

# Clinical QBS Diagnosis and Primary Prevention of Brain Disorder 'Inherited Real Risk' and Alzheimer Disease

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## **Introduction**

Quantum Biophysics Semeiotics, QBS, is a new discipline in medical field, extension of the classical semeiotics with the support of quantum and complexity theories, a scientific approach first described by Stagnaro (1-8), based on the 'Congenital Acidotic Enzyme-Metabolic Histangiopathy', CAEMH (1-4), a unique mitochondrial cytopathy, present at birth and subject to medical therapy.

According to the research of Stagnaro, today doctors should be able to evaluate, at the bedside, simply using the stethoscope and Auscultatory Percussion of the stomach and of ureteres(2), mitochondria functionality, as well as the functionality of all biological systems. It is now possible, since the moment of birth to bedside detect the presence of the Inherited Real Risk of many diseases linked with QBS Constitutions (3), so that an intelligent prevention strategy can be implemented only on those subjects with Inherited Real Risk.

Quantum Biophysical Semeiotics, in addition to the most severe disease diagnosis as, for example, solid and liquid forms of cancer, type 2 diabetes mellitus, heart diseases, hypertension, osteoporosis, is able to make the diagnosis of Inherited Real Risk – IRR - of brain disorders, and in the present paper we show the ways to detect the IRR of brain disorders especially related to Alzheimer Disease - AD. QBS is able to make a diagnosis of AD not only at the first very initial stages, usually very difficult to do, but even many years before that such disease could appear, allowing so an efficacious primary prevention.

## Quantum Biophysical Semeiotics priors: CAEMH, QBS constitutions and Inherited Real Risks

According to Stagnaro (2), genome's information are transmitted simultaneously both to parenchyma and related micro-vessels, so that mutations in parenchymal cell n-DNA and mit-DNA are the *conditio sine qua non* of the most common human disorders, like diabetes, CAD, and cancer, today's epidemics.

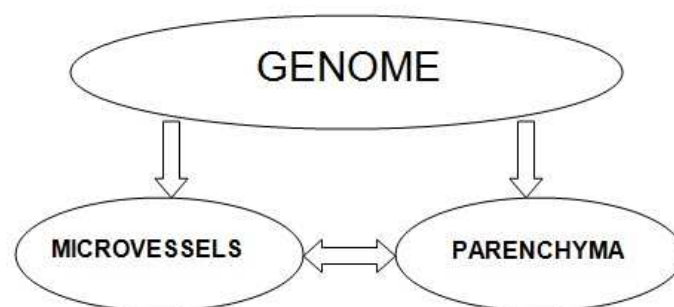
In fact, all these diseases are based on a particular congenital, functional, mitochondrial cytopathy, mostly transmitted through mother, and defined Congenital Acidotic Enzyme-Metabolic Histangiopathy, CAEMH (2, 45).

The contribution of these modifications to the relative pattern, based always on genetic or inborn errors – CAEMH - is different from patient to patient and during the disorder's evolution. For instance, in case of diabetic syndrome, insulin-secretion increases silently for years or decades, before appearing as Type 2 Diabetes Mellitus - T2DM, at the fifth and final stage of its natural history (11, 12, 13, 43).

This pre-clinical stage is not detectable through usual clinical tests, so it is necessary to explore new approaches, such as that introduced by Quantum Biophysical Semeiotics – QBS – (2), which through bed-side evaluation, can assess the existence of pre-metabolic syndrome<sup>i</sup>, that can last for years or decades, pre-clinical stage of the disease still potential or on training (evolution to pathology, pre- morbid state or gray area), so allowing an effective prevention (Scheme 2).

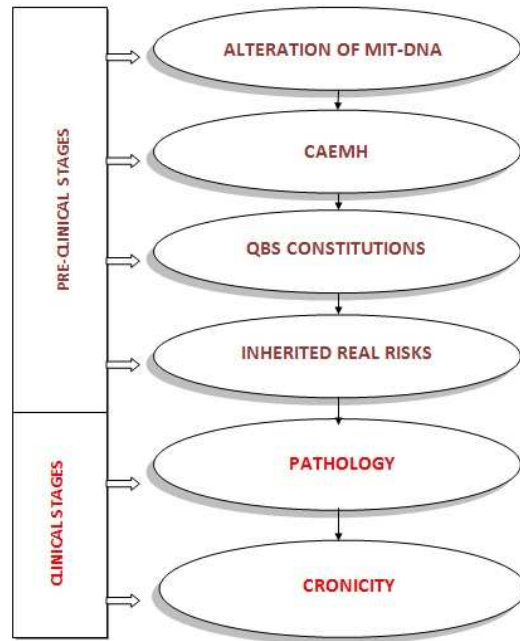
In addition, parenchymal gene mutations cause local microcirculatory remodeling, so doctor can evaluate it at the bedside in a reliable manner, gathering indirect information on inherited modifications of relative parenchymal cell, since biological system functional modifications parallel gene mutation, according to Angiobiopathy theory (Appendix A).

The presence of intense CAEMH – termed CAEMH-‘alfa’ - in a well-defined area, i.e., myocardium, involved by gene mutations in both n-DNA and mit-DNA, is the ground for one or more biophysical semeiotics constitutions<sup>ii</sup> (3, 45) which could brings about their respective congenital Real Risks - RR (Scheme 4) characterized by microcirculatory remodeling from QBS viewpoint, especially intense under environmental risk factors.



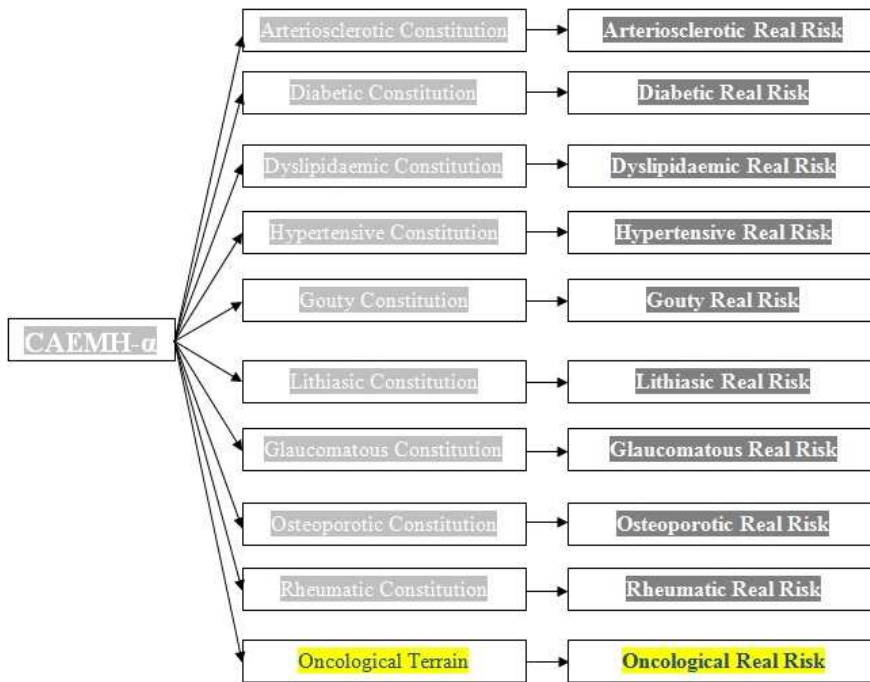
Scheme 1. Genome affects both micro-vessels and parenchyma

In Scheme 1 it is shown that genome affects both micro-vessels and parenchyma, according to Stagnaro's Angiobiopathy theory. Investigating the micro-vessels, whose behavior is typical of dissipative systems far from equilibrium, this is a way to get indirect information from the state of health of their respective parenchyma.



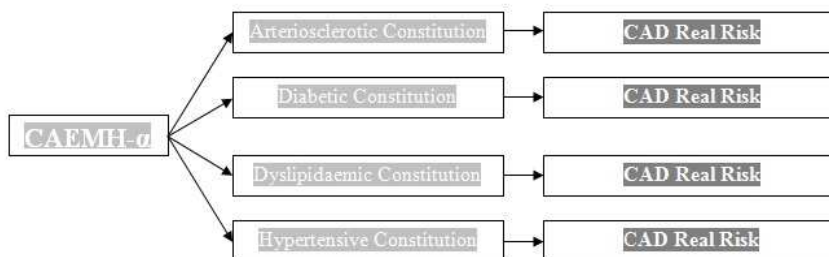
*Scheme 2. Pre-clinical and clinical stages of diseases depending on mit-DNA alteration*

The congenital micro-vascular remodeling, shows since birth interesting structures, i.e., newborn-pathological, type I, subtype b), Endoarteriolar Blocking Devices, EBD, localized in small arteries, according to Hammersen (42). As a consequence of above, briefly referred remarks, physicians are able nowadays to demonstrate the presence of typical pathological EBD in well defined micro-vessels, which play a central role in Inherited Real Risks (Appendix B).



Scheme 3. CAEMH- $\alpha$ , QBS constitutions and its Inherited Real Risks

Through the objective QBS examination, it is possible to recognize in a few minutes and quantify if a patient has got any QBS constitution and congenital Real Risk (RR) to have a disease (Scheme 4, QBS constitutions, ground of the IRR of CAD).



Scheme 4. CAEMH- $\alpha$ , QBS constitutions and Inherited Real Risk of CAD

Through the objective QBS examination in a few minutes, it is possible to recognize and quantify if a patient has got any congenital Inherited Real Risk (IRR) to have a disease by means of the observation of EBD, type I, subtype a) cancerogenous (Scheme 3, in yellow) b) nonspecific (Scheme 3, in gray, present in all the other more frequent and severe disease).

It is therefore now possible, since the moment of birth, to make a diagnosis in order to detect the presence of the Inherited Real Risks (20) of many diseases linked with QBS constitutions (3), so that an intelligent prevention strategy can be implemented only on those subjects with Inherited Real Risk.

## **‘Inherited Real Risk’ of brain disorders**

There are many cases of brain disorders, i.e., Alzheimer disease, depending on QBS constitutions (i.e., diabetics constitution), so that CAEMH and QBS constitutions are at the base of inherited real risk of brain disorders.

