A SHORT HISTORY OF THE METABOLIC SYNDROME DEFINITIONS

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Some researchers tend to think of the metabolic syndrome (MS) as being the most important medical problem of the 21st century beginning.
The metabolic syndrome is rather difficult to estimate because of the numerous existing points of view regarding the elements needed for the diagnosis.
It isn't about a singular disease, but an association of impairments that can appear simultaneously or gradually in the same individual, caused by associating the genetic and environmental factors (+ lifestyle) with the insulin-resistance, considered as the fundamental pathogenic component.
The first definition of the metabolic syndrome was formulated in 1998 by a group of researchers from OMS (the group being concerned with studying diabetes). Starting with that first definition (initial one) of the metabolic syndrome a range of alternative definitions was suggested. The most widely accepted definition was formulated by EGIR (European Group for the Study of Insulin Resistance) and NCEP (USA National Cholesterol Education Panel).

Key words: Metabolic syndrome; Anthropometry; Obesity.

INTRODUCTION

Such a great interest taken in this theme starts from the increased prevalence of the metabolic syndrome and its association with a decreasing hope for a longer lifespan, especially by the increasing of the cardiovascular mortality, the increasing of diabetes, myocardial infarction and cerebrovascular disease risk.

Some researchers tend to think of the metabolic syndrome as being the most important medical problem of the 21st century beginning. Recent studies showed the epidemic proportions that this affection reached worldwide (global numbers show a prevalence of 20–25%). The diagnosis, clinical evaluation and efficient treatment of such a big number of patients are heavily trying the public health systems. On the other side, the delaying in curing the metabolic syndrome leads to an increasing of the cardiovascular diseases and type 2 diabetes incidences, with disastrous consequences over the human society. Passing to a food that is rich in refined products, food of animal origin and fats plays an important part in the worldwide epidemics of obesity, diabetes mellitus and cardiovascular diseases (non – transmissible chronic diseases).

It was noticed that the probability to develop metabolic disorders, including MS, increase with obesity level. For example, in comparison with normal weight subjects, the probability to have MS increases 5.2 times for overweight subjects, 25.2 times for moderate obese subjects and 67.7 times for severe obese subjects [1, 2].

Medical definition of obesity requires, with all the rigor, being able to assess the fat mass. But fat mass cannot be measured with satisfactory precision in any other way than by sophisticated methods (the measurement of body density, the assessment by dual energy X ray absorptiometry,

tomodensitometry, magnetic resonance) too expensive to be available for routine. In clinical practice, the obesity is defined using a corporality index, which takes account of weight and stature (BMI) that has become the international reference to define obesity [3,4].

To define obesity, besides BMI, we can also use other anthropological parameters:

- Thickness of skin folds
- Waist circumference *
- The waist / hip ratio

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DEFINITION

According to the encyclopedic dictionary of the Romanian language the term "*syndrome*" = *group of signs and symptoms that appear together during a pathological process, giving it the characteristic note.*

The metabolic syndrome expresses a complex disturbance of the genetic metabolism of the organism, including disturbances of the lipid metabolism (obesity, dyslipidemia), the carbohydrate metabolism (altered tolerance to glucose/ type 2 diabetes mellitus), the protein metabolism (hyperuricemia), as well as the arterial hypertension (a hemodynamic disturbance having a metabolic starting point)[5].

TERMINOLOGY

The term "syndrome" derives from the Greek word *sundromos* (sun-syn + dromos= to run) and it means *"to run together"*.

* According to EGIR > 80 cm for women and > 94 cm for men or according to NCEP-ATPIII ≥ 88 cm for women and ≥ 94 cm for men of European (caucasian) origin. For South Asia have been proposed: for men > 90 cm, for women > 80 cm; China: men > 90 cm, women > 80 cm; Japan: men ≥ 85 cm, women ≥ 90 cm.

The metabolic syndrome was diversely named in time: the plurimetabolic syndrome, the X syndrome, the X plus syndrome, the X metabolic syndrome, the cardiovascular metabolic syndrome, the insulin-resistance – dislipidemia syndrome, the atherogenic metabolic syndrome, the syndrome of atherogenic factors' agglomeration, the deadly quartet). Recently, there was used the MetS acronym as replacing the term of Metabolic Syndrome.

