGA-3 FATTY ACIDS IN THE MANAGEMENT OF CHRONIC DISEASES

Jing X. Kang

Director of Laboratory for Lipid Medicine and Technology (LLMT), Professor at Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

The growing threat of chronic diseases to global health calls for safe and effective measures to conquer current health problems. The association of chronic diseases with nutrient metabolism points to the possibility of certain dietary factors as underlying causes of today's disease epidemic. Identification of the risk factors and development of nutritional interventions to target the disordered metabolism may be an important approach to the management of chronic disease.

A potential cause of the modern prevalence of chronic disease is an increase in dietary intake of omega-6 fatty acids and a decrease in consumption of omega-3 fatty acids. These changes in omega-6 and omega-3 fatty acid intake have dramatically shifted the omega-6/omega-3 fatty acid ratio in our bodies from the human evolutionary ratio of ~1:1 to the modern imbalanced ratio of 10:1 or higher. This shift in the omega-6/omega-3 ratio has profound implications on human health, as these two classes of essential fatty acids are key components of cellular membrane structure and function, and have opposing effects on many physiological and pathological processes – including chronic inflammation, gut microbiota, adipogenesis and lipogenesis, and energy metabolism – which underlie the development of many chronic diseases. In general, increased tissue omega-6 fatty acid content confers higher risk for chronic diseases, while increased tissue omega-3 fatty acid status suppresses the development of chronic diseases. A growing body of evidence from molecular and animal to human levels shows that a high tissue ratio of omega-6/omega-3 fatty acids is detrimental to health and promotes development of chronic diseases, while balancing or reducing the omega-6/omega-3 ratio can have preventive as well as therapeutic effects on chronic diseases. Furthermore, recent studies demonstrate that high doses of omega-3 fatty acids are indeed effective in treating certain clinical conditions. We therefore propose that the tissue ratio of omega-6/omega-3 fatty acids is an important determinant and biomarker of health, and that balancing the ratio by decreasing omega-6 fatty acids and increasing omega-3 fatty acids may be a promising solution to modern health problems.

PREVENTION OF METABOLIC COMPLICATIONS IN PREGNANT WOMEN - OBESITY, METABOLIC SYNDROME AND GESTATIONAL DIABETES

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The metabolic dysfunction suffered in utero by the fetus of a mother affected by Gestational Diabetes (GD) will have a life-long impact on the metabolic and cardiovascular condition of the future adult.

In addition to this GD, if untreated, is associated with late gestational hypertension or maternogenic preeclampsia probably caused by the same low-grade inflammatory stress.

An extensive literature has reported both increased risk and greater protection in the association between specific nutritional factors and type 2 diabetes in non-pregnant women.

In the Nurses' Health Study II two dietary patterns are described, the pattern of the Western diet, characterized by a high intake of red meat, processed meat, refined grains, sweets, chips, pasta, pizza and the prudent dietary pattern characterized by high consumption of fruit, nuts, vegetables, fish and poultry, and reduced consumption of red meat and dairy products.

Strong positive associations were observed between the score obtained by the Western dietary pattern and the risk of developing gestational diabetes,

The link between maternal condition and insulin resistance is determined by the chronic inflammation of visceral and deep subcutaneous adipose tissue, and by the unbalanced ratio between saturated and polyunsaturated fats (OMEGA-3) with a background of other dietary factors, antioxidants, vitamins, minerals and fibre as well as physical activity.

A special role among antioxidants is played by polyphenols that are associated with a reduced incidence of type 2 diabetes in humans. The fruit from *Aristotelia chilensis* (Maqui) is extremely rich in anthocyanins. Purified extracts of the maqui berry have been shown to reduce glycaemia upon an acute carbohydrate challenge and to reduce oxidative stress under chronic administration.

We started a randomized trial in pregnant women at high risk of gestational diabetes, with the aim to assess the impact of Omega-3, Polyphenols and maltodextrines when added to a standard Mediterranean diet, modified according to the Healthy Eating Plate recommendations by the Harvard University- School of Public Health, and in agreement with the requirements (LARN 2014) of Italian Ministry of Health.