In summary everything takes origin from a genetic alteration of mit-DNA, as shown in Scheme 2, which is responsible of a well defined cell cytopathy, CAEMH. CAEMH spreads in several QBS constitutions, and one or more QBS constitutions are at the base of the Inherited Real Risk of a disorder, i.e., as shown in Scheme 4 for the ‘Inherited Real Risk’ of CAD (42).

As a prove of this fact, for example, maternal infection during pregnancy increases the risk of severe neuropsychiatric disorders, including schizophrenia and autism, in the offspring. We must reflect on two paramount points: firstly, not all maternal infection during pregnancy brings about neuropathies, like autism; secondly, the relative QBS constitution-dependent ‘Inherited Real Risk’ of most common diseases really exists, regarding also brain disorders (1-6).

As a consequence, we must add at above referred phrase: ...in children involved by brain microcirculatory remodeling, characterized by newborn-pathological, type I , subtype a) oncological, and b) aspecific, Endoarteriolar Blocking Devices, cerebral ‘Inherited Real Risk’ is based on!

By the same way, as also recognized by several papers in recent medical literature, Alzheimer disease has been considered as linked with Artery hypertension, dyslipidaemia, hyper-cholesterolemia and Diabetes Mellitus.

QBS experimental and clinical evidences show that the ‘Inherited Real Risk’ of brain disorder, or better the ‘Inherited Real Risk’ of Alzheimer disease is linked, i.e., with Diabetics Constitution, with dyslipidaemic Constitution and with hypertension constitution. The cause of Alzheimer disease is related therefore to genotype and to CAEMH, as defined by Quantum Biophysical Semeiotics.

The ‘Inherited Real Risk’ of brain disorders can provoke different cerebral diseases, i.e. epilepsy (2), Parkinson disease (32), Alzheimer disease, but there are specific QBS signs and tests which can reveal from the moment of birth, specifically the ‘Inherited Real Risk’ of brain disorder linked exclusively with Alzheimer disease, as we will see in next chapters.

## **QBS Diagnosis of Alzheimer’s Disease**

According with Quantum Biophysical Semeiotics is possible an early QBS Diagnosis of Alzheimer’s Disease”. We gathered interesting data, due to the fact that there is notoriously an association between high serum cholesterol, raised blood pressure and, finally, -insulin-resistance. Briefly, in healthy, from the microcirculatory point of view, during stress test both vasomotility (chaotic-deterministic oscillations of arterioles) and vasomotility (chaotic-deterministic fluctuations of nutritional capillaries and post-capillary venules) particularly in

hippocampus, pre- frontal and parietal cerebral regions are maximally activated. (2, 3, 4, 5). On the contrary, in individuals with a family history positive for Alzheimer's disease and, of course, in patients in the first stages, under identical conditions appears a particular form of microcirculatory activation, characterized by increased vasomotility and decreased vasomotion (namely dissociated type). In a few words, the flow- and flux-motion in the cerebral microcirculatory bed appears to be clearly decreased, due to the dangerous phenomenon of the so -called "microcirculatory blood-flow centralization". Unfortunately, it is generally admitted that diagnosing Alzheimer's disease, particularly in initial stages, is very difficult. The test of acute pick of insulin secretion (2, 3) proves to be reliable in bed-side recognizing this (and other numerous) disorder, even in its first stage. Although insulin isn't necessary in the glucose utilizations of cerebral neurons, surely in both cerebral cortex and hippocampus there is a largely amounts of insulin receptors (6). In initial stages of the disease has been demonstrated a scarce glucose metabolism in cerebral tissue: venous glucose level appears to be slightly decreased (6). The authors, in addition, demonstrated that O<sub>2</sub> consumption is unchanged, due to the fact that the neurons utilize other "endocellular" substances rather than glucose, probably causing neurons death (7). Although insulin isn't necessary in glucose utilizations of cerebral neurons, however in both cerebral cortex and hippocampus there is surely a largely amounts of insulin receptors (6). In addition, in the initial stages of the disease has been demonstrated a scarce glucose metabolism in cerebral tissue: venous glucose level appears to be slightly decreased (6). These authors, moreover, demonstrated that O<sub>2</sub> consumption is unchanged, due to the fact that the neurons utilize other "endocellular" substances rather than glucose, probably causing neurons death. In summary, in the complex and non completely understood pathophysiology of Alzheimer's disease does exist a fault response of cerebral insulin receptors, while the hormone acts likely as a growth factor. From these work hypothesis, in a previous clinical research we observed that acute pick of insulin secretion (2, 3, 4) in healthy activates the microcirculation in all biological systems, while in patients at "real" risk of Alzheimer's disease and, naturally, in patients involved by the disease, even in early stage, microcirculatory activation is totally absent. Importantly as well as interestingly, in no other cerebral disorders, including cerebral arteriosclerosis, it has been observed the absence of insulin-receptors response, i.e. the absence of microcirculatory activation, type I, associated. From the above remarks, it is well considered the A.R. Koudinov's et al. theory (41) according to which cholesterol is implicated in Alzheimer's disease (AD). In fact, their own recent studies show that accurate neuronal cholesterol dynamics is critical for the synaptic plasticity and neural degeneration. These data also imply the link between neuronal lipid metabolism and tau and amyloid beta neurochemistry and propose that the classical AD brain lesions are functional consequences of the neuronal cholesterol and possibly phospholipids biological mis-regulation. In addition, I think that also insulin-receptors are less responsive to insulin under such circumstances, as I demonstrated in my research. In my opinion, we have to pay all attention to this intriguing theory, that finally enlightens the physiopathology of the biophysical-semantic man oeuvre, specific in diagnosing AD, even in early pre-clinical stage.

The central role of QBS Constitutions and of the Inherited Real Risk of Brain disorders in aging people disease occurrence is due also especially if Co Q10 deficiency is present. QBS diagnosis at bed-side of Co Q10 deficiency syndrome, we have described earlier (16-19), could

be very helpful in risk stratification to predict functional decline in Older Adults. In fact QBS has demonstrated that doctors can clinically recognize with the aid of a stethoscope subjects involved by Ubidecarenone deficiency, even initial and symptomless, causing damage of tissues due to the increase levels of free radical (17).

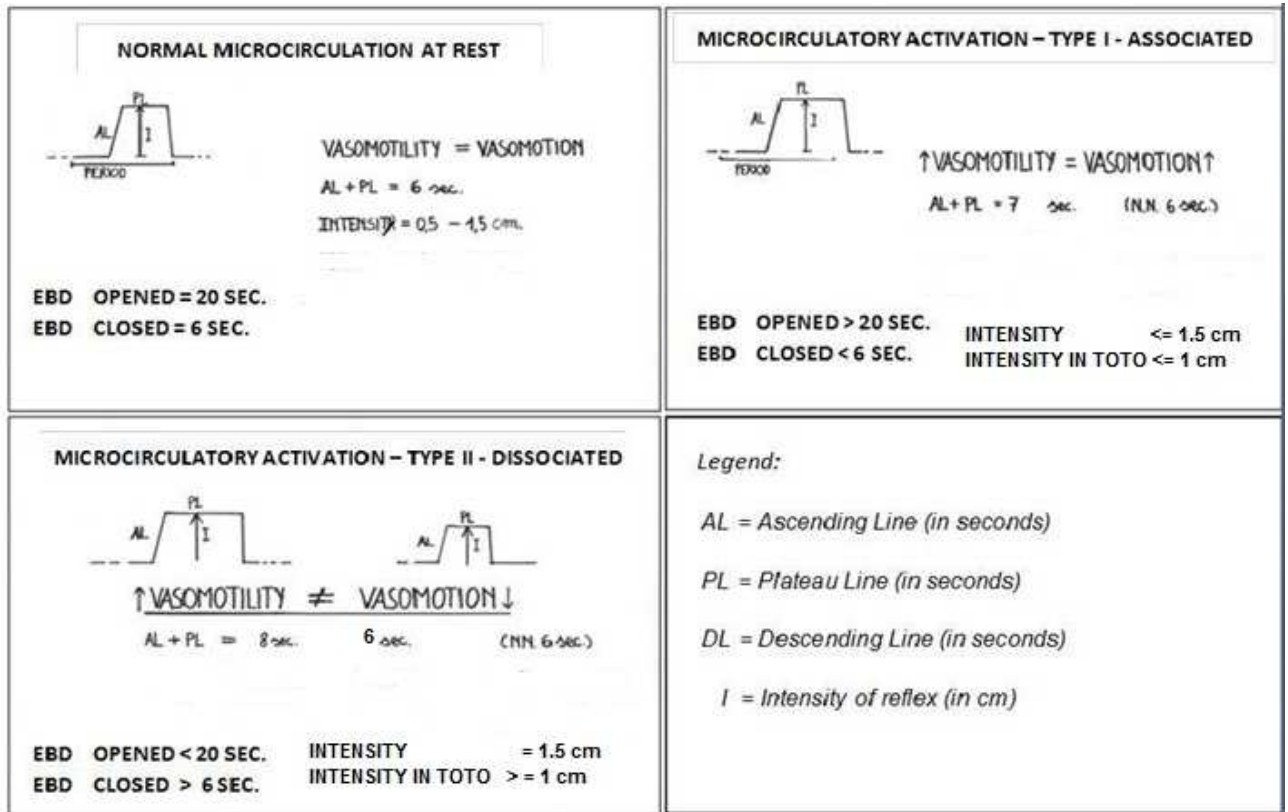
Such as diagnosis, made clinically for the first time, proved to be really efficacious and reliable in avoiding dangerous administration of statine to individuals without clinical symptomatology, even involved by ubidecarenone deficiency, notoriously worsened by anti-cholesterolemic drugs. In addition, physicians are able to recognize since birth whatever Constitution-Dependent Inherited quantum-biophysical-semeiotic Real Risk, including oncological, diabetic, and Alzheimer Disease one (5-8), based on microvascular remodeling, characterized by newborn-pathological, type I, subtype a), oncological, and b) aspecific Endoarteriolar Blocking Devices, which predispose to the related disorders. Finally, only individuals with inherited cerebral quantum-biophysical-semeiotic Inherited Real Risk (5) may be involved by functional decline, like Alzheimer Disease (8), particularly in presence of Co Q10 deficiency syndrome.

## **Alzheimer's Disease: early bed-side diagnosis by means of microcirculatory activation of the brain**

Clinical Microangiology allows to localize from the moment of birth the locations of Microcirculatory Activation (limbic region, pre-frontal area, parietal and occipital cortex) where we are able to make the diagnosis of IRR of brain disorders, based on microcirculatory remodeling.