Out of the numerous terms suggested to define this nosologic entity, the World Health Organization (WHO), the International Diabetes Federation (IDF) and other international bodies agreed upon the term "metabolic syndrome". Nevertheless, from a semantical point of view, this term is not correct; let's not forget that the metabolism *per se* represents a natural phenomenon. Thus, if we refer to its dysfunction, it would be logical to call it "dysmetabolic" (ex: we call the disturbance of the lipid metabolism "dyslipidemia", not "lipidemia")[6].

HISTORY

As early as 250 years ago, long before the MS description, the Italian physician and anatomist Morgagni identified the association between visceral obesity, HTA (arterial hypertension), atherosclerosis, the high levels of uric acid in the blood and the frequent respiratory disorders during sleep (the obstructive apnea) [7].

In 1920, Nicolae Paulescu, speaking about obesity and diabetes, said "most frequently, the obese people become glycosuric, as if the two affections (obesity and fat diabetes) represent two consequent phases of the same pathological process" [8].

In 1927, Maranon, the founder of modern endocrinology in Spain, explicitly described the fact that the arterial hypertension is a pre-diabetical stage and this concept is similarly applied to obesity. Maranon also underlined the fact that food is essential for preventing and treating these disturbances [7].

At the middle of the 20th century (1947), Vague, a French physician, was the first to identify android obesity (adiposity of the superior part of the body) as being the condition the most frequently associated with diabetes mellitus and cardiovascular diseases.

The often-simultaneous presence of obesity, the high level of blood lipids, diabetes mellitus and arterial hypertension was first mentioned under the name of plurimetabolical syndrome in the 60's.

In the 70's, Moga, Orha, Haragus [9,10] supported the idea of the existence of a close connection among the components that constitute the metabolic syndrome at present, correlating them to the cardiovascular diseases. From the point of view of the school from Cluj, the atherosclerosis is represented by a complex disturbance of the metabolism, vaso-motility, coagulation and hydro-electrolytic and mineral equilibrium [11].

The cardiologists were the first to notice the connection between the major disturbances of the metabolic syndrome. Making an inventory of the risk factors for the coronary diseases, alongside with HTA they recorded dyslipidemia (hypercholesterolemia / hypertriglyceridaemia), obesity, diabetes and hyperuricaemia, as well as food factors, the sedentary lifestyle, environment factors, psychosocial factors, etc.

Towards the end of the 80's, the assembly of glucose, insulin metabolism disorders, obesity, dyslipidemia and arterial hypertension received the mysterious name of "X syndrome". In 1988, Reaven G., an endocrinologist physician from Stanford University, was the one who took a big stride forwards, interpreting the association of diabetes, obesity, dyslipidemia and arterial hypertension by their pathogenic relationship with the peripheral insulin-resistance. He named this association "X syndrome", the name underlining the doubtfulness that accompanied the emitting of the apparently new concept[12]. The insulin resistance and the compensatory hyperinsulinism were associated with each component of the metabolic syndrome, offering thus a physio-pathological connection between them. Continuing this logical chain, one can naturally reach the conclusion that the metabolic syndrome represents a complex disturbance of the energetic metabolism, in close connection with the insulin secretion altering, influenced in its turn by the sensitivity / resistance to insulin [5].

Ferranini and collab. resumed this idea, confirming that this assembly of disturbances is provoked by the insulin–resistance and, after several years, they called it the "insulin – resistance syndrome" [7].

Afterwards, it was found out that the spectrum of metabolic disturbances is larger. Zimmet and Serjentson [13] speak about the "plus X syndrome" signaling the association with hyperuricaemia, sedentariness and old age. The X syndrome generates high degrees of free radicals, which are harmful to the cell, causing a premature aging. The blood glucose level tends to increase with age, accelerating aging by connection to proteins [14]. During mid 70's, the biologist Anthony Cerami discovered the fact that the chronically increased glucose levels represent the main trigger in the chemical process of manufacturing the final glycolsylation products (AGE = Advanced Glycosylation End). AGES are involved in the processes of normal and accelerated aging, by chemical reactions between glucose and molecular proteins, producing serious damages at the level of cellular membranes and collagen fibers [15].

The appearance of the metabolic syndrome notion was due to the fact that, more often than not, the risk factors associate for the same individual. This suggests that, on the one side, there is possible a common etiopathogeny, and, on the other side, it was considered that it offers a better capacity to predict risks and, therefore, to intervene.