Eligible women will be identified according to Primary RISK FACTORS: and Secondary RISK FACTORS for GD.

Eligible pregnant women at their first obstetric counselling will be invited attend a focus group directed by a nutritionist supported by dedicate by formative brochures.

Treatment by placebo or nutraceutical supplementation will start at 16 weeks of gestation at the time of the first Oral Glucose Tolerance Test with 75 g of glucose (OGTT)

The main outcome of the study will be both clinical and metabolic, among which: OGTT at 28 weeks of gestation, glycemic profile that requires metformin or insulin treatment, fetal growth profile and amniotic fluid and urine isoprostane at term, Homa Index, HBA1c1.

Third Session

POSITIVE NUTRITION FOR SPORTS PERFORMANCE

Chairman: **Rodolfo Tavana**

MD Specialist in Orthopedics, Traumatology and Sports Medicine. Healthcare manager Torino FC.

REMEMBERING ENRICO ARCELLI

It's all too easy when remembering someone who is no longer with us to exalt their many qualities using well worn words: a towering figure, a lesson to us all, generous, a dear friend, always ready to lend a hand. But Enrico - the unforgettable professor Enrico Arcelli, the mythical 'Racing Professor' as he was called by his many champions, Olympic medallists, athletes, admirers, and supporters - was truly kindly, generous, well mannered in words and approach, simple, and unfailingly unpretentious. It was this lack of pretension that set him apart from others. It made him unique in a world where arrogance and bluster seem to prevail. Enrico in contrast was soft-spoken, but the words he spoke struck home. He spoke of Science, with a capital "S", to which he dedicated a life that was a lesson to us all. He was a retiring person despite the fact that life could have prompted a very different attitude, born as he was - on 5th March 1940 - into a noble family and given the auspicious name of Enrico Arcelli di Monteventano e di Montebisagno - a fact he never boasted of.

Giving an account of Enrico's many achievements in and outside the world of sport is no easy task. He graduated in medicine in 1967, subsequently specializing in sports medicine, nutritional science and occupational medicine, becoming Associate Professor of Motor Sciences at Milan University teaching football techniques, the basic principles of training, and the science of team sports. It was in Varese, where he lived with his wife Angela and sons Francesca and Marco, that he began applying his research on the field, becoming the doctor of the city's football team, Varese Calcio. In 1971, he started applying his experience of physiology to improving athletic performance with specific exercises, paving the way for the profession of athletic trainer. After his experience with football, he transitioned to the Ignis Varese basketball team. He subsequently returned to the Varese football team, then to Bologna, Monza and Como, finally becoming a consultant with Juventus, Chelsea and Milan. Lately, he was on the technical staff of the Inter football team. But Enrico's world was not just football. Over the years he became an authoritative reference point for the whole world of sport, respected by everyone, a pioneer in many fields, going from one discipline to another - skiing, mountaineering, fencing, team sports, sailing - always leaving his mark. He became a towering figure, however, in athletics, the Italian Track and Field Association's director of middle-distance and long-distance running and competition walking. His expert teaching allowed a long list of champions of yesterday and today to excel and take their place in the history of world sports; people like Sara Simeoni, Maurizio Damilano, Jonas Svensson, Gelindo Bordin, Manuela Di Centa, Alberto Tomba, Diego Armando Maradona, Jean Alesi, Stefano Baldini, Valentina Vezzali, Clemente Russo, Elisa Di Francisca, Daniele Molmenti and, last but not least, Alex Zanardi, for a total of more than 30 Olympic medals, world championships and world records. But his teachings were especially appreciated by amateur sportsmen. He gave essential insights into the physiology of the human body and the best way to train. An example is his book "Correre è bello" (Running is Fun) that was in the line-up for the Bancarella Book Award in 1999, and still today is the most popular Italian book on sports ever written. This was the first of some 23 other books Enrico was to write, some of them even translated into Russian and Chinese. To this must be added his long-standing collaboration with major newspapers like Corriere della Sera and Gazzetta dello Sport, as well as specialist titles like Correre, Nuovo Calcio, Scienza e Sport.