A lot of years ago, for the first time clinically, we have demonstrated that in healthy, in middle age, cerebral microcirculation in the frontal, parietal, temporal, and occipital lobes may be activated physiologically, according to type I, associated (words coined afterwards) during numerous dynamic tests, as mentally calculating, thinking disappointing events, simulating speaking to a large audience, and so on (1-6, Appendix A,B,C).

From the microcirculatory point of view, in health (Scheme 5, M.A., type I, associated), during stress-tests both vasomotility (fluctuations of the arterioles and small arterioles, according to Hammersen: upper ureteral reflex) and vasomotion (fluctuation of capillaries and post-capillary venules: lower ureteral reflex) of the above-mentioned cerebral regions show the duration (AL + PL) of 7-8 sec. ( length of upper and lower ureteral third, caused by digital pressure of "mean" intensity, applied on the scalp of an individual in supine position), oscillation intensity 1,5 cm. (*highest spikes*), Endoarteriolar Blocking Devices (EBD, evaluated as fluctuations of middle ureteral reflex under identical stimulation conditions of cerebral trigger-points, above-mentioned), at rest functioning normally, during the stress-tests show a prevalent opening phase (mean ureteral reflex duration > 20 sec. (NN = 20 sec.), and closure duration (i.e. reflex disappearing) < 6 sec.(NN = 6 sec.). Ureteral "in toto" reflex (= interstitial space) is  $\leq 1$  cm., normal value (Scheme 5, Microcirculatory activation, type I).



Scheme 5. microcirculatory activations

On the contrary, in people with family history of Alzheimer's disease (Scheme 5, M.A. type II, dissociated) and particularly in the asymptomatic sub-group, involved by initial knowledge disorder and/or short term memory impairment, during the stress-tests mentioned above, appears microcirculatory activation more intense in the above-cited cerebral regions but exclusively as far as vasomotility is concerned, i.e. ureteral superior reflex fluctuates for a duration of 8-9 sec. (basal value = 6 sec.) of maximal intensity (in cerebral small arteries and arterioles, according to Bucciante,  $AL + PL = 8-9 \text{ sec.}$ ), while in the vasomotion (lower ureteral reflex, i.e. capillaries and post-capillaries venules) the duration lasts for only 6-7 sec. initially, indicating microcirculatory activation type second, dissociated, in which EBD are either not activated or show as prevalent the closure phase (ureteral middle reflex disappears for  $> 6 \text{ sec.}$ ;  $NN = 6 \text{ sec.}$ ). Consequently, under the later condition, parameters value of numerous cerebral reflexes, which inform about local tissue oxygenation, do not improve or, at least, ameliorate in a non statistical manner, as show instrumental, sophisticated semeiotics (PET, MNR). Ureteral "in toto" reflex (= interstitial space) results pathologically intense already as basal value ( $> 1 \text{ cm.}$ ;  $NN \leq 1 \text{ cm.}$ ), demonstrating the anomalous situation, genetically transmitted.

The activation of the local microcirculation aims to increase the flow-motion and consequently the blood supply to yet normally functioning neurons. However, from the above remarks, based also on our earlier original researches (6), dissociated activation, type II, does not improve the flow-motion and then neurons metabolism, if still intact, representing, in my mind, the primary cause of slow and progressive worsening of the local cerebral microvessel system and consequently of neurons, as I described in previous articles (1-6).



In conclusion, interestingly Quantum Biophysical Semeiotics allows doctor to recognize and assess EBD dysfunction in cerebral microvessels at rest, which worsens during dynamic tests, starting from very initial phase of Alzheimer's disease, so that takes form of the principal expression of genetic error.

## **The test of insulin secretion acute peak in bed-side QBS diagnosis of Alzheimer's disease**

The diagnosis of Alzheimer's disease, particularly in the early stage, is notoriously difficult. *Clinical Microangiology*, by means of insulin secretion acute peak (2), allows doctors to make the early correct diagnosis, even in asymptomatic patients (6).

If mit-DNA and n-DNA are not normal, i.e., if there is their genetic alteration, the glycocalyxes (9, 24, 25) at level of nervous cells or neurons, do not run simultaneously during the test of insulin secretion peak.

In order to understand all the importance of this test, avoiding to consider the physiopathology of QBS signs, which is not the aim of this article, one has to reflect on the role played by insulin in both glycidic metabolism and memory, compromised in aging as well as in Alzheimer's disease (7). In effect, now a days the authors do not agree on this aspect of insulin activity, so that even those, who uphold insulin theory, are not in agreement on hormone action mechanism (8).

It is sure, however, that in both cerebral cortex and hippocampus there is a large number of insulin receptors, by which the hormone brings about the well-known effects on the memory, as demonstrated some experiments in animals, since 1980 (8).

As a matter of fact, the authors agree until now on the neurons uptake of glucose without the need of insulin (which is also a growth factor) (9). In the initial stages of Alzheimer disease, in fact, there is impairment in the neurons utilization of glucose, as shows it clearly the usually slight lowered level of blood glycaemia in venous cerebral vessels (9). Because of the unchanged O<sub>2</sub> consumption authors have suggested that neuron utilizes other metabolites different from glucose, as neuron makes use of its internal metabolites and consequently the cells become damaged and finally die. Therefore, the disease may be the result of this process (9).

In other words, on the basis of Alzheimer's disease could be an impairment of neurons response to insulin, that explain the increasing of cerebral blood glycaemia, due to the lowering of insulin receptors and/or of their response.

Based on this working hypothesis, I performed the test of insulin secretion acute pick in early diagnosing senile dementia and all other forms, gathering really intriguing results.

## ***Methods***

In up-to-date practice doctor assesses, at base, following reflexes caused by digital pressure of different degree, as indicated in bracket:

- 1) oculo-gastric aspecific and –caecal reflex (pressure degree mean-intense upon eyeball, closed of course) (Fig.1);
- 2) cerebral-gastric aspecific reflex type I (the same);
- 3) cerebal-upper, mean, lower ureteral reflex ( pressure degree light-mean);
- 4) carotid-gastric aspecific and –caecal reflex (the same);
- 5) carotid- upper, mean, lower ureteral reflex (the same);
- 6) cerebral *preconditioning* (after 5 sec. interruption from the end of basal evaluation doctor assesses for the second time the above-mentioned reflexes, comparing these parameters value with the basal ones.

In order to apply the insulin secretion test, doctor, after assessing the parameters basal value of the above-described reflexes, immediately thereafter stimulates by lasting pinching the skin of VI thoracic dermathomere (i.e., the crossing point between emiclavear line and costal arch, at right or left) for 15 sec., repeating the evaluation of the identical reflexes: in both health and patients involved by senile dementia, vascular in origin or mixed, the test improves “always” the numerous parameters mentioned above, although in different manner, of course. For instance, in case of “initial” and asymptomatic senile decay, latency time of the cerebral-gastric aspecific reflex inceases from 5-6 sec. (NN = 6 sec.) to 6-7 sec. (NN  $\geq$  8 sec.) (Fig 1).

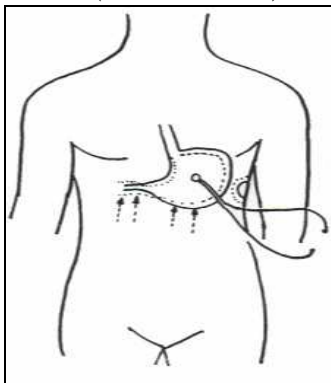


Fig.1

*The figure shows the precise location of the bell-piece of stethoscope and the lines upon which doctor must apply digital percussion in order to delineate a small tract of the low part of inferior great gastric curvature. Gastric aspecific reflex: in the stomach both fundus and body are dilated, while antral pyloric region contracts.*

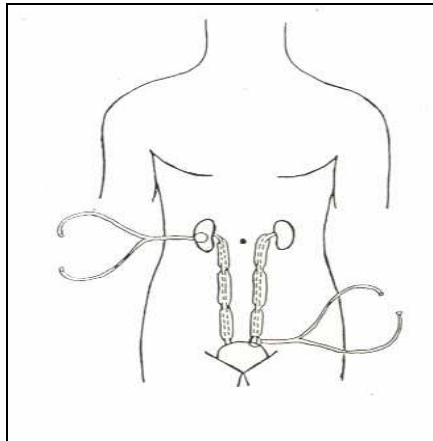


Fig. 2

*The figure shows the correct position of the bell-piece of stethoscope unavoidable in performing auscultatory percussion of kidneys and ureters and evaluate the ureteral reflexes (Appendix C)*

On the contrary, in Alzheimer's disease, starting from the very initial stage without clinical symptomatology, over years or decades, the acute pick of insulin secretion does not improve at all the above-mentioned parameters values of reflexes, which are identical to those of basal assessment.

In practice, in an easiest manner, doctor has to evaluate cerebral-gastric aspecific reflex type I at the base (at rest), in a patient in supine position and psycho-physically relaxed and soon thereafter the insulin secretion test. Digital pressure is applied on skin projection area of parietal and/or temporal and/or frontal and/or occipital cerebral cortex: the parameters value persist the same also after the test (lt 5-6 sec., e.g.).

Particularly, vasomotility and vasomotion, evaluated as upper and, respectively, lower ureteral reflexes oscillations (Fig. 2), even pathological at rest (as basal values), appear to be unchanged: AL + PL 5-6 sec. (opening duration = ureteral reflex duration) in the two assessments.

We never observed this behaviour of the cerebral microcirculation in anyone involved by other cerebral disorders, different *in origine*. Therefore, this sign proved to be in a long experience a "typical" sign of Alzheimer's disease.

As a matter of fact, the incidence of this disease is not greater among diabetic patients than among non-diabetic. In my opinion, the reduced response of insulin neuronal receptors in the Alzheimer disease (insulin functions also as growth factor) must not be considered primary, but secondary to the initial apoptic neuronal events, recently demonstarated in the Alzheimer disease (10), which enlighten the pathophysiology of alterations, both functional and structural, at receptor and post-receptor level.

In healthy, all parameters value of the above-described biophysical semeiotic signs (and of the numerous others not illustrated because of the reader's actual biophysical semeiotic knowledge) improve clearly, while they persist either unchanged, in initial stage and/or in individuals at risk, or get worse after the disease onset, even asymptomatic.

