## Editorial

# Influence of Nutrition on Premetabolic Syndrome and Vascular Variability Syndrome

Sergio Stagnaro<sup>\*</sup> and Ram B. Singh

## Biophysical Semeiotics Reaearch Laboratory, Halberg Hospital and Research Institute, Moradabad, India

The metabolic syndrome (MS) is a constellation of abnormalities including central obesity; glucose intolerance, and type 2 diabetes; hypertension; and a dyslipidemia characterized by increased serum triglycerides, decreased high-density lipoprotein (HDL) cholesterol, and increased small, dense low-density lipoprotein (LDL) particles [1-6]. Presence of biophysical-semeiotic constitution, and related inherited real risks evolving slowly towards relative disorders, may be defined as premetabolic syndrome. The metabolic syndrome affects more than 27% of adults in the United States [6] and increases the risk of cardiovascular disease 2- to 3-fold, but exclusively in individuals with biophysical-semeiotic constitution-dependent, inherited, coronary real risk, which has been described in the former paper on this website, thus not in all patients with MS [7-12]. More precisely speaking, all components of metabolic syndrome may occur exclusively in subjects with congenital acidosic enzyme metabolic histangiopathy (CAEMH), as well as with either "some" or all CAEMH-dependent, biophysical-semeiotic constitutions [4, 5, 7, 9-12]. As a consequence, not all patients with metabolic syndrome are equal. Biophysical-semeiotic constitution may be characterised with abnormal vasomotion in the microcirculation.

I recently expressed my views [5] about the Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes [13], underscoring some important points. While some of the views were acceptable, critically important information was missing to warrant its designation as a syndrome [13].

Despite the alarming prevalence of the metabolic syndrome and the magnitude of risk it confers, defining the pathogenic links between the metabolic syndrome and cardiovascular disease, has been difficult, and whether they are united by some common underlying patho-physiology remains a matter of intense debate. It is possible that Quantum Biophysical Semeiotics can explain such relation [4, 5, 11, 12, 14, 15].

In fact, now clinicians should evaluate and treat all CVD risk factors, without regard to whether a patient meets the criteria for diagnosis of the metabolic syndrome [13]. The fact is that early recognition of pre-metabolic syndrome is now possible, It has been proposed earlier, that identify a metabolic marker, which may follow the former, is of paramount importance [14, 16-18]. In addition, in all components of these syndromes, i.e., pre-metabolic [4, 7] and metabolic syndrome, there are both parenchymal and microvascular inherited alterations, in some biological systems since birth, which (i.e. the latter) parallel the former, according to a new theory of angiobiopathy, which completes Tischendorf's Angiobiotopy theory [4, 15].

It is interesting to emphasize the presence of dual realms, in all biological systems, including the entire vascular tree. Besides the local realm, non-local realm has been recently demonstrated in biology, highlighting a large number of biophysical-semeiotic reflex, manoeuvre, test patho-physiological mechanisms, not known until now [19-26]. The most interesting is Lory's experiment, which parallels Aspect's experiment, performed in sub-atomic world. It acts on two entangled electrons: apart from

#### Editorial

their distance, betwin biological systems react in identical way, under stimulation of precise trigger-points of only one of them [27].

Finally, the hepatic insulin receptor resistance [4, 25] is not associated with all metabolic disorders in all the patients. It depends on dysfunction of PPARs in the liver, skeletal muscle, and adipose tissue, [4, 7, 19]. In arteriosclerosis microcirculatory theory [24], the mechanism of the association between ATS and metabolic syndrome has been explained, that it can occur exclusively in presence of biophysical-semeiotic ATS constitution [4, 14, 19-24].

It is possible that microscopic and macroscopic functions are continuously interacting in body, which may be disturbed when cellular free energy is reduced due to impaired mitochondrial respiratory function. On the contrary, under physiological conditions, mitochondrial function, non-local realm is widespread in biological systems. Analogously, micro- and macro-vessels are interacting, which is clear from microvessel theory of ATS [24].

It is known that interventions involving lowering of blood pressure, glycaemia, serum cholesterol, and other risk factors (such as clinically diagnosed IIR) reduce the risk of cardiovascular disease (CVD), and decrease the risk factors as much as possible. However, it may be suggested that we must go beyond the known risk factors. In fact, primary prevention of CVD, depends especially upon easy and immediate bedside detection of individuals at "inherited real risk," from birth, which is always dependent on biophysical-semeiotic constitutions, assessed clinically in a quantitative way [4, 7, 9-12, 19-21, 25, 26].