In 1998, the first definition of the metabolic syndrome was formulated by a group of researchers from the WHO (World Health Organization), the group being concerned with studying diabetes. One year later, the WHO definition was accompanied by a criteria list meant to the clinical diagnosis. It made precise the fact that the syndrome is defined by the presence of type 2 diabetes mellitus or the altered tolerance to glucose combined with at least 2 other factors (hypertension, increased level of blood lipids, obesity and microalbuminuria).

The definition of the MS according to WHO [16]

- Diabetes mellitus/ IFG* / IGT** / insulin resistance (evaluated by the euglycemic

*__IFG__ (Impaired Fasting Glucose) = (basal) à jeun glycemia modified/affected (110–125 mg/dl) (OMS classification 1998). Increased à jeun glycemia values that are over the normal level, but without reaching diagnosis values for the diabetes mellitus; at 2 h after administering 75 g of glucose per os, the glycemia level is normal.

**__IGT__ (Impaired Glucose Tolerance) = tolerance altered to glucose (glycemia at 2 h after oral loading with 75 g of glucose 140–199 mg/dl) (WHO classification 1980, 1985). Non - diabetic values of the à jeun glycemia (from normal values to increased ones, but <126 mg/dl of the venous plasma) and increased glycemia values of over the normal level at 2 h after the oral administrating of 75 g of glucose (between 140 and 199 mg/dl), without reaching, though, the values that characterize the diabetes mellitus.

During the last years, IGT and IFG were reunited under the term of **prediabetes.**

***The method of the hyperinsulinemic/euglycemic clamp represents a truthful indicator of the sensibility/resistance to insulin. This is determined during a continuous perfusion of a solution that contains insulin in a concentration that allows the

clamp method[***]) and at least 2 of the following parameters:

- BMI>30 kg/m^2 or the waist/hip ratio > 0.90 for men
  >0.85 for women
- Plasmatic triglycerides (TG) ≥ 150 mg/dl (>1.7 mmol/l) or
  HDL-cholesterol < 35 mg/dl (<0.9 mmol/l) in men
  < 39 mg/dl (< 1.0 mmol/l) in women
- The rate of excretion of the urine albumin > 20 μg/min or albumin/creatinine ratio ≥30 mg/g
- Blood presure ≥ 140/90 mmHg.

In 1999 EGIR (European Group for the Study of Insulin resistance) proposed a change in the WHO definition, establishing that insulin-resistance is the principal cause of this syndrome [17]. EGIR attached bigger importance to the abdominal obesity than WHO, but excluded the patients with diabetes mellitus type 2.

EGIR definition [18]

Insulin-resistance or hyperinsulinemia *à jeun* >25% and, at least, 2 of the following parameters:

- Plasmatic glucose *à jeun* ≥ 6.1 mmol (excluding diabetes)
- Blood presure ≥ 140/90 mmHg or treatment for HTA
- Plasmatic triglycerides ≥ 2 mmol/l or HDL cholesterol < 1 mmol/l or treatment for dyslipidemia
- Waist circumference ≥ 94 cm for men and ≥ 80 for women.

In 2001 NCEP-ATP III (the USA Cholesterol Education Panel, Adult Treatment Panel III) introduced alternative clinical criteria for defining MS. The ATP III criteria don't require the demonstration of the insulin-resistance presence [19].

keeping of insulinemia constant at a value of 50, 75 or 100μU/ml. This increased concentration is accomplished in order to ensure an as high as possible occupying of the insulin receivers from the peripheral tissues. Normally, the maintaining of this insulinemia would rapidly lead to hypoglycemia. Its avoiding, in parallel with the insulin administrating, is done by introducing i.v. with the help of a pump of controllable capacity (delivery rate), a glucose quantity (variable) that is necessary to keep glycemia within normal and constant values. The quantities of glucose administered for preserving euglycemia indirectly reflect the sensibility to insulin; the higher the glucose need is, the better the tissue insulin - sensibility. The lower the insulin need is (owing to the low peripheral using), the higher the insulin resistance.

The definition of the MS according to NCEP ATP III (the USA Cholesterol Education Panel, Adult Treatment Panel III) [20]

At least 3 of the following parameters:

– Waist circumference > 102 cm for men
  >88 cm for women
– Plasmatic triglycerides ≥ 150 mg/dl (>1.7 mmol/l)
– HDL cholesterol < 40 mg/dl (1.0 mmol/l) in men
  < 50 mg/dl (1.3 mmol/l) in women
– Blood presure ≥ 130/85 mmHg
– Serous glucose ≥ 110 mg/dl (> 6.1 mmol/l)

Other definitions of the metabolic syndrome were suggested, complicating the possibility of an accepted international definition.