In conclusion, the employment of acute pick insulin secretion test in bed-side recognizing Alzheimer's disease, even in initial stage 6), by means of QBS, proved to be reliable and useful due to the fact that exclusively in this cerebral disease there is not any

favourable modification of the cerebral microcirculation, induced by the test, otherwise always observed in both physiology and pathology, although of different intensity. Finally, it is necessary to underline the importance of Endoarterial Blocking Devices (EBD) impairment, mentioned above briefly from the biophysical semeiotic point of view, that is ascertained over years or decades before the onset of this and all other most common human disorders, proving to be an very useful tool in diagnosing and primary prevention: the cerebral- mean ureteral reflex duration at rest results  $\leq 20$  sec. (NN = 20 sec.) and disappearance duration  $\geq 7$  sec. (NN = 6 sec.), indicating clearly the impairment of local Microcirculatory Functional Reserve of different degree, due to the altered cerebral vasomotion, provoked principally by EBD dysfunction. At the beginning of December 2001, the authors has been informed about the interesting Alexei R. and Natalia V. Koudinov's work, reading the article "BRAIN CHOLESTEROL PATHOLOGY IS THE CAUSE OF ALZHEIMER'S DISEASE", posted in Clinical Medicine & Health Research; January 5, 2001, Published online: November, 2001.

"Inhibiting cholesterol production in the brain might inhibit amyloid (A $\beta$ ) production, and reduce the accumulation of A $\beta$  that causes Alzheimer's disease (AD)". As Koudinov et al. show and discuss in their paper cholesterol homeostasis biological misregulation itself has a key role for synaptic plasticity impairment, neuronal degeneration and is the primary cause for several AD hallmarks not limited to brain amyloid (23). Moreover, Alzheimer's changes in neurochemistry of amyloid beta, tau, neuronal cytoskeleton, and oxidative stress reactions likely represent physiological transitory mechanisms aiming to compensate impaired brain cholesterol dynamics and/or associated neurotransmission and synaptic plasticity failure. I am grateful to these colleagues because their theory enlightens the physiopathology of the biophysical semeiotic method above described.

## **Quantum Entanglement Sign of Inherited Real Risk of brain disorder**

The ureteral reflexes are not so easy to evoke in practice, and usually the doctors approach the QBS first learning the Auscultatory Percussion of the Stomach, easier to understand and to apply in the daily practice. The test of microcirculatory activation of the brain implies the knowledge of ureteral reflexes, while the test of insulin secretion acute pick implies the knowledge of several reflexes, not always so easy to evoke for beginners.

There is one more reflex, very easy to evoke, and this is called cerebral-gastric aspecific reflex in case of intense pressure on the trigger points of brain. This reflex is called Quantum Entanglement Sign, because is correlated with the non-local quantum behavior of biological systems.

In health, in case of intense pressure on brain's trigger points if the reflex appears just after 16 seconds, there is not any inherited real risk of brain disorders.

In case of intense pressure on brain's trigger points related to Alzheimer disease ((limbic region, pre-frontal area, parietal and occipital cortex) if the reflex appear simultaneously there is an Inherited Real Risk of brain disorder linked to Alzheimer disease, but only if the intensity

of the reflex is more than 1 cm (otherwise if the intensity is of 0.5 cm this is just the sign of positive CAEMH).

<b>INTENSE DIGITAL PRESSURE ON BRAIN TRIGGER POINTS – QES – QBS CEREBRAL-GASTRIC ASPECIFIC REFLEX</b>	<i>CAEMH</i>	<i>INHERITED REAL RISK OF BRAIN DISORDER (ALZHEIMER DISEASE)</i>	<i>HEALTH</i>
<i>Latency time (in seconds) – Lt</i>	<i>Lt = 0</i>	<i>Lt = 0</i>	<i>16</i>
<i>Intensity (in cm) – In</i>	<i>In ≈ 0.5</i>	<i>In ≥ 1</i>	<i>-----</i>

*Table 1. Quantum Entanglement Sign - QES*

The intense Auscultatory Percussion of the Stomach (both real and virtual in case of Psychokinetic Diagnostic) upon the lateral region of the front (pre-frontal areas), upon the temporal-parietal region (3 cm above the external auditory meatus), etc. provoke in fact a brain-gastric aspecific reflex with an intensity of at least 1 cm in case of Inherited Real Risk of brain disorder. This is an aspecific sign, but it becomes specific if the remodeling is present in the typical areas of Alzheimer disease: pre-frontal areas, limbic region, and so on.

This is a similar behavior to other inherited real risks of disorders, such as diabetics, rheumatic, gouty one, where the remodeling is characterized by new-formed aspecific pathologic EBD, all equals in term of structure and function, but they turn specific in relation with their tissue location.

## **Primary Prevention of Alzheimer Disease**

The diseases are divided into treatable and incurable, according to current scientific knowledge. Alzheimer disease is one of the incurable diseases, so that any actual medical treatment is oriented just to slow the progress of the disease. Quantum Biophysical Semeiotics is a modern and original way to make the diagnosis of AD at bed-side, in its very initial stages, but furthermore QBS is able to detect the Inherited Real Risk of brain disorder, with regard to Alzheimer disease too, so that is possible to suggest an efficacious primary prevention only on those subjects at Risk of this incurable disorder. If the primary prevention is done before the disease occurs, the Inherited Real Risk can become residual or even completely disappear.

The primary prevention is the best therapy for any disorder, included the treatable disorders. In order to transform the IRR of brain disorder in its residual variant QBS emphasizes the importance of taking conjugated-melatonin according to the recipe of 'Di Bella-Ferrari', in conjunction with other appropriate preventive therapies, designed in the etymological sense: i.e., to avoid tobacco smoke, sedentary lifestyle and overweight, and at the same time to favor an healthy lifestyle, using for instance a custom Mediterranean diet, encouraging a daily physical activity and body movement. Vitamins and NIR-LED treatments are also recommended. All these treatments aim to improve mitochondrial oxygenation, so that a better breathing cell do not allow the disease to appear. It needs to be understood in fact that

the CAEMH reveals the state of suffering of the cell, particularly with respect to mitochondrial DNA, and thus the mitochondria, responsible for cell oxygenation. In case of alteration of mitochondrial DNA, it is clear that the mitochondrial oxygen becomes deficient. The genetic alteration continues to be anyway still present, so that the preventive therapy just above mentioned must be daily constant and continuous.

There is a recent discovery, still under experimental evaluation, which is very promising in the sense that just one application of quantum treatment done with a quantum device able to capture the personal frequencies of the suffering part of the body, is able to reverse the genetic alteration of mit-DNA. This means that, at least in the sample of patients under observation, this quantum treatment allows to reverse. i.e., the positive CAEMH. If the CAEMH becomes negative, all QBS constitutions and related 'Inherited Real Risks' disappear, because at the base we eliminate definitively the genetic alteration of mit-DNA. In the specific case of this paper, it is easy to understand that in accordance with the promising experimentation in progress, with just one quantum treatment it is possible to eliminate the 'Inherited Real Risk' of Alzheimer disease. If this experimentation will be confirmed and validated in the next future, it will be possible an effective and efficacious primary prevention just on all the subjects at risk of Alzheimer disease.

## Conclusions

Quantum Biophysical Semeiotics is able to make the diagnosis of 'Inherited Real Risk' – IRR - of brain disorders, and in particular through the Auscultatory Percussion of the typical areas of Alzheimer disease, i.e., pre-frontal areas, limbic region, this original semeiotic can reveal if any subject, from the moment of birth, is at risk of such disorder.

There are two main QBS tests able to do it: the test of microcirculatory activation of the brain, and the test of insulin secretion acute peak. Furthermore, there is a Quantum Entanglement Sign (QES), which can reveal the 'Inherited Real Risk' of brain disorder, specially related to Alzheimer disease.

Alzheimer Disease is not reversible by medical treatments, and the current research is concentrated just on genetic and histological clinical tests, while QBS is able for the first time to provide for such disorder a biological evaluation, because biological system functional modification parallels gene mutation. Furthermore QBS is able to make a diagnosis of AD not only at the first very initial stages, usually very difficult to do, but even many years before that such disease could appear, allowing so an efficacious primary prevention, according to the Manuel's Story.

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## APPENDIX A - Elements of Clinical Microangiology

*According to Tischendorf's concept of Angiobiotopie (Curri, 1986), biological tissue-microvascular system can be described as formed by single units: the tissue-microvascular units.*

*In its turn, the tissue-microvascular unit (T.M.U.) is made up by three fundamental components:*

- 1) *microvessels, diameter < 100 μ,*
- 2) *the blood, flowing in them,*
- 3) *perivascular connective, periangium, interstitium or "environment" in which microvessels are placed, formed by water, free- and bound- water, cells and connective fibers, and interstitial matrix, glucosaminoglycanes.*

*Microvessels can be subdivided as follows (Pratesi, 1990):*

- 1) *Para-microcircle: small arteries and arterioles, according to Hammersen, venules of I, II, III order, shunts or Arterio-Venous Anastomoses (AVA), functionally speaking (Bucciantè, 1949);*
- 2) *Microcircle: nutritional capillaries, post-capillaries venules, "meta"- arterioles.*

*With the aid of Biophysical Semeiotics, doctor is able to evaluate, in dynamic manner, T.M.U. of every biophysical system, from both structural and functional view-point, according to a synergistic<sup>iii</sup> pattern, i.e. the clinical evaluation of microvascular dynamics.*

Notoriously the microvessels carry on a motor activity, autoctonous and deterministic chaotic, which represents one of the most remarkable manifestations of microcirculatory hemodynamics, characterized by a flow-motion and hematocrit rhythmically fluctuating due to the particular behaviour of both vasomotility and vasomotion<sup>iv</sup>.

A biological system, as the tissue-microvessel system, so much highly evolved and well differentiated, as regards anatomy and physiology, can not react to attacks, different in origin, which involve it, by a lot of ways.

As far as tissue-microvessel unit is concerned, cells, transformed in smooth muscle cells and in ramified smooth muscle cells, when stimulated, either contract or dilate, although there is a residual possibility of further response.