## MODIFIED MEDITERRANEAN DIET AND PRE-METABOLIC SYNDROME

The association of diet with chronic diseases of affluence has attracted since ever much attention among authors. Recently, interest has concentrated on dietary patterns, because they can address the complex interplay of nutrients within a diet [1-3, 8, 27, 28]. Dietary patterns have often been studied in relation to the mortality of elderly people, because of interest in this important age group and because of methodological considerations, for example, the cumulative effects of diet over an extended period and the high frequency of deaths. The Mediterranean diet has been used in many studies because several of its components have been related to common chronic diseases, and ecological evidence suggests that such a diet may be beneficial to health, and variants of this diet have improved the prognosis of patients with coronary heart disease [1-3, 8, 27-36].

The modified Mediterranean diet is characterised by a high intake of vegetables, legumes, fruits, nuts and cereals (largely unrefined); a moderate intake of fish; a low intake of saturated lipids but high intake of unsaturated lipids, particularly olive oil; a low to moderate intake of dairy products, mostly cheese and yogurt; a low intake of meat; and a modest intake of ethanol, mostly as wine [32]. Interestingly, in women, the frequent association of osteoporotic biophysical semeiotic constitution with Pre-Metabolic Syndrome [4, 19, 20], has been observed in association with increased intake of refined foods, cola drinks and w-6 fatty acids.

Increased intake of calcium, the major mineral constituent of bones, appears to be important in the primary prevention osteoporosis in people with osteoporotic constitution. Novel vitamin D analogues are useful for the prevention or treatment of bone disorders such as osteoporosis. At this point, we must emphasize the importance of also w-3, magnesium and antioxidants [33-36].

Calcium is found in food of both plant and animal origin. Rich sources are dairy products, such as milk, cheese, yoghurt, and small fish, particularly in their bone. Isoflavone containing compounds are also used for the treatment of osteoporosis and inflammatory joint disease. Calcium is central to a variety of functions in the body, such as nerve and muscle activity, as well as bone metabolism. In addition, osteoporosis is seen by the authors as an outcome of calcium deficiency, in that such as deficiency may lead to the development of a lower peak bone mass. Unfortunately, not all physicians know Quantum Biophysical Semeiotics, and thus ignore biophysical semeiotic constitutions and related congenital real risks.

Briefly, adherence to a Mediterranean diet proved to be efficacious in preventing most common cardiovascular diseases, diabetes, osteoporosis and cancer [27-36].

However, we have to care an "unique" individual, a "single patient" with particular biophysical-semeiotic constitutions, Single Patient Based Medicine is based on. In fact, we must consider accurately in the "single" patient its (her) entire biophysical semeiotic constitutions; dislipidaemia, diabetese, hypertension, gout, osteoporosis, and cancer [4, 5, 19].

Such diet, in association with physical exercise, walking about 40 min. day; avoiding tobacco smoking and alcoholism, may enhance survival among older people, especially when modified by adding, omega-3 rich foods or nutraceuticals. However, to achieve remarkable advantages in clinical decision making, we must know significance of microcirculatory remodelling, characteristic of inherited risk of osteoporosis and other common disorders [4-6, 14, 15].

It may be emphasized, once again that dietary modification and daily physical exercise, may be of paramount importance in ameliorating endothelial dysfunction. A protective role has also been implicated to coniugated-Melatonin, because it can influence brain-heart connection [4, 5, 21-26].

The endothelial cells, play a important role in highlighting some overlooked action mechanisms of physical exercise. Exposure to shear stress or stretch results in a range of electrophysiological, biochemical, and genetic dysfunction. If the stimulus is sustained, often result in predictable changes of cell morphology. It is possible that, unidirectional shear stress elongates endothelial cells in the direction of the shear in a force- and time-dependent fashion, whereas stress applied at a highly variable frequency, duration, and magnitude (e.g., in turbulence) induces a polygonal morphology without preferred orientation. *In vivo*, cells align with the flow in region where the flow is unidirectional. In contrast, morphology abruptly changes to polygonal at the border of flow separation regions where recirculation is created and where the shear stresses vary in direction and magnitude throughout the cardiac cycle. When endothelial cells are subjected to mechanical stimuli, diverse responses are generated, some of which are extremely fast, while others develop over hour or days. Rapid changes in ionic conductance, inositol triphosphate generation, G-protein activation, and intracellular free calcium and magnesium in response to stresses occur. Many of these rapid responses are similar to second-messenger responses that result from agonist-receptor coupling, and this suggests that the mechanical and agonist responses may share common transduction pathways [37, 38] In conclusion, diet and physical exercise act synergesticaly on endothelial function, among patients with stress, apart from anti-inflammatory cytokine production, such as interleukin(IL)-10 and IL-4, adiponectin, which have a beneficial effect on osteocyte and bone metabolism as well as on other cardiovascular risk factors ( www.semeioticabiofisica.it).