In 2003 AACE (American College of Endocrinology) revised the NCEP-ATP III criteria, redirecting the MS diagnostic to insulin-resistance [21]. The major criteria were: IGT or IFG, increased triglycerides, low HDL-cholesterol, higher blood tension and obesity. The number of the factors involved in diagnosis was left to clinical judgment. According to AACE, after establishing the diagnostic of type 2 diabetes, the diagnostic of metabolic syndrome is no longer applied.

AACE definition (American College of Endocrinology) [22]

The presence of at least 1 factor out of the following:

– Diagnosis of cardiovascular diseases, hypertension, polycystic ovary syndrome, nonalcoholic fat liver or acanthosis nigricans disease
– Family history of type 2 diabetes mellitus, hypertension or cardiovascular diseases
– Gestational diabetes history or intolerance to glucose
– Non-Caucasian ethnic
– Sedentariness
– BMI > 25 kg/m^2 and/or waist circumference > 102 cm for men and > 88 cm for women
– Age > 40 years.

And at least 2 out of the following parameters:

– Plasmatic triglycerides (TG) ≥ 150 mg/dl
– HDL cholesterol < 40 mg/dl in men
  < 50 mg/dl in women
– Blood pressure ≥ 130/85 mmHg
– *À jeun* glucose 110 – 125 mg/dl or at 2 h postprandial 140 – 200 mg/dl (diabetes is excluded from the AACE definition).

In 2005 IDF (the International Diabetes Federation) modify the ATP III definition, publishing the new criteria. The IDF recorded an important achievement in MS physiopathology and diagnosis, suggesting that the key element is the *central obesity* [23]. The presence of other 2 factors from ATP III list establishes the MS diagnostic.

The IDF definition [23]

The central obesity (defined by the waist circumference ≥ 94 cm for men and ≥ 80 cm for women, of European origin, with characteristics values for various ethnic groups) and ≥ 2 of the following parameters:

1) Low level of the TG ≥ 1.7 mmol/l (150 mg/dl) or drug treatment for hyperlipidemia
2) Low level of the HDL – cholesterol
   < 1.03 mmol/l (40 mg/dl) in men and
   < 1.29 mmol/l (50 mg/dl) in women or drug treatment for dyslipidemia
3) Arterial hypertension, systolic blood pressure ≥ 130 mmHg or dyastolic blood pressure ≥ 85 mmHg or cure for hypertension that was previously diagnosed.
4) The increased levels of the venous glycemia* ≥ 5.6 mmol/l (100 mg/dl) or previously diagnosed type 2 DM (with values > 5.6 mmol/l or 100 mg/dl, there is recommended an oral test of tolerance to glucose, but it isn't needed for defining the MS presence).

The measurement of the abdominal circumference was proposed for use for both adults and children, as an indicator of abdominal obesity, closely correlated with the occurrence of the MS and of the obesity co-morbidities in general.

The IDF brought forth a number of other parameters that seem to be connected to MS, and that should be included into the research studies in order to ascertain the predictive power of these supplementary factors for the cardiovascular diseases and / or diabetes [24]:

- General obesity
- Fat cell products: high leptine levels, low adiponectine levels
- High Apolipoprotein B levels
- High LDL – cholesterol levels
- High free fat acids (FFA) levels
- Microalbuminuria
- Proinflammatory status [high PCR, high inflammatory Citokins (TNF - ∝, IL -6)]
- Prothrombotic status (high PAI – 1, high fibrinogen).

In 2005 both IDF and AHA/NHLBI attempted to reconcile the different clinical definitions. In spite of this effort, their separate recommendations contained differences related to waist circumference. The IDF dropped the WHO requirement for insulin resistance but made abdominal obesity necessary as 1 of 5 factors required in the diagnosis, with particular emphasis on waist measurement as a simple screening tool. The AHA/NHLBI definition slightly modified the ATP III criteria but did not mandate abdominal obesity as a required risk factor.

The IDF recommended that the threshold for waist circumference to define abdominal obesity in people of European origin should be ≥94 cm for men and ≥80 cm for women; the AHA/NHLBI, in contrast, recommended cut points of ≥102 cm and ≥88 cm, respectively, for the 2 sexes.