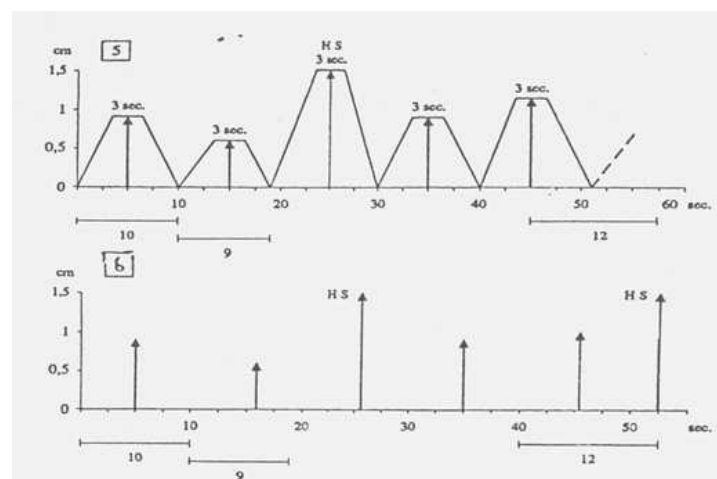
On the contrary, smooth muscle cells of the media of great arteries – elastic and muscular – which are less differentiated, react to various stimuli, even, de-differentiating and, then, evolving towards cells with secretory activity (Simonescu 1990, Gimbrone 1997).

These concepts account for the reason of the restricted number of tissue-microvascular unit reactions, doctor can observe at the bed-side by biophysical semeiotics and Clinical Microangiology<sup>v</sup>.

According to biophysical semeiotics, in a supine healthy subject, psycho-physically relaxed, with his (her) open eyes, aiming to inhibit melatonin secretion, digital pressure of “low-mean” intensity, applied upon the skin projection area of heart, brings about upper, middle, low-ureteral-, gastric aspecific-, caecal-, and choledocic- reflexes, i.e., upper-, mean, low-ureter as well as stomach, caecum, and choledocus dilate, the latter three after a latency time of 8 seconds.

In health, the dilation of upper and low ureteral reflexes, appears after 6 seconds and lasts for 6 seconds, while all other reflex duration is less than 4 seconds. The latter parameter value proved to be of paramount importance, from diagnostic viewpoint, informing precisely about local microvascular structures and function, as well as microvessel remodeling. In fact, such as digital pressure brings about “low-mean” stimulation of coronary trigger-points, inducing “rapidly” oscillations of upper and choledocic reflexes (small arteries, according to Hammersen) and subsequently those of lower ureteral (arterioles, nutritional capillaries), which parallell fluctuations of the related microvessel structure, according to a synergetic model (Stagnaro, 1994).

The oscillations of “upper” reflexes define the vasomotility – the general dynamics of microcirculatory vessels, while those of “lower” one express the vasomotion – capillary- venules dynamics (Figure 1).



**Figure 1:** Physiology fluctuations of upper and lower ureteral reflexes, at rest (vasomotility and vasomotion); HS stands for Highest Spike or highest oscillation

In figure 1 we can see how are practically evaluated vasomotility and vasomotion. Drawing a Cartesian diagram, in the x-axis is represented the reflex's duration (in seconds), while in y-axis is represented the reflex's intensity (dilation of parenchyma, in cm). Interestingly, the period of oscillations is not fixed or constant: under physiological condition, it varies from 9 seconds to 12 seconds showing 6 cycles per minute. The average duration of fluctuations is 10.5, i.e., a fractal number. Furthermore, the intensity of "normal" oscillation is variable in a unpredictable manner, varying in health from 0.5 cm to 1.5 cm. Physiologically, after two normal, different in intensity, unpredictable fluctuations, we observe an highest oscillation - highest spike (HS) – that corresponds to "quantic", maximal, periodic adrenalin and nor-adrenalin discharge from autonomic nervous system endings, which occurs exactly every 25 seconds. Finally, these signs can usefully be evaluated under stress tests (Stagnaro, 1996).

Vasomotility and vasomotion of every T.M.U. physiologically show an highly complex type of variability, "constrained randomness", reminiscent of chaos (Goldberger, 1991, Murry, 1986), which may be evaluated nowadays at the bed-side with the aid of biophysical-semeiotics, as demonstrated for the first time clinically (Stagnaro, 1994).

Quantum Biophysical Semeiotics allows doctor to detect the chaotic behavior of both intensity and period of ureteral (and choledocic) oscillations, i.e. vasomotility (upper ureteral reflex: small arteries) and vasomotion (low ureteral reflex: nutritional capillaries) of the microcirculatory bed of all organ and tissue, including the heart (Figure 1).

In addition, more intense stimulation provokes numerous, pressure-dependent, middle ureteral reflexes, informing respectively on different types of EBD and AVA, according to Bucciante (1949). Middle ureteral reflexes are correlated with EBD both physiological and newborn-pathological (Table 2). Furthermore, low ureteral reflex oscillations give information on nutritional capillaries. Interestingly, mean digital pressure upon Th-1 – Th-2 dermatomes stimulates cardiac  $\beta$ -adreno-receptors. Physicians assess the capillary diameter as intensity of low ureteral reflex. Highest spike (HS) intensity divided for minimal oscillation gives a ratio 3/1 under physiological condition. This value is unavoidable in calculating biophysical-semeiotic fractal Dimension ( $fD$ ) of microvascular deterministic chaotic systems. It is perfectly identical to the value of differential latency time of heart-specific gastric and –caecum-reflex, surely easier to be evaluated (table 1).

#### Middle ureteral reflexes

Low intense stimulation: 1 cm.; 7 sec. duration;  
6 sec disappearing time. = type II EBD.

Mean-moderate intense stimulation: 1,5 cm.; 15 sec. duration;  
6 sec. disappearing time = type I, A, AVA

Moderate-intense stimulation: 2 cm.; 20 sec. duration;  
6 sec. disappearing time = type I normal and newborn-pathological, subtype b) EBD.

Mean intense stimulation: 1,5 cm.; 15 sec. duration;  
6 sec. disappearing time = type II, AVA.

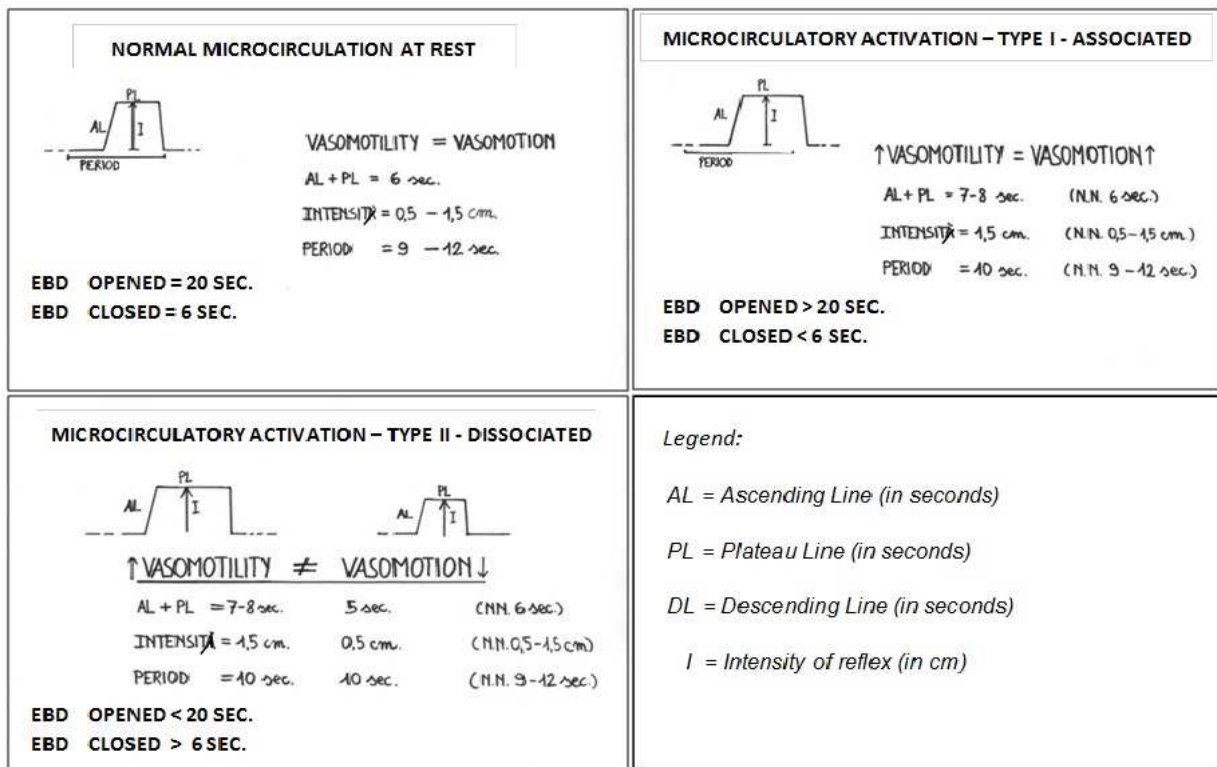
Intense stimulation: 2,5 cm.; 20 sec. duration; 6 sec.  
disappearing time = type I, newborn- pathological, subtype a) EBD.

**Table 2:** parametric values of different middle ureteral reflexes as well as their significances

Numerous conditions, physiological and pathological, bring about “rapidly” modifications of deterministic-chaotic fluctuations of the small arteries, arterioles, nutritional capillaries, post-capillaries venules, and AVA, functionally speaking, in particular EBD, ubiquitous structures, essential in causing flow-motion in the microcircle of biological systems. It is easy to understand that such microcirculatory modifications aim to adapt in a better way the biological system to new conditions. Obviously, the activation of “peripheral heart” aims to realize and maintain a sufficient flow-motion in nutritional capillaries in relation to actual functional situations of local parenchyma, whose local microcircle has to supply material-energy-information in a perfect way.

