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Lectio Magistralis,

Two Clinical Evidences Corroborating Microcirculatory Quantum-Biophysical-Semeiotic Theory of Atherosclerosis.

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Introduction.

In the medical field, wide and fascinating, of Biophysical Semeiotics, far away from having reached the borders of its domain, *Clinical Microangiology* plays a primary role, from both theoretical and practical view-point, due to its excellent results, collected at the bed-side in original and refined manners, allowing me to formulate the Microcirculatory Theory of Atherosclerosis (1-3).

After 55 years of biophysical semeiotic research and practical performance of this method, I have demonstrated that Biophysical Semeiotics is a scientific theory, characterised by multiple values of efficaciousness and beauty, so that it must be considered a scientific progress.

Until now, the Microangiology is overlooked by almost all physicians, as my friend Prof. Claudio Allegra states rightly "Microcirculatory this unknown".

However, by Quantum Biophysical Semeiotics, it will surely become cultural heritage of every open-minded doctor, who will be able to collect at the bed-side numerous, original and reliable data, obtaining excellent results on diagnosis, differential diagnosis, clinical research and ultimately therapeutic monitoring (4).

Clinical Microangiology represents the clinical study of deterministic chaos of *vasomotility*, i.e., sphygmicity of small arteries and arterioles, according to Hammersen, and, then, of *vasomotion*, sphygmicity of capillaries and post-capillaries venules, in all biological systems.

This new discipline of Medicine, unavoidable to understand ATS onset, according to our Microcirculatory Theory of Arteriosclerosis, we have recently up-dated (55-57), is based exclusively on clinical evaluation, i.e., using a stethoscope and assessing ureteral reflexes, of autonomous and autoctonus movements of all structures of tissue-microvascular-units, among them Arterio-Venous Anastomoses (AVA), including Endoarteriolar Blocking Devices, that are AVA from the functional view-point, of every organ, gland, and tissue (5, 6).

Importantly, in the interest of General Practitioners we are going to describe also an easy method, based on evaluating the gastric aspecific reflex, whose parameters parallel those of more refined, but more difficult, microcirculatory evaluation.

Under basal physiological conditions, tissue-microvascular-unit fluctuations show an high degree of deterministic chaos, i.e. highest *fractal dimension* or *dimensionality* (fD), which is its measure.

The calculation of this parameter, essential in *Clinical Microangiology*, by easy and practical way, can be performed with the aid of evaluation of disappearing time of gastric aspecific reflex: by elegant and refined way doctor quantifies in sec. "differential latency time" of gastric aspecific reflex, which parallels its disappearance, as will be described in details later on.

When a biological system, due to whatever disease, different in origin, evolves slowly towards pathological condition, both functional and structural, since function and structure must be considered as the poles of the same equation, according to Leuckart, characteristic modifications of deterministic chaos happen in both local *vasomotility* and *vasomotion* and, at macroscopic level, in volume fluctuations of organ, gland, and tissue, where disorder is localized, allowing to draw, even mentally, related diagrams, illustrated in the site pages, dedicated to Quantum Biophysical Semeiotics, and, therefore, yet known to reader.

In fact, these physiological oscillations (trajectories) appear modified at microscopic as well as macroscopic level, causing progressive lowering of the *fractal dimension* or *dimensionality*, that