The Enervit Team was created at the beginning of the 1980s by Dr Paolo Sorbini, a man of science and a brilliant innovator, and his son Alberto, now Enervit's President – and by Enrico. What prompted it? The cycling hour record achieved by Francesco Moser in Mexico City on 23rd January 1984. At Enrico's suggestion, an independent company of doctors, athletic trainers, nutritionists and athletes was created to apply scientific findings in the development of products to meet, then as now, the increasingly demanding requirements of sportsmen and women as well as all those who lead active lives.

The Enervit Team's focus is the human machine, that prodigious set of organs and systems able to deliver performance excellence. Top performance only comes, however, with the right diet, the most rational training methods, and most suitable materials. They can help a champion go that all-important extra inch, gain that essential second, or point, produce that added thrust that clinches a medal, breaks a record or simply improves a placing. Still today, years of study and experience lead to the investigation of new products. It was here that Enrico excelled and innovated. An example is Enervit Protein, developed to help athletes recover after intense training, and everyone else to stay 'strong and lean'.

For Enrico Arcelli, teamwork was a *sine qua non*. Especially in the world of sports, and especially in certain disciplines where no single individual, however expert and well prepared, possesses the full range of knowledge needed to help an athlete perform at his very best. Enrico knew that athletic preparation, especially of a champion, can only be carried out by a closely-knit team. Although an apparently obvious concept, it is still one that struggles to find general acceptance.

Our mild mannered Professor Arcelli, calmly but with great determination of purpose succeeded in just this: catalyzing the Mexico team to work together to allow Francesco Moser shatter Eddy Mercks' seemingly unbeatable record. That was the first of many other great victories where the science and wisdom of Enrico were fundamental. His last challenge was with Alex Zanardi in Hawaii for an exceptionally long triathlon. Still following Enrico's precious advice, Zanardi went on to win two gold and one silver medals at the Rio Paralympics at the age of 50.

Although Enrico enjoyed much fame, success and satisfaction during his life, he never let it go to his head. Discretion was Enrico's hallmark right to the end, on 30th June 2015. He left us on a Tuesday in Sardinia, a sunny day that did little to warm the cold chill that crept over us at the unexpected news. Ciao Enrico, a formidable mentor on the sports field but especially in life.

NUTRACEUTICALS ROLE IN SPORTS NUTRITION

Fabrizio Angelini

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The nutritional plan for athletes, both amateur and elite, can be integrated with supplements before, during and after performance, provided there is sufficient evidence on the mechanism of action and safety of these supplements. In the last few years, some nutraceuticals have proved to be particularly useful in nutrition applied to physical exercise. With reference to hydration, for example, studies have shown that one light or low-alcohol beer, not more than 4% alcohol, could be an excellent recovery drink, especially in endurance sports. This is because it is a natural source of fluids, with a high content of mineral salts and carbohydrates. It could therefore be a useful tool to replenish the fluids that have been lost during exercise. However, we must remember that all studies on the intake of alcohol, including beer, before exercise are all against its use, because of the negative effect on glycogen store replenishment and on the stimulation of the M-Tor system induced by anabolic exercise.

In the recovery phase, it is now agreed that the meal ensuring excellent recovery after activity, must be made of a mixture of carbohydrates and proteins. Milk is recommended as the ideal natural mix of these nutrients and it is therefore considered as a functional food. Some nutraceuticals have been proved to counter the negative effects of exercise-induced inflammation. For example, cherry/sour cherry juice was shown to reduce elevated levels of IL6 and CRP and to decrease the risk of Upper Respiratory Tract Infections after an endurance effort. Omega 3 fatty acids have been used for some time in sports because of the benefits they can provide to athletes. Indeed several investigations showed that daily Omega-3 supplementation can have an anti-inflammatory effect, improve muscle vascularization, improve mental focus and can also promote optimization of body composition, thanks an improvement in the ratio between fat mass and fat-free mass through an increase in insulin-sensitivity and an adaptogenic action on the levels of cortisol that rise during intense and prolonged activity. Beet juice attracted special attention, because of its high nitrate content and its ability to increase nitric oxide production in muscles. Betaine, that is found in large amounts in vegetables like spinach, is thought to promote muscle trophism by means of an IGF1 mediated mechanism.