The normal microcirculation at rest can become physiologically active when the parenchyma starts to work. The important set of microvascular dynamic events, related to microcirculatory activation - M.A., can be subdivided in three types (scheme 11):

- type I or “associated”, “physiological”, in which both the vasomotility and vasomotion result increased and consequently blood-flow in nutritional capillaries and post-capillary-venules is augmented, due also to right AVA reaction; (e.g. during parenchyma work);
- type II or “dissociated”, “pathological”, in which the vasomotility shows increasing of both intensity and oscillation duration, while the vasomotion shows a highly differentiated behaviour, in relation to the presence of microcirculatory “compensation” or “decompensation” (failure), as we will say later on. (e.g. during pathological conditions);
- type III or “intermediate”, when vasomotility is activated, while vasomotion shows basal activity, and hemoderivative structures are not activated. The transition from type I to type II goes through numerous intermediate stages, which from the compensation reach the total irreversible decompensation of microcirculation, showing a large variety of different and significant forms.



Scheme 11. Vasomotility and vasomotion. Microcirculatory activation types

*M.A.* - type I shows the increasing of oscillation waves: the sum of  $AL^{vi}$  (ascending line) and  $PL^{vii}$  (plateau line) duration is equal to 7-8 seconds, maximal intensity (1.5 cm) as well as a period of 10 seconds. Arrows indicate the activation<sup>viii</sup> of both vasomotility and vasomotion. Consequently, fractal dimension appears clearly reduced (scheme 11). The under curve area “shows” microvessel sagittal surface during their highest and prolonged opening phase so that, under such condition, microcirculatory blood-flow is greatest.

In healthy, who is invite, e.g., to bend and extend repeatedly homolateral foot or, more easily and refined, to “think” of perform such movements, adventitial arterial microcircle of common femoral artery moves rapidly from basal microcirculatory condition, characterized by microvessels deterministic-chaotic oscillations, revealed by upper and lower ureteral reflex fluctuations (figure 1), where  $fD$  is 3,81, to the typical type I, associated, activation, in which all fluctuations show the same, greatest, intensity (highest spikes) and fractal dimension lowers from 3,81 to 1,5 (figure 2).

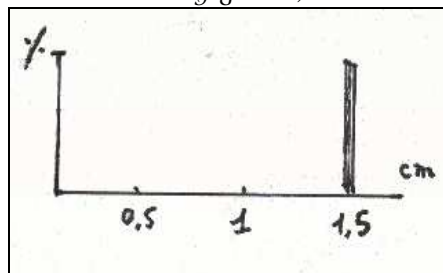


Figure 2

Figure 2 illustrates the “at far column” type of Fourier’s transformation of oscillations observed in the *M.A.*, type I, associated, in which capillary as well as arteriolar fluctuations intensity are all identical and highest, showing value of about 1,5, as conventional measure.

Among microcirculatory structures, a primary role in the microvessel blood-flow is played by Endoarterial Blocking Devices (EBD), which are largely present in human body (scheme 12).

**Physiological Endoarteriolar Blocking Devices**  
**Type I and Type II: location**

**Type I and Type II:**

**Skeletal Muscle, right cerebral hemisphere  
(individuals positive for CAEMH-alpha), etc.**

**Type II: really UBIQUITOUS**

**Brain (without CAEMH-alpha), Heart, Lung, Stomach,  
Duodenum, Liver, Gall-Bladder, Prostate, Womb and Ovaries,  
Endocrine Glands, e.g., Adrenal, Pituitary, Thyroid Glands,  
Diencephalic NeuroneCenters, Adipose Tissue, etc.**

**Scheme 12:** Doctor who knows the exact location of physiological type I EBD (skeletal muscle, right emisphere of individuals CAEMH-positive, conjunctival mucosa) can recognize in easier way the type I pathological DEB, that play a pivotal role in diagnosing biophysical-semeiotic real risk of most common and serious human disorders

Both physiology and anatomy of EBD, evaluated “clinically” for the first time, play a primary and pivotal role in diagnosis and prevention of the most common and serious human diseases, including diabetes, hypertension, ATS, CVD, and cancer, permitting, for the first time “clinically”, to define the link existing between genetic factor and phenotype, according to the theory of Angiobiopathy (Stagnaro, 2004).

EBD, derived from arteriolar medial layer, and located in a single point of vascular wall with two (arterioles) or more (small arteries, according to Hammersen) layers of smooth muscle cells, protruding to the lumen, show very different structure and form, under physiological and pathological conditions: small cushions with wide base, polypoid formations, generally pedunculated, sphincteric formations, intimal contractile architectures (figure 3).

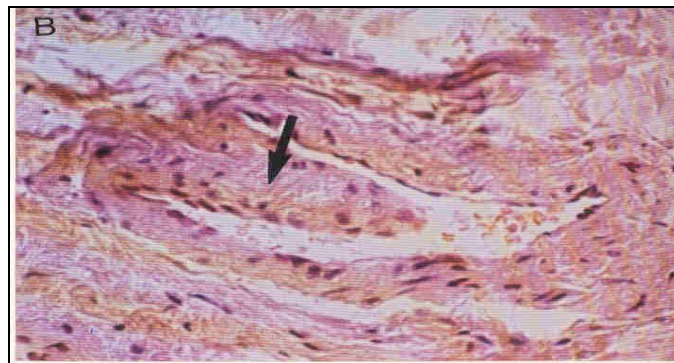


Figure 3. For kind permission of Curri S.B. (1986), the figure shows a refined imagine of EBD with a large base of the type “proboscide”

They are ubiquitous since they are located in all biological systems; more precisely speaking, only type II, normal, EBD, localized in arterioles, according to Hammersen, are ubiquitous. EBD are playing a primary role in the regulation of local microcirculatory flow-motion, as the following clinical evidence demonstrates: when abnormal, at least from functional biophysical-semeiotic viewpoint, EBD bring about impairment of MFR, which contribute to conditioning the “real risk” of disorders, like CAD, whose onset will possibly occur after years or decades.

EBD contraction, i.e. the contraction of its muscular cells, at the base of mean ureteral reflex (arteriolar opening), brings about blood flow increase in the capillaries, microcirculatory stasis and, then, if lasting, possible hypertensive damage of related capillary net, and subsequently dilation at first, and, thereafter, basal membrane thickening. In case of microcirculatory activation type I, associated, EBD contribute significantly to increasing matter-energy-information supply to parenchyma, according to the physiological behaviour.

During M.A, type I, associated, EBD are “open” mean ureteral reflex, brought about by “middle” digital pressure on the artery, lasts for  $> 20$  seconds (NN = 20 seconds), i.e., for a time longer than that observed at baseline, and, moreover, reflex disappearing (EBD decontraction, expressed by reflex cessation from biophysical-point of view) is  $< 6$  sec. (NN = 6 seconds). These functional “vasomotion” modifications aim to increase the blood-flow in nutritional capillaries of arterial wall external, outward third and, consequently, to remove efficaciously  $H^+$  as well as various catabolites.

On the contrary, M.A., type II, dissociated, in which vasomotion is reduced, is always associated to EBD dysfunction, indicating pathological local microcirculation: microcirculatory bad distribution of blood flow<sup>ix</sup>, according to S.B. Curri (1986).

In M.A., type II, dissociated, pathological, in which occurs the microcirculatory phenomenon of the so-called “blood-flow centralization”, due to the greater opening of AVA, and subsequent removal of

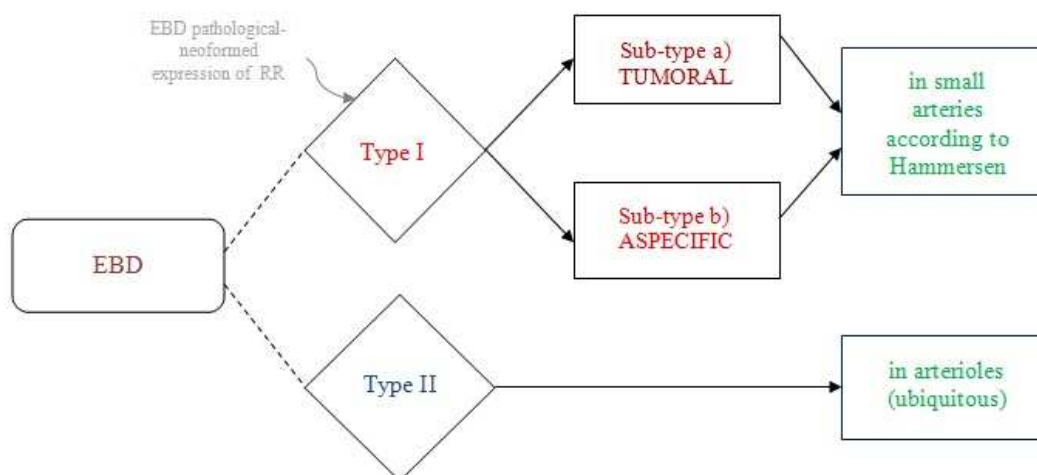
capillary blood, we observe an insufficient blood-flow to parenchyma, that flows mostly in AVA, shunting therefore it away from parenchymal cells.

For instance, in case of chronic arteriopathy, arteriosclerotic as well as of other origin, it is present the dissociated type of activation, which brings about tissue acidosis, recognized at the bed-side by caecal, gastric aspecific and upper ureteral reflexes.

## APPENDIX B – The Endoarteriolar Blocking Devices (EBD)

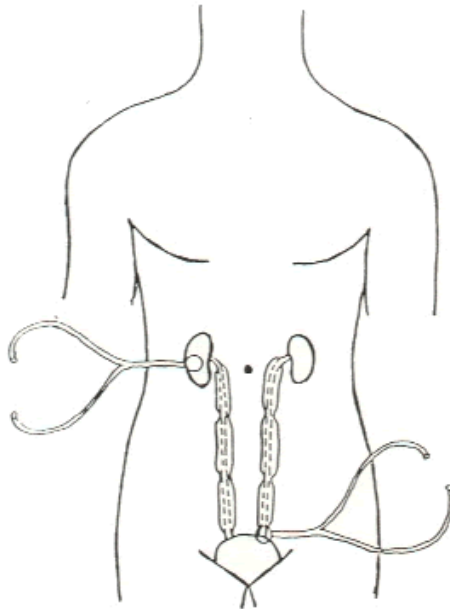
The EBD is a kind of dam which opening or closing itself regulates blood flow in microvessels directed to the parenchyma (tissue, substance of a body). With a simple stethoscope it is detectable if there is a clear genetic predisposition to have a disease such as cancer, diabetes or CAD, and it is possible to quantify and monitor it over time since birth. So there is the possibility of implementing a prevention on a huge hall in individuals clinically finally selected in a rational way. This new way of prevention will not allow to materialize physical illness, which can be anyway potentially present (or be RR as "residual") at potential level. As similarity we can think of butterfly valves that regulate the flow and mixture of air and gasoline in car engines, since the EBD are dams that are simply regulating blood flow to the parenchyma<sup>x</sup>, precisely cells of various tissues. If these DEB are tough, rigid, inelastic, there is RR.