In 2009, the International Diabetes Federation and the American Heart Association/ National Heart, Lung and Blood Institute (AHA/NHLBI) were agreed that the measure for central obesity there should not be an obligatory component, but that waist measurement would continue to be a useful preliminary screening tool. Three abnormal findings out of 5 would qualify a person for the metabolic syndrome [25]:

1) Elevated waist circumference†
2) Elevated triglycerides ≥150mg/dl (1,7 mmol/l) or drug treatment for elevated triglycerides is an alternate indicator
3) Reduced HDL-cholesterol < 40 mg/dl (1,0 mmol/l) in males and < 50 mg/dl (1,3 mmol/l) in females or drug treatment for reduced HDL-cholesterol is an alternate indicator
4) Elevated blood pressure systolic ≥130 mmHg and/or diastolic ≥85mmHg (antihypertensive drug treatment in a patient with a history of hypertension is an alternate indicator)
5) Elevated fasting glucose‡ ≥100 mg/dl (drug treatment of elevated glucose is an alternate indicator)

* In clinical practice IGT is also accepted, but to assess this criterion, all epidemiological reports concerning the prevalence of the MS must use only fasting venous blood glucose and the presence of previously diagnosed diabetes.

† It is recommanded that the IDF cut points be used for non-Europeans and either the IDF or AHA/NHLBI cut points used for people of European origin until more data are available.

‡ Most patients with type 2 diabetes mellitus will have the MS by the proposed criteria.

The WHO and EGIR definitions are limited like applicability and clinical acceptability. The most accepted definition was the NCEP-ATP III one because of his simplicity.

However, for international comparisons and to facilitate the etiology, it is critical that a commonly agreed-upon set of criteria be used worldwide, with agreed-upon cut points for different ethnic groups and sexes (an exception being the waist perimeter which requires further researches).

As we can see there is no agreement among the researchers on the parameters that define the metabolic syndrome. From an anthropological point of view, the MS can be defined only by means of anthropometry because the anthropological population / racial studies are still in the early stage. Anthropometry represents the cheapest, non-invasive and universally applicable method for determination of size and body composition.

Lately, attention was directed more and more to use anthropometry for estimation of the overweight and obesity, the adipose tissue distribution and the risk of developing chronic diseases.

Between 2007–2009 the Institute of Anthropology "Francisc I. Rainer" underwent a study among overweight / obese adults with / without type 2 diabetes.

An adult population was chosen for the study because the MS definition wasn't established for children. In their case, the problem is more vague because we talk about children of different ages and in different stages of development. Waist circumference, triglycerides, HDL-cholesterol, blood tension, glycemia – are moving targets in children; there were no firmly established criteria as regards normality or abnormality.

Our objectives were:

- depiction of nutritional status in different population groups and its variations according to demographic characteristics and socio-economics changes (age, gender, geographic location, finance);
- assessing the prevalence of MS depending on ponderal status;
- identification of the population groups at risk, towards which the public health policies should be directed;
- monitoring the evolution trends of nutritional status.

The anthropometric form included 13 measurements (stature, real weight, neck circumference, arm circumference, bust girth, waist circumference, hip circumference, thigh circumference, ankle circumference, and measurements of bicipital, tricipital, supraspinale and abdominal skin folds). The degree of obesity (calculated by bio-impedance method), body fat mass, percent body fat and ideal weight were also determined using a Body Composition Analyser-Biospace Inbody 3.0.

For diagnosis of the MS we used the IDF-AHA/NHLBI definition [25].

The partial results we obtained confirm data from literature: BMI correlates with weight, waist circumference and do not correlates or correlates poorly with waist/hip ratio and biochemical and hemodynamic parameters. The prevalence of the MS in overweight/obese group without type 2 diabetes mellitus is 67% for men and 49,6% for women. The most common criteria were: waist circumference followed by systolic tenssion for men and waist circumference and HDL-cholesterol for women. An observation, unconfirmed yet (because statistic processing of these data is still in work) can be drawn: the first parameter which presents a variation with changing of ponderal status (increase of BMI) seems to be TG.

The results could lead to discovery, between different parameters used, of some correlations stronger than those currently known. Using these factors in research could change the present definitions, if this is necessary, and validate a new clinical definition.

Although anthropometric measurements may indicate the existence and the dimension of the nutritional problems and can serve as markers of risk in the health – disease relation, the information provided by them cannot explain, only by itself, the specific causes of the nutritional problems and the mechanisms of associations between anthropometric status and the subsequent risk of morbidity or mortality.