Medicinal mushrooms, which have been used for a long time in the Chinese Traditional Medicine, can be employed in sports nutraceuticals for their ergogenic and immunomodulant and effort-adaptogenic properties. In particular Cordyceps and Ganoderma Lucidum are the two medicinal mushrooms that seem to provide these benefits.

Vitamin D is essential in the field of sports for its role in improving muscle trophism and strength and bone mass peak. It has an interesting effect on immune modulation and insulin sensitivity. This is why vitamin D supplementation is recommended when its measurement in blood reveals a shortage during the sports season.

Take Home Messages

- Nutraceutical supplementation in sports is very interesting because it is mostly made of “natural” substances. But their intake must be based on scientific evidence.
- Some nutraceuticals can be very useful in the run-up phase and also in the recovery after physical exercise. In particular, some nutraceuticals are able to modulate inflammatory responses after prolonged and repeated efforts. Hence they are able to protect athletes from cases of overreaching/ overtraining, muscle and tendon injuries and some post-exercise disorders like Upper Respiratory Tract Infections (URTI)), especially in endurance sports.
- As is the case for all supplements, nutraceuticals must be recommended only after a careful assessment of athletes, including anthropometric measures, hematochemical and hormonal data and general physical condition.

SPORTS NUTRITION OF THE FUTURE

Asker Jeukendrup

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Director of Mysportscience and co-founder of CORE Nutrition Planning

The future of sports nutrition may depend on the viewpoint and although there are overlapping interests, there will be different views for industry, science and the media. From a scientific, and applied science, point of view the main two areas of development will be in periodized nutrition and personalized nutrition. Periodized nutrition refers to the short and long term planning of nutrition and integrating nutrition with training. Interventions include promoting training adaptations in the muscle, but can also include methods that improve other organs that ultimately affect performance (brain, gut etc). The concept of “personalized” medicine is being extended to the field of nutrition. It is now accepted that nutrients (i.e., macronutrients, micronutrients) alter molecular processes such as DNA structure, gene expression, and metabolism, and these in turn may alter disease initiation, development, or progression. Undoubtedly there are also links to human performance and therefore personalized nutrition is gaining momentum within the field of sports sciences. Individual genetic variation can influence how nutrients are assimilated, metabolized, stored, and excreted by the body and this in turn could have effects on adaptation, performance or recovery. Although the use of nutrigenomics in sports nutrition is sometimes suggested to be the future, it is important to recognize that the field of sports nutrition is in its infancy and there are a number of drawbacks that currently make this technique less useful. It is also important to realize that other factors are far more important drivers of nutritional needs for performance. These factors will inform what the most appropriate nutrition advice is for an athlete. For example, the goals of the individual, the exercise intensity and the duration, and the weather conditions all dictate the nutritional needs to a larger degree than the genome. It is essential to move away from generic recommendations and take into account the factors mentioned above, combine this with preferences and tolerances of the individual to create a personalized nutrition plan for the individual athlete. This talk will give some examples of ways to personalize nutrition with the tools we currently have available. Personalized nutrition plans can be created. Although there is some progress in this field, there is a lot to be discovered and a lot of work that needs to be done before we can really make “personalized sports nutrition” accessible to all athletes.