from the physiological value, i.e., 3,81, lowers to about 2,57, as in the case of pancreas during Metabolic syndrome, classic or "variant", we described previously as Reaven's Syndrome, slowly evolving to diabetes mellitus (7, 8).
Interestingly, dividing *physiological dimensionality and fractal dimension* of Reaven's syndrome slowly evolving to DM, or other disease, of course, the result oscillates around a 6,18, ϕ, or *golden mean*. In our opinion, such magic numbers, really numerous in clinical microangiological evaluation, underline clearly the scientific value of the chaos in Medicine.
In fact, according to many authors, biological, physiological and pathological structure shows its chaotic nature (7). The study of single patient, according to the Single Patient Based Medicine (11-13) has to be performed not by principles valid for the group of individuals, population in general, according to the standards of Evidence Based Medicine (EBM), but to the SPBM, based on the deterministic Chaos (10).
It is nowadays clear that the best knowledge of an individual, under physiological and pathological situations, is acquired by a method based on the sensitivity to initial conditions, on interaction, complexity, standards totally ignored by EBM, as we suggested in a lot of previous articles (15-20).
Data of my researches, performed over the past decades by Biophysical Semeiotics, in a way as easy as possible, aiming to a practical utilization at the bed-side, hopefully demonstrating that phenomena observed in a single individual very often are not identical to those evaluated in the "group" of comparable subjects, on the base of an evidence, which allows to forecast in probabilistic and statistic manner exclusively by great numbers.
Finally, to demonstrate above referred data, it is necessary to say that in the course of chronic disease, *dimensionality* of local tissue-microvascular-units fluctuations and, then, the fractal dimension of macroscopic oscillations of related biological systems, are equal to 1, i.e. topological dimension.
From the above remarks, it results clearly the usefulness and originality of *Clinical Microangiology* in bed-side diagnosis, prevention, research and therapeutic monitoring.
Functional activity, both physiological and pathological, of a biological system is strictly related to its microcirculatory blood-flow pattern. Therefore, it is possible to assess function and structure of the former by evaluating function and structure of the later, according to Angiobiopathy Theroy (21-24). Such study represents the aim of *Clinical Microangiology*, originated with the aid of Quantum Quantum Biophysical Semeiotics, which is its method or operative tool.

The biological significance of microcirculatory deterministic chaos.

Chaos, a mathematical concept, has been described as "deterministic randomness", meaning that a chaotic system is deterministic, but so complicated that looks random. Chaos theory tells us that it is impossible to predict the long term behaviour of very complex systems, because all the conditions are not known with precision at any time and uncertainty increases with time (25) .
It is well known that electrocardiograms, for example, of healthy hearts, constantly vary, however slightly, in an unpredictable way. But in dying patient the intervals between beats (R-R) become practically identical and electrical signals predictably cyclic (26) .
We described in previous papers, for the first time clinically, spleen- (26), liver., kidney- and pancreas- (27, 29) chaotic oscillations, partly due to Autonomic Nervous System activity.
More precisely speaking, organ and tissue oscillations are related to their local microvessels chaotic activity, i.e. the complexity of the dynamism of the firsts corresponds exactly to that of the second. In addition, the physiologically functioning organ presents complex, chaotic oscillations, constrained to a "strange attractor" in the phase space (See later on).
On the contrary, in a diseased organ there are cyclic, periodic, regular, identical, predictable and low oscillations without *highest spikes* (HS).

In conclusion, the tissue microcirculatory unit and consequently the related organ, as biological dynamic system, lose complexity, it lose its adaptative capacity and ability to respond (29, 30).

Interestingly, biophysical-semeiotic evaluation of the complexity degree is very important as regards prevention, diagnosis and therapeutic monitoring.

As mentioned above, the chaotic volume fluctuations of kidney, pancreas, liver, spleen, aorta, heart (obviously, regardless systo-diastolic movements), a.s.o. are due to their congestion and decongestion (6 cycles per minute) as clinical and experimental evidence suggests.

In facts, organs chaotic oscillations are strictly analogous and synchronous with related microvessels fluctuations, presenting really identical behaviour .

Consequently, we are allowed to state that chaotic behaviour of local nutritional capillaries and venules brings about volume random changing of the related organs, mentioned above. Therefore, it is easy and reliable to assess in a precise manner oscillations of about all organs and tissues by means of the evaluation of corresponding microvessels fluctuations.

In other words, besides kidney, pancreas, heart, spleen, liver, a.s.o., chaotic oscillations assessment, it is practical, useful and reliable to evaluate the "oscillations" of important tissues, organs and glands, such as bone-marrow, prostate, lungs, gall-bladder, breast, urinary-bladder, stomach-duodenum, a.s.o. (31), evaluating *vasomotility* and *vasomotion* of related microcirculatory bed.