#### REFERENCES

- Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998; 339: 229-34.
- [2] Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 2004; 109: 433-38.
- [3] Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care 2005; 28: 1769-78.
- [4] Stagnaro S. Teoria Patogenetica Unificata. Ed. Travel Factory: Roma, 2006
- [5] Stagnaro S. Epidemiological evidence for the non-random clustering of the components of the metabolic syndrome: multicentre study of the Mediterranean Group for the Study of Diabetes. Eur J Clin Nutr 2007; 61(9): 1143-44.
- [6] Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. Diabetes Care 2004; 27: 2444-49.
- [7] Stagnaro S. Pre-metabolic syndrome: the real initial stage of metabolic-syndrome, type 2 diabetes and arteroscleropathy. Cardiovasc Diabetol 2004; 3:1.
- [8] Hedley AA, Ogden CL, Johnson CL, Carroll MD, Curtin LR, Flegal KM. Prevalence of overweight and obesity among US children, adolescents, and adults, 1999-2002. JAMA 2004; 291: 2847-50.
- [9] Stagnaro-Neri M, Stagnaro S. Deterministic chaos, preconditioning and myocardial oxygenation evaluated clinically with the aid of biophysical semeiotics in the diagnosis of ischaemic heart disease even silent. Acta Med Medit 1997; 13: 109.