THE ROLE OF BETAINE ON BODY COMPOSITION AND PERFORMANCE

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Betaine is a natural nutrient found in most living things. In the human body, betaine has a dual role as a methyl donor for several reactions essential for normal cell function and as an organic osmolyte to help cells maintain normal water balance. Betaine has a long history of safe use in animal and human nutrition and many health benefits are associated with betaine consumption. In the EU, betaine has an authorized health claim related to cardiovascular health for homocysteine lowering. Betaine also promotes liver health. This presentation will focus on the benefits natural betaine (derived from sugar beets) has for sportsmen and sportswomen; specifically, for body composition and sports performance.

Though long used as a nutrient to improve body composition in animal nutrition, recent research demonstrates a similar benefit in humans. A 2013 study demonstrated that lean body mass increased while fat mass decreased in exercising subjects who consumed 2.5 g of betaine daily for six weeks compared to a placebo (Cholewa et al. *J Int Soc Sports Nutr.* 2013; 10:39). Two prior studies did not report any body composition changes following betaine supplementation but both failed to incorporate exercise into the study protocol, which likely contributed to the differential results (Cholewa et al. *Amino Acids.* 2014; 46:1785-1793).

Betaine supplementation may increase lean body mass by one or more mechanisms including direct and/or indirect effects on mediators regulating protein synthesis, an influence on cell hydration, stimulation of growth hormone secretion, or by improving insulin and IGF-1 receptor signaling. The observed fat mass decrease in subjects may be attributed to enhanced carnitine levels found in muscle following betaine supplementation. Carnitine transports fatty acids into the mitochondria to be burned via β -oxidation. Ostensibly, enhanced β -oxidation would contribute to decreased intramuscular fat stores and a decrease in overall body fat mass. More research is required to understand the mechanisms by which betaine supplementation improves body composition.

Sports performance can be improved with both acute and chronic betaine supplementation including muscular strength, power, and endurance. Acute studies have been performed in both runners and cyclists. Dehydrated subjects who were rehydrated with a carbohydrate-electrolyte (CE) solution or water tended to sprint longer following 75 min of treadmill running compared to the same CE drink or water without betaine (Armstrong et al. *J Strength Conditioning Res.* 2008; 22(3):851-860). Cyclists consuming a similar CE solution supplying betaine maintained significantly more leg strength compared the CE or placebo (water) groups following two hours of cycling and a 15-min time trial (Millard-Stafford et al. *Med Sci Sports Exerc.* 2005; 37(5):S28).

Chronic betaine supplementation with 2.5 g of betaine daily for two weeks resulted in increased power and force in the bench press movement, vertical jump power, and squat force compared to placebo (Lee et al. *J Int Soc Sports Nutr.* 2010; 7(1):27). Another study using a similar design showed an increase in the number of squat repetitions and in the number of squat repetitions performed at 90% peak power in subjects who ingested betaine compared to placebo (Hoffman et al. *J Int Soc Sports Nutr.* 2009; 6(1):7-17).

Betaine supplementation can also enhance anaerobic power. Pryor and others had men and women

complete four 12-sec sprint tests on a cycle ergometer at baseline and after one week of supplementation with 2.5 g of betaine daily or a placebo. Compared to baseline, peak and mean anaerobic power significantly increased when subjects ingested betaine but not placebo (Pryor et al. J Int Soc Sports Nutr. 2012; 9(1):12-18).

Taken cumulatively, research supports that betaine supplementation improves sports performance. As with body composition however, specific mechanisms of action remain elusive and more research is necessary to understand the positive impact betaine supplementation has on muscle strength, power, and endurance.