The lack of a minimal consensus regarding the basic elements of the metabolic syndrome expresses the different levels of thoroughgoing into and interpreting of the syndrome by the researchers in the domain; we exclude the priority subjectivisms and the hierarchic differentiation vainglory of the organizations.

During the last years, by carefully analyzing the elements (original or further – on – added ones) that make up the metabolic syndrome, there was found out that they have a different significance. Some of them are "primary" genetic disturbances (the insulin-resistance and hyperinsulinism), others are the metabolic consequences of these disturbances and,

finally, the last category includes the final complications of the syndrome, which are represented by the generalized cardiovascular disease.

Recently, the controversies on the MS intensified themselves. An all-inclusive (and official) analysis regarding the metabolic syndrome was published by Kahn and collaborators [26]. The authors present a series of criticisms concerning the definition and the physio-pathological basis of the MS:

I. Some of the criteria used for defining MS are ambiguous or incomplete. For example, it is not clear if the definition of the blood pressure refers to values of the systolic pressure that has to be > 130 mmHg or of the diastolic pressure > 85 mmHg, or if both conditions have to be fulfilled; also, there isn't either specified the way blood pressure should be measured (in clino- or orthostatic–postural-position). Such ambiguities affect the sensibility and specificity of the diagnosis and, undoubtedly, led certain physicians to wrong diagnoses (+).

II. It is clear that the definition of the syndrome differs in the listed criteria. For example, micro-albuminuria appears in the WHO definition, but not in the ATP III one; the insulin–resistance is relevant for the WHO definition, but not for the NCEP ATP III one. Until at present, there has been published no survey of the clinical records in favor of including or excluding any criterion for any of the definitions.

III. Certain criteria (for example the waist circumference, HDL–cholesterol) differ by gender, implying the fact that the relationship between the risk factor level and the results differs as depending on gender; there was found no proof that could justify the establishing of certain guide marks by taking into account one's gender (used as criteria the way those connected to cardiovascular diseases are). For example, it is not known if the same mass of adipose intra-abdominal tissue carries various risks in men as compared to women. An analogous reason can be put forth as concerns the variation of these criteria depending on race and ethnic group.

IV. Finally, the reason supporting the criteria is that the syndrome components are associated with the insulin– resistance [16, 18], but one could notice the fact that not all the subjects with the metabolic syndrome are insulin– resistant. Recently, the ATP III definition went through reviewing, enlarging the MS etiological basis from the "insulin–resistance" taken singularly, to "obesity and disturbances of the adipose tissue", as a "constellation of independent factors" that indicates specific MS components [22].

V. The studies also illustrate another deficiency of the present dwelling upon the MS diagnosis. Both the WHO definition and the ATP III one weigh each risk component equally; still, it is obvious that certain risk factors that are included into the definition have a bigger predictive importance than others. It is extremely important to know from a list of all the cardiovascular risk factors (known ones) the hierarchy of the combination having the highest predictive value.

Briefly, the conclusions reached by Kahn and collaborators pursuant to the carried out analysis are the following:

1) The criteria are ambiguous or incomplete. The motivation for thresholds (limit values) is badly defined.
2) The insulin – resistance as a unique etiology is unsure.
3) There is no clear basis for including or excluding other risk cardiovascular factors.
4) The value of the cardiovascular risk is varying and depending on the specific risk factor presence.
5) The cardiovascular disease risk, associated with the syndrome, doesn't seem to be higher than the sum of its component parts.

There are needed subsequent studies that should ascertain if modifying the actual MS definition, with adding the risk parameters for the cardiovascular disease, could optimize its predictive value. Identifing a cluster of cardiovascular disease risk factors that confer a higher risk when analyzed together proves an unrealistic purpose at present [24, 27].

INSTEAD OF CONCLUSION

The symptoms of the metabolic syndrome are not immediate and direct ones (of the cause – effect type), but they are shifted in time and more finely interconnected, so that, although the deteriorations are obvious, it is quite hard to

establish with absolute certainty how they were got to, the decisive factors having still to be properly elucidated.

Metabolic syndrome necessitates more thorough-going studies, before its definition as a "syndrome" would be fully justified and before its clinical usability would be adequately defined.

From an anthropological point of view, the metabolic syndrome can only be defined by anthropometry, as the populational/racial anthropo-logical studies are, for the time being, at an incipient stage.

Paraphrasing the eminent scientist Jean Rostand, one may say that, the more various the aggressions that the human body has to endure are, the more various the measures taken for protecting it should be.

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