- [10] Stagnaro S. A clinical efficacious manoeuvre, reliable in bed-side diagnosing coronary artery disease, even initial or silent, as well as "heart coronary risk". 3rd Virtual International Congress of Cardiology, FAC 2003; http://www.fac.org.ar/tcvc/marcoesp/marcos.htm
- [11] Stagnaro S. Biophysical-semeiotic bed-side detecting cad, even silent, and coronary calcification. 4to Congreso International de Cardiologia por Internet. 2005; http://www.fac.org.ar/ccvc/marcoesp/marcos.php.
- [12] Stagnaro S. Bedside recognizing diabetics with or without CHD real risk or silent CHD. BMC Cardiovasc Disord 2006; 6: 41.
- [13] Kahn R, Ferrannini E, Stern M. Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2005; 28: 2289-304.
- [14] Stagnaro S. Hypertensive constitution accounts for the existence of diabetics with and without hypertension. Cardiovasc Diabetol 2006; 5: 19.
- [15] Stagnaro S, West PJ, Hu FB, Manson JE, Willett WC. Diet and risk of type 2 diabetes. N Engl J Med 2002; 346: 297-98.
- [16] Biddinger SB, Hernandez-Ono A, Rask-Madsen C, et al. Hepatic insulin resistance is sufficient to produce dyslipidemia and susceptibility to atherosclerosis. Cell Metab 2008; 7: 125-34.
- [17] Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. Lancet 2005; 365: 1415-28.
- [18] Grundy SM, Brewer HB, Cleeman JI, Smith JI, Smith SC, Lenfant C. Definition of metabolic syndrome. Report of the National Heart, Lung and Blood Institute/American Heart Association Conference on Specific Issues Related to Definition. Circulation 2004; 109: 433-8.
- [19] Stagnaro S. Pivotal PPARs Activity Bed-side Evaluation in Pre-Metabolic Syndrome and Metabolic Syndrome Primary Prevention. Cardiovasc Diabetol 2005; 4: 13.
- [20] Stagnaro S. Mitochondrial genome of the mastodon highlights human constitutions. PLoS Biol 2007; http://biology.plosjournals.org/perlserv/? request=read-response&doi=10.1371/journal.pbio.0050207#r1725.
- [21] Stagnaro S. Bedside Evaluation of CAD biophysical-semeiotic inherited real risk under NIR-LED treatment. EMLA Congress, Laser Helsinki August 23-24, 2008. "Photodiagnosis and photodynamic therapy", Elsevier 2008; Vol. 5 (suppl 1) August 2008.
- [22] Stagnaro S. Biophysical-semeiotic diabetic "and" dyslipidaemic constitutions and primary prevention. Ann Fam Med http://www.annfammed.org/cgi/ eletters/4/5/427.
- [23] Stagnaro S. Manzelli's intelligibility of nature. PLoS Biol. http://biology.plosjournals.org/perlserv/?request=readresponse&doi=10.1371/journal. pbio.0060025.
- [24] Stagnaro S. Arteriosclerotic constitution. Microcirculatory theory of the arteriosclerosis, 2006;http://www.semeioticabiofisica.it/semeioticabiofisica/ Documenti/Eng/Costituzione%20arteriosclerotica%20engl.doc
- [25] Stagnaro S, West PJ, Hu FB, Manson JE, Willett WC. Diet and Risk of Type 2 Diabetes. N Engl J Med 2002; 24; 346(4): 297-8.
- [26] Stagnaro S. New bedside way in reducing mortality in diabetic men and women. Ann Int Med 2004; http://www.annals.org/cgi/eletters/0000605-200708070-00167v1.
- [27] Trichopoulou A. Orfanos P, Norat T, et al. Modified Mediterranean diet and survival: EPIC-elderly prospective cohort study. BMJ 2005; 330: 991 (30 April), doi:10.1136/bmj.38415.644155.8F (published 8 April 2005).
- [28] Huijbregts P, Feskens E, Rasanen L, *et al.* Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and the Netherlands: longitudinal cohort study. BMJ 1997; 315: 13-7.
- [29] World Cancer Research Fund and American Institute for Cancer Research. Food, nutrition and the prevention of cancer: A global perspective. Washington DC: WCRF and AICR, 1997.
- [30] Knoops KT, de Groot LC, Kromhout D, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: The HALE project. JAMA 2004; 292: 1433-9.
- [31] Stagnaro S. Endothelial cell function can ameliorate under safer drugs, such as Melatonin-Adenosine. BMC Cardiovasc Disord 2004; http://www.biomedcentral.com/1471-2261/4/4/comments.
- [32] De Logeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditionalrisk factors and the rate of cardiovascular complications after myocardial infarction. Final report of the Lyon Diet Heart Study. Circulation 1999; 99: 779-85.
- [33] Pella D, Dubnov G, Singh RB, Sharma R, Berry EM, Manor O. Effects of an Indo-Mediterranean diet on the omega-6/omega-3 ratio in patients at high risk of coronary artery disease: The Indian paradox. In Simopoulos AP, Cleland LG, Eds. World Review of Nutrition and Dietetics. Karger 2003, 92, pp. 74-80.
- [34] Singh RB, Niaz MA, Agarwal P, Beegum R, Rastogi SS. Effect of antioxitant rich foods on plasma ascorbic acid, cardiac enzyme and lipid peroxide levels in patients hospitalized with acute myocardial infarction. J Am Diet Assoc 1995; 95: 775-80.
- [35] Singh RB, Rastogi SS, Verma R, et al. Randomized, controlled trial of cardioprotective diet in patients with acute myocardial infarction: results of one year follow up. BMJ 1992; 304: 1015-9.
- [36] Singh RB, Niaz MA, Sharma JP, Kumar R, Rastogi V, Moshiri M. Randomized, double blind, placebo controlled trial of fish oil and mustard oil in patients with suspected acute myocardial infarction: the Indian Experiment of Infarct Survival-4. Cardiovasc Durg Ther 1997; 11: 485-91.
- [37] Davis PF, Barbee KA, Lal R, Robotewskyj A, Griem ML. Hemodynamics and Atherogenesis. Endothelial Surface Dynamics in Flow Signal Transuction. Recent Advances in Atherosclerosis Research. Ann N Y Acad Sci 1995; 748: 86-103.
- [38] Stagnaro S, Manzelli EP. L'Esperimento di Lory. Scienza e Conoscenza, Nº 23, 13 Marzo 2008. http://www.scienzaeconoscenza.it//articolo.php?id= 17775

## Sergio Stagnaro

Biophysical Semeiotics Reaearch Laboratory, Via Erasmo Piaggio 23/8, 16039 Riva Trigoso (Genoa) Italy, Tel: (+39) 0185-42315 E-mail: dottsergio@semeioticabiofisica.it

Received: October 5, 2009

Revised: October 12, 2009

© Stagnaro and Singh; Licensee Bentham Open.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/3.0/) which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.