HYDRATION MANAGEMENT FOR TRAINING AND COMPETITIONS: NEW PROSPECTS

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The issue of hydration has always played an essential role in nutritional support to physical exercise. Each athlete is aware of the importance of maintaining adequate hydration, in particular to avoid the onset of medical problems and to maximize one's own exercise potential. In the most recent years, however, other important benefits originating from appropriate hydration have been highlighted and some of the old certainties in terms of knowledge and habits have been questioned. In particular, while attention was originally focused on the role of hydration in maintaining performance levels, now a broader approach is adopted and hydration is viewed as essential in the athlete's life, including training days, not just during competition. On the contrary, in the past the recommendations on hydration that athletes received were less stringent in "ordinary" days. This substantial change was due to the increasing evidence of the impact that hydration status has on exercise adaptation processes, hence on the actual effect of training on performance improvement. It turned out that maintaining an appropriate hydration status is required for the proper synthesis of macromolecules, including proteins, glycogen and nucleic acids, and for enhancing the ability to prevent oxidative stress. At the same time, new evidence was also gained on the impact of dehydration on sports performance, both on its physical component and the part more closely related to the nervous system. The evidence obtained triggered a debate on new working hypotheses as to how the highest possible performance level can be achieved. More specifically, greater attention was paid to maintaining proper hydration in those disciplines where the "nervous" component of performance must be enhanced. Other hypotheses have been put forward on the possibility to have a less stringent control of hydration in those disciplines in which the athlete's weight must be kept as low as possible. These hypothesis, however, are still preliminary and are not yet scientifically demonstrated.

COCOA FLAVANOLS AND ENDOTHELIAL FUNCTION: WHAT PERSPECTIVES IN SPORTS

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A large body of evidence supports that the dietary intake of polyphenols - particularly of flavonoids and the specific class of flavonoids named flavanols - might be able to exert some beneficial vascular effects and reduce the risk for cardiovascular morbidity and mortality. The review of epidemiological and mechanistic studies supports the role of flavonoids, particularly cocoa and tea flavanols, in protecting the cardiovascular system against cardiovascular disease. Nevertheless, flavonoids are an heterogeneous group of natural molecules differently represented in fruit and vegetables. Cocoa flavonoids are able to reduce cardiovascular risk, by improving endothelial function, and ameliorating insulin resistance.

Further, a growing interest has been addressed to flavonoids as potential nutraceuticals with interesting results from nutritional intervention trials and molecular studies also on the possible role of cocoa and chocolate consumption on sport performances. According with this, we recently showed that long-term low-dose flavanol-rich dark chocolate administration improved endothelial function, arterial stiffness and reduced blood pressure, suggesting that daily dark chocolate consumption, without additional calories intake, might be responsibly incorporated into a dietary approach, representing a reasonable tool in cardiovascular prevention. Moreover recent studies suggest that flavanoli-rich cocoa administration improved maximum work achieved and VO₂ max in sedentary subjects and also chronic supplementation with dark chocolate was able to reduce the oxygen cost of moderate intensity exercise being an effective ergogenic aid for short-duration moderate intensity exercise.