There are EBD Type I - located in small arteries, according to Hammersen - and Type II – they can be found in the arterioles that are, according to Hammersen, between small arteries and capillaries -: only type II is ubiquitous, in the sense that it is observed everywhere, in all arteries (scheme 12). Even these physiological types get sick or old. However, the other types, pathological-neoformed, are expressions of the RR, of potential disease, they occlude more, but through therapy they can be transformed from the subtype a) tumoral, to subtype b) aspecific, and then in "physiological" type, decreasing gradually their amount<sup>xi</sup>.



Scheme 4. Endoarterial Blocking Devices (EBD)

## APPENDIX C- *The ureteral reflexes*



*In order to learn Clinical Microangiology, and therefore the chance to investigate the way of being and functioning of all parenchyma, i.e., genetic alterations provoke biological alteration, by means of the evaluation of the activity of the related microvessels, in accordance with Angiobiopathy theory, the physician must know the Auscultatory Percussion of Ureteres.*

***In order to delimit the ureteres*** in accordance with the Technical Page n.5 ([www.semeiomaticabiofisica.it](http://www.semeiomaticabiofisica.it) –english version), this is as follow. As far as kidney's and ureter's auscultatory percussion is concerned, a simple method, useful in bed-side detecting cutaneous projection are of both kidney and ureter, is the following: in a subject, psycho-physically relaxed and in supine position, applied the bell-piece of a stethoscope on abdomen lateral anterior region, right and than left, doctor performs digital percussion of slight intensity directly upon centripetal lines, starting from the external area towards the bell-piece of stethoscope (Fig. 1).

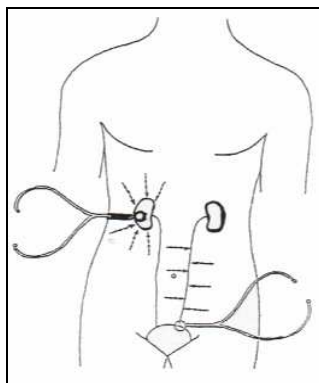


Fig. 1



*Figure shows the correct position of bel-piece of stethoscope in order to perform auscultatory percussion of both kidney and ureter.*

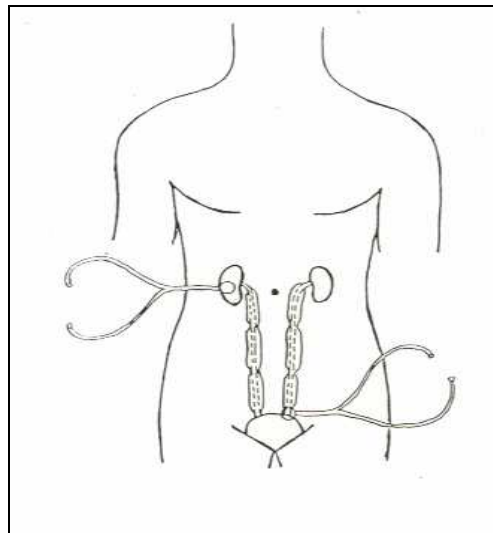
*When the percussion is applied “directly” on the precise cutaneous projection area of the kidneys, doctor perceives the percussion sound more clear, hypophonetic, and intense, “as originating near to doctor’s ears”.*

*Really, there are two ways of applying auscultatory percussion (A.P.) of the urinary tract: anterior and posterior, in relation to the location of the drum-piece of stethoscope.*

*In addition, as regards the posterior way, there is an interesting “variant” form: patient is sitting on visiting-bed with the legs down and doctor performs AP of the kidney, beside that of lung and spleen. In my opinion the useful AP of kidney must be a necessary component of the common physical examination.*

*The anterior way of kidney AP allows doctor to perform also AP of ureters, which permits to draw cutaneous projection area of the urinary tract, even only in mind.*

*Thus it is easy to recognize three interesting ureteral reflexes, i.e. upper, middle, and lower ureteral reflex, fundamental on Clinical Microangiology, since their accurate assesment, over the two last decades, have allowed me to found this new branch of Medicine, i.e. bed-side study of the microcirculation in all biological systems with the aid of **QBS** (Fig. 2).*



*Fig. 2*

*Figure indicates clearly upper, middle, and lower ureteral reflexes, cause by”light” stimulation of the trigger-points of whatever biological system.*

*Moreover, kidney’s and ureter’s AP evaluation allows to perform an original bed-side assessment of renal function, related in a satisfactory way to RPF and GFR, i.e. **bed-side renal functionality test by water load** (See also **Medscape: Internal Discussion**).*

*At first, in a individual in supine position and psycho-physically relaxed, doctor assesses renal diameters, evaluated as minimal degree of renogram, i.e the chaotic-deterministic fluctuations of kidney besides period, duration and intensity of ureteral peristaltic wave.*

*In healthy, data are observed as follows: 6 cm. x 12 cm., Phase C (kidney congestion) duration 6 sec., oscillation intensity varying between 0,5 cm. and 1,5 cm. in a chaotic-deterministic manner, period fluctuating between 9 sec. and 12 sec.*

*In addition, the ureteral peristaltic wave period at base-line is 18 sec., intensity < 1 cm. and, finally, duration of ureter dilation is 3 sec. exactly. Soon thereafter, subject is administered 250 cc. water and then, after a latency time of 3 minute, the degree of above- mentioned parameters, are*

evaluated for a second time. “Minimal” kidney diameters increases ( $> 6$  cm. and respectively  $> 12$  cm.), renogram appears to be of “vagal” type, i.e. Phase C is clearly augmented with 7-8 sec. duration and all fluctuations are identical, as far as intensity and period are concerned.

In addition, ureteral peristaltic wave shows an increased intensity (more than 1 cm.) lasting for 6 sec. (doubled than that at base-line) and a period decreased to 12 sec. exactly. Actually, the degree of the numerous renal parameters are related in a satisfactory manner to RPF, while ureteral parameters are correlated with GFR.

Where do we place the drum of the stethoscope? The drum of the stethoscope is placed over the region of the upper side of the abdomen, i.e. above the anterior axillary line, just below the costal arch, corresponding to the projection of the kidney. The position of the drum in front is less practical, because the sound is weaker! By this way is possible to do the Auscultatory Percussion of all the urethra.

In the figure 2 you can see clearly how must be done the stimulation of the uretra through the percussion of the lines drawn.

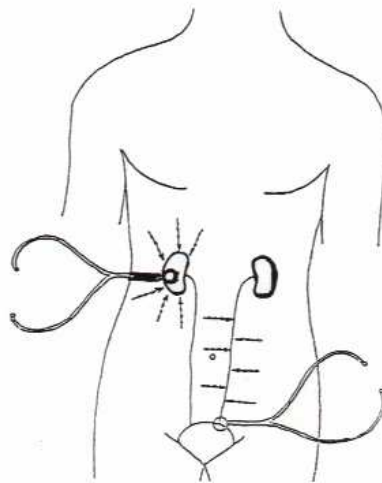
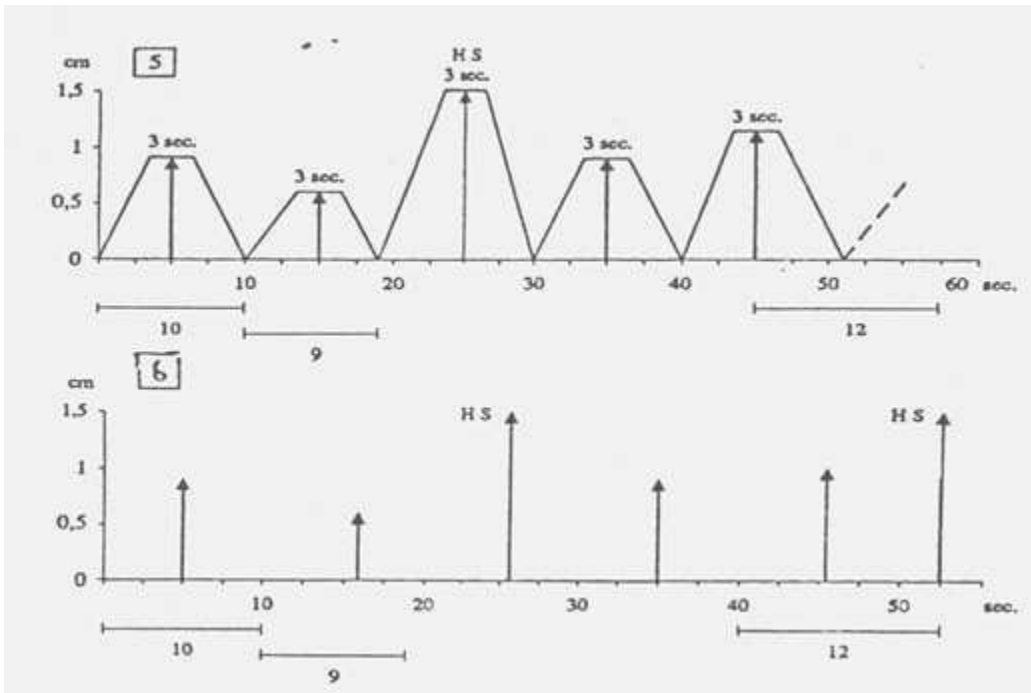


Fig 2

About the reflexes, the Latency time is just 1 seconds, and then we have to evaluate the elasticity of the reflex. There is the physiological dilatation, and microvessels oscillation whose behaviour is typical of chaotic deterministic dynamical systems. There are alternate dilatations with contractions with 6 cycles per minute.