As regards bone marrow and breast, for example, digital pressure upon the middle line of breast-bone (and/or hyliac crests) and mammary gland, respectively, in healthy, brings about choledocic "arteriolar", "venular" reflexes as well as ureteral reflex (= nutritional capillaries), which fluctuate in a chaotic manner, as mentioned above.

Interestingly, AP values of marrow- and mamma-oxygenation and Co QlO levels (28) are in perfect relation with chaotic choledocic and ureteral fluctuations.

At this point, it appears relevant to outline that during acute disorder, flogistic in nature, local periodic microvascular oscillations (choledocic and/or low ureteral reflexes) show the most intense degree, almost equal to that of the *highest spikes* (HS), demonstrating clearly the real biological nature of oscillating complexity, namely the adaptative capacity and ability to respond.

In fact, during phlogistic process, the interstitial oedema increases both vasomotility and vasomotion. (33-36). In other words, chaos theory has stimulated some important technical developments in the way we can analyze and interpret medical and other time series data. (37)

As regards the above-mentioned "strange attractors" of chaotic dynamic systems, a key concept is "fractal dimension", very different from the topological one, as demonstrates the generation of Koch's curve (37, 38), which, as the name implies, was developed for fractals, but the practical applications of which has emerged as a byproduct of attempts to prove that certain systems have strange, chaotic, fractal at-tractors, by analyzing time evolution data. (39).

When brain wave data, e.g., in rats are "re-constructed", the attractor for a healthy rat is computed to have a "dimension" of about 5,9 while that for the same rat in epileptic seizure has a dimension of only 2,5. (40). The suggestion is that the "dimension" correlates with the flexibility and adaptability of the organisms: the larger number implies a chaotic system with well developed flexible response to different stimuli, whereas the low value associated with the seizure can be regarded as evidence of suppression or malfunction of a number of key elements of the rat's physiology.

A somewhat similar argument can be applied to quantum-biophysical-semeiotic data, as regards, e.g., pancreatic oscillations in case of classical or "variant" Reaven's syndrome in diabetic evolution (41) as well as in diabetes mellitus (42). It must also be remembered that fractal dimension (fD) and system complexity are directly correlated.

Quantum-Biophysical-Semeiotic morphological Analysis of Vasomotility and Vasomotion under both physiological and pathological Conditions.

From the practical point of view, it is sufficient and reliable to evaluate periods, as well as intensity of upper and low ureteral reflex oscillation (= vasomotility and respectively vasomotion), as described above, for example during “small” digital pressure, applied – for instance - upon the middle third of biceps muscle, compressing it between thumb and other fingers, of a supine individual, psychophysically relaxed with open eyes (to reduce melatonin secretion). The muscle pressure allows doctor to examine resistance microvessels dynamics and flow-motion of nutritional capillaries.
Interestingly. “small” pressure allows to recognize the microvessel dynamics at rest; “mean” pressure stimulates microvessels, which are working as under stimulation tests; “mean-intense” pressure abolishes microvessel fluctuation: it is particularly useful in investigating arterial wall properties; “intense” pressure allows to assess artery compliance.
Finally, “most intense” pressure has to be utilize, e.g., in evaluating type I, group 2 AVA, according to Bucciante.
Importantly, the mentioned adjective, are really quantitative, rather than qualitative, because they are directly related to the dyne/surface unit, necessary to stimulate single structures of microcirculatory bed. From such a remark, all adjectives aren’t qualitative at all!
However, the original morphological analysis of vasomotility and vasomotion, i.e the precise evaluation of upper and low ureteral reflex oscillations, reveals at the beside the actual condition of related tissue-micro vascular-units, according to a synergetic model.

Interestingly, physicians not skilled in Quantum Biophysical Semeiotics have to know that reliable data can be easily gathered with a stethoscope by assessing the parameter values of gastric aspecific Reflex (Fig. 2, 3).