ANTI-INFLAMMATORY DIET AND INJURY RISKS IN ATHLETES

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Running is the most popular type of physical exercise in the world. However, the risk of injury for runners is very high (ranging from 19.4% to 79.3% in different studies). Athletes that have been training for a shorter time are more at risk than those who have trained for more years (17.8% vs 7.7% injury risk respectively, per 1,000 hours of running). If training is frequently discontinued because of injuries, performance is negatively affected. After intense exercise, the level of pro-inflammatory molecules in blood grows substantially. At the end of a marathon, IL-10, IL-6 and IL-8 grow 200, 42 and 10 times their baseline values respectively. According to the model by Allen and Proske, intense or extreme eccentric muscle work induce mechanical sarcomere damage with subsequent release of Ca^{++} in muscle fibers. This turns on a first inflammatory phase that is characterized by neutrophil and macrophage infiltration in muscle. These cells, after exercise induced muscle damage (EIMD), remove damaged proteins, proteolytic enzymes and cell residues by means of phagocytosis mechanisms. In the process, reactive oxygen species (ROS) are released. Furthermore, pro-inflammatory molecules, including IL-6, IL-8, TNF- α , IL-4, IL-1, are synthesized and enter the blood stream. In this way local inflammation becomes systemic. Alongside these pro-inflammatory molecules, after EIMD, there is an increase in the blood levels of other molecules, including IL-10, IL-1ra, IL-12, cortisol, G-CSF, that are able to resolve inflammation. An appropriate balance between pro- and anti-inflammatory molecules is required to trigger repair and regeneration mechanisms through proliferation and differentiation of "satellite cells". Exercise induced severe muscle damage, as is the case after strenuous activity or closely repeated intense exercise sessions, produces even higher levels of pro-inflammatory molecules. Substantial inflammatory activation translates into insufficient regeneration and necrosis of muscle fibers with subsequent formation of scar tissue. This results in inadequate muscle adaptation. These mechanisms occur in any tissue that has undergone trauma, and this applies to bones too. It is well known that omega-6 fatty acids are precursors of inflammation-inducing molecules, such as leukotrienes, prostaglandins and lipoxins; while omega-3 fatty acids are precursors of molecules that resolve inflammation, such as resolvins, protectins and maresins. A correct balance between omega-6 and omega-3 is required for the activation and resolution of inflammation with the aim of optimizing regeneration and repair mechanisms after damage has been caused. A review of the literature by Urso in 2013 showed that complete resolution of inflammation by means on non steroidal anti-inflammatory drugs (NSAIDs) has a negative impact on muscle repair following injury. On the contrary modulation of inflammation through omega-3 fatty acids and polyphenols promotes faster recovery of strength. At the same time muscle fiber damage and pain are controlled more rapidly. We wanted to understand if the AA/EPA ratio and omega-3 Index could be related to a higher risk of overuse injury (self-reported, according to IDCF consensus: bone microfracture, muscle rupture and tendon rupture). To this end we are currently carrying out an observational horizontal retrospective study denominated "Arachidonic EPA ratio and lipids in athletes injuries: ARCELLI registry" in a population of Italian runners and triathletes. Subjects must be at least 18 years old and have trained at least twice a week for the last 12 months. Those who volunteered to take part in the study were asked to fill in a questionnaire indicating age, sex, BMI, use of omega-3 fatty acids (at least 1 gram for at least three months), years of

training, training sessions-hours-kms per week, previous overuse injury (self reported according to ICDF consensus): at least once in the previous six months. On the same day they underwent measurement of the AA/EPA ratio and omega-3 index on whole blood (Dried Blood Spot; U.S.A., NU-CHECK PREP, INC). A preliminary analysis was performed on a sample of 275 individuals. 26% were women, mean age was 41.2. 17.1% of them reported injury in the previous 6 months and 21.1% were taking Omega-3 supplements. As regards training, on average, subjects had trained for 8.5 years and were running 49.5 km a week. Preliminary analysis performed with multivariate linear regression showed that a higher training volume per week (expressed as number of kms run per week) was associated with a higher AA/EPA ratio in plasma (Beta 0.18, Sig. 0.008) and a lower omega-3 index (Beta -0.214, Sig. 0.003). This is due to a decline in plasma levels of omega-3 fatty acids (EPA and DHA; respectively, Beta -0.219, Sig. 0.014; Beta -0.307 Sig. 0.001). No significant correlation with AA has emerged. Furthermore, as previous studies showed, we observed a drop in AA/EPA ratio in older subjects (Beta -0.119 Sig. 0.002).

Supplementation with omega-3 fatty acids is able to rebalance the AA/EPA ratio in our athlete population as well (Beta -0.454, Sig. \rightarrow 0.001). Lastly, the multivariate logistic regression analysis shows that a rise in AA/EPA, normalized based on specific variables, increases likelihood of injury such as bone microfracture/muscle sprain/tendon rupture. No significant correlation with the omega-3 index was found. Therefore we seem to be able to say (with the caution required by a retrospective study with self reported injuries) that disrupting the proper balance between omega-6 and omega-3 fatty acids seems to increase injury risk in runners and triathletes.

To conclude, an appropriate balance between pro- and anti-inflammatory molecules is required to promote the best possible activation of tissue regeneration mechanisms, after trauma has been experienced. The use of omega-3 fatty acids and polyphenols seems to improve repair mechanisms by rebalancing the AA/EPA ratio in athletes.



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