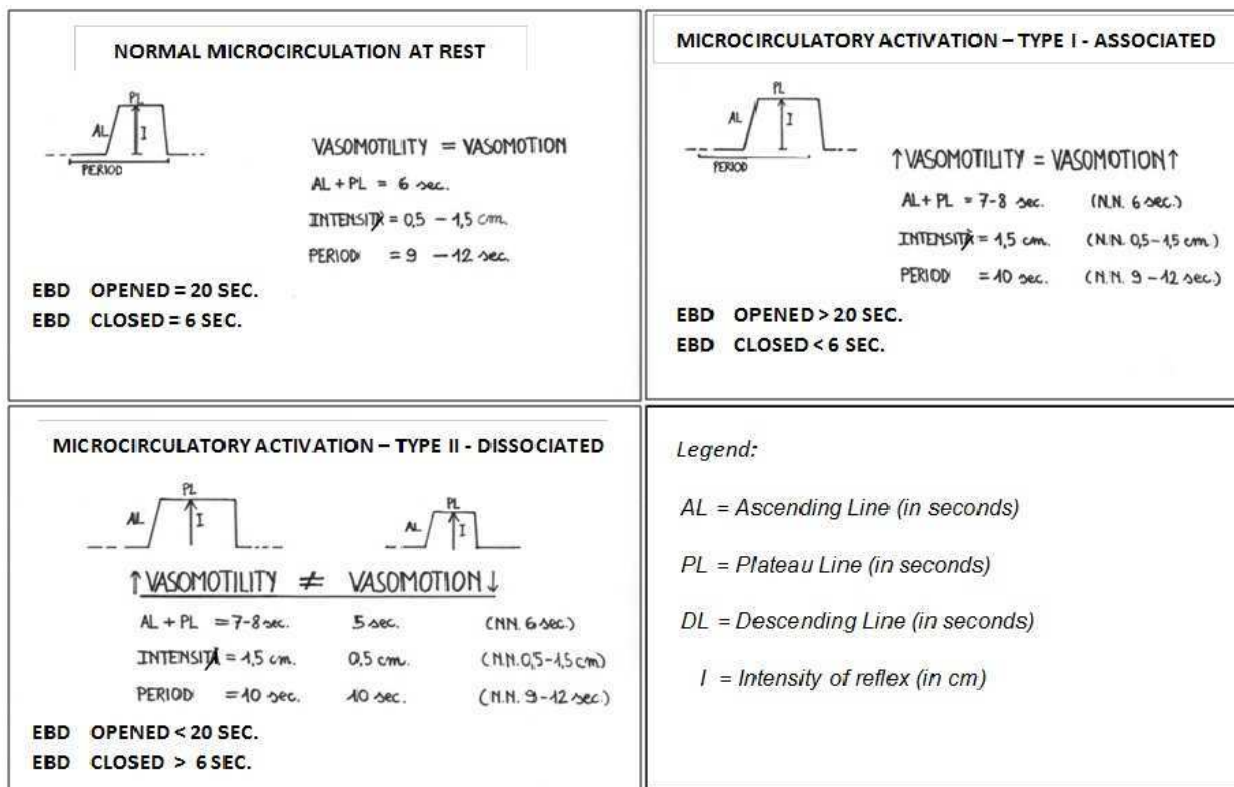
For example, to visualize the TMU (Tissue Microvascular Unit) of the prostate, while you do a lingering pinch to the right (or left) groin for the respective prostate lobe, you can observe the vasomotility (oscillation of upper uretra) and vasomotion (oscillations of lower uretra).



By this way, the doctors continue to do the Auscultatory Percussion of the ureteral segment they are interested in (Upper or Lower uretra) and they observe the dilatation and following contraction.

Pay attention: just after the beginning of the initial stimulation of trigger points, but just in this moment, we observe a latency time of 3 seconds. During these 3 seconds just the upper segment of uretere (small arteries and arterioles) shows a first small dilatation. Later on, a second small dilatation lasts for 3 more seconds, and during this time (3seconds + 3 seconds) the lower segment of uretere (capillaries) does not move. Just after 6 seconds from the beginning of Auscultatory Percussion of Uretere, the oscillations begin.

Microcirculatory Activation "type I or "associated", "physiological", stands for both the vasomotility (AL+PL) and vasomotion (AL+PL) result increased and consequently blood-flow in nutritional capillaries and postcapillary- venules is augmented, due also to right AVA reaction; (e.g. during parenchyma work).



$AL+PL = 6$  seconds stands for normal microcirculation at rest, without percussion of trigger points, so that there is not yet microcirculatory activation, the oscillation of microvessels is physiological (6 seconds) and then there is a contraction less than 1 cm, and than one more cycle ( $AL+PL$ ). There is a fast contraction is physiological situations.

Microcirculatory Activation is related to Microcircular Functional Reserve: if the first one is compromised, the latter one is compromised too.

$AL+PL = 7-8$  seconds stand for M.A. type I, associated, so it is physiological. Both in vasomotility and vasomotion the small arteries and arterioles work more to push the blood to the capillaries and venules, which of course dilate and contraction passively, in fact in the capillaries there are not smooth muscle cells.

In turn, in M.A., type II, dissociated, we can observe a movement to pathology. In fact, the small arteries and arterioles are pulsing less intensively, but the blood flow inside capillaries and venules is augmenting always less, so their oscillations is not anymore like in small arteries and arterioles (dissociated activation). It is taking over slowly the failure even of small arteries and arterioles, and therefore the tissue death.

<sup>i</sup> Metabolic syndrome is a combination of medical disorders that increase the risk of developing cardiovascular disease and diabetes. It is also known as metabolic syndrome X, syndrome X, insulin resistance syndrome, Reaven's syndrome. The pre-metabolic syndrome, as defined by Stagnaro, is the syndrome that precedes the metabolic one, and is linked with congenital real risks and their associated biophysical semiotics constitutions.

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<sup>ii</sup> Biophysical semeiotic constitutions, detectable since birth, are the inherited congenital ground or terrain of well defined potential diseases clinically hidden, which can last several years before appearing, in the slow transformation process from potential (pre-metabolic syndrome, pre-clinical stages) to effective pathology (metabolic syndrome)

<sup>iii</sup> The *synergetics* enables us to study the relation between microscopic level and the macroscopic one, with the principle of “self-organization”. This is possible exclusively if, at microscopic level, complex system can modify in qualitative manner; let’s think about the fluids in Bénard’s cells and the laser. Technically speaking, we define “order parameters” macroscopic observables, which describe the macroscopic behaviour of a system, and “enslavement principle” the behaviour of microscopic elements, according to which it becomes defined when originate “macroscopic observables”.

The laser gives us the best example, that illustrates the general rule: the casual emission of waves, under a defined current supply, becomes coherent; when it is exceeded, however, the emission moves toward a deterministic chaotic behaviour. The synergetics, therefore, studies the characteristics of “complex” systems, without considering the nature of their elements, outlining strict analogies between the macroscopic behaviour of the complex systems in spite of the fact that they are really different.

<sup>iv</sup> In all tissues, a part from their local different architecture, microvessel diameter oscillates rhythmically during time. The term *vasomotility* refers to small arteries and arterioles sphygmnicity, according to Hammersen, and *vasomotion* is the subsequent oscillation of capillaries and post-capillaries venules diameter.

<sup>v</sup> Book in progress. See [http://www.semeioticabiofisica.it/microangiologia/common\\_eng.htm](http://www.semeioticabiofisica.it/microangiologia/common_eng.htm)

<sup>vi</sup> It is called ascending line because the reflex’intensity is growing for few seconds.

<sup>vii</sup> It is called plateau line because reflex’intensity is steady for few seconds.

<sup>viii</sup> Microvessels with diameter of 100  $\mu$  show a motor activity of 2-3 circles/min. and diameter oscillation intensity of 10-20%. As far as vascular diameter lowers, motor activity progressively becomes more intense and rapid; in terminal arterioles, the frequency is 10-20 circles/min. and the width can reach 100% of mean diameter, causing periodically opening and closure of the microvessel.

This rhythmic activity is mainly spontaneous and direct consequence of periodic contraction of smooth muscle cells of arterioles with 20-90  $\mu$  of diameter. Diameter oscillations of small vessels is due to the properties of smooth muscle cells, which have a labile membrane potential and, then, depolarize periodically.

Smooth muscle cells activation by well-known polarization-depolarization processes, which bring about periodic vasoconstrictions, is caused by nervous, hormonal, local biochemical stimuli and also by myogenic stimuli, characteristic of myocytes. These stimuli provoke in smooth muscle cells of small arteries and arterioles, according to Hammersen, the onset of depolarization and consequent ionic fluxes and, then, intracellular storage of  $Ca^{++}$ , partially due to release from cytoplasmic and membraneous storages, which bring about the phosphorylation of myosine, that in turn interact with actine, to start contraction mechanism in presence of phosphorylated nucleotides with high caloric content, produced in mitochondria.

The “vasomotion” varies in relation to temperature fluctuation,  $O_2$  concentration, pH variations, ionic concentration of vascular wall. In fact, it has been demonstrated that  $Ca^{++}$  and  $K^+$  fluxes, due to channels voltage-dependent and, respectively, voltage and calcium dependent, at the base of the periodicity of these transports, brings about the rhythm of arteriolar contractions, ruled also by transmural pressure (Gonzalez-Fernandez J.M., Ermentrout B. On the origin and dynamics of the vasomotion of small arteries. *Mathematical Biosciences*. 119, 127-167, 1994).

<sup>ix</sup> Likely, typical *vasomotion* behaviour of dissociated activation, type II, pathological, represents a *defence* mechanism against increased endocapillary pressure. In other words, one may suggest the hypothesis that the lowered *vasomotion*, secondary to blood increased supply (*increased vasomotility*) to capillary net or *microcirculatory maldistribution*, could be caused by a less elastic, more tonic state, with subsequent functional damage of endothelial as well as myocellular mitochondria of EBD and of local microvascular wall, including local periangium, under these circumstances edematous. As a matter of fact, the described microcirculatory situation ends into interstitial obstruction, first, and subsequently into basal membrane thickening of capillaries themselves. From the above remarks, it does exist a strict relation between “vasomotion” and EBD behaviour, under physiological and pathological conditions, and the abnormalities of EBD is counterbalanced, for months or years, by the increase only of vasomotility, which aims to preserve a physiologic *vasomotion* (dysassociation); this fact explains the importance of such structures as regards the regulation of microcirculatory blood-flow, corroborated *clinically* for the first time.

<sup>x</sup> The parenchyma is a characteristic substance of the bodies such as the liver and the lung parenchyma.

<sup>xi</sup> See Microangiologia in <http://www.semeioticabiofisica.it>