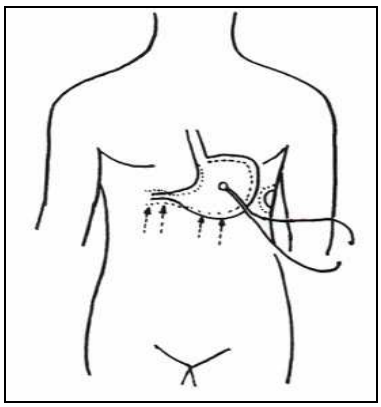
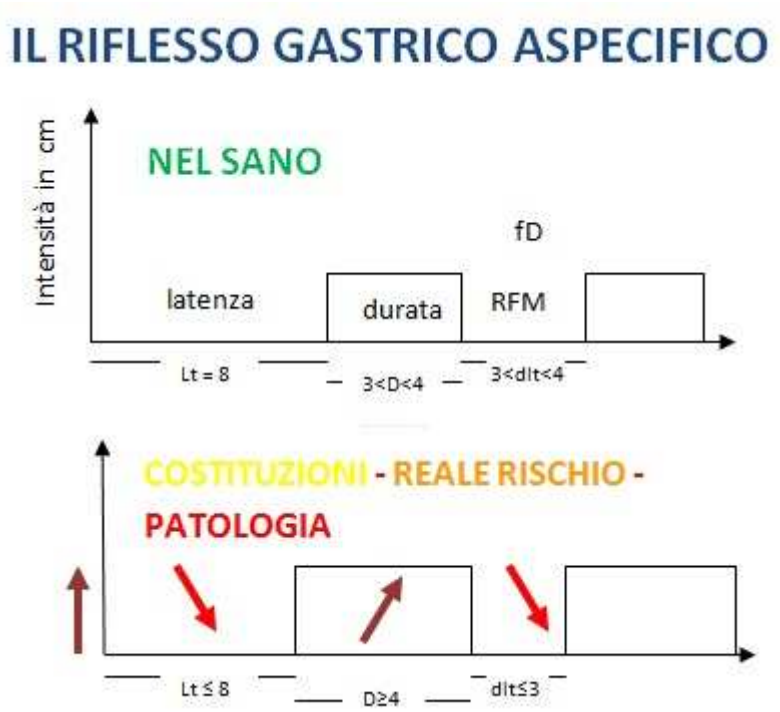


Fig. 2
Figure shows the gastric aspecific Reflex. Physician has to assess Latency Time, Intensity, Duration, and the Duration of Disappearance before the following reflex.



a) Latency Time (in sec.): tissue oxygenation, tissue pH
b) Intensity (in cm.): seriousness of underlying disorder
c) Reflex Duration (in sec.): Microc. Function. Reserve
d) Disappearing Time (in sec.): important parameter value, which parallels fractal Dimension of upper and lower Ureteral Reflex Oscillations, i.e., vasomotility and vasomotion

In order to realize microvessel oscillation analysis it is unavoidable to transfer upon cartesian coordinates intensity (ordinate, cm) and duration (abscisse, sec.) of three successive fluctuations of low ureteral reflex, observed for example in the above-mentioned situation, during biceps muscle microvascular units stimulation. In healthy subject we observe a characteristic diagram (Fig. 1).

Interestingly, in 2 sec (ascending line: AL) it is reached the highest intensity (NN = 0,5-1,5 cm); the "plateau" line (PL) lasts physiologically 3 sec, then in 1 sec (descending line: DL) the line returns to basal value (i.e. abscisse), where persists for > 3 sec. < 4 sec. (= fractal Dimension), varying the periods from 9 to 12 seconds under physiological condition. The fluctuations show the typical chaotic-determinist pattern.

On the contrary, in pathological situations, e.g. essential hypertension, the diagram results interestingly modified (Fig. 3): AL as well as DL are normal, 3 sec. and 1 sec respectively; intensity is approximately 0,5 cm, in a "predictable" manner; the physiological highest waves, i.e. highest spikes of 1.5 cm intensity (HS), are absent. All oscillation are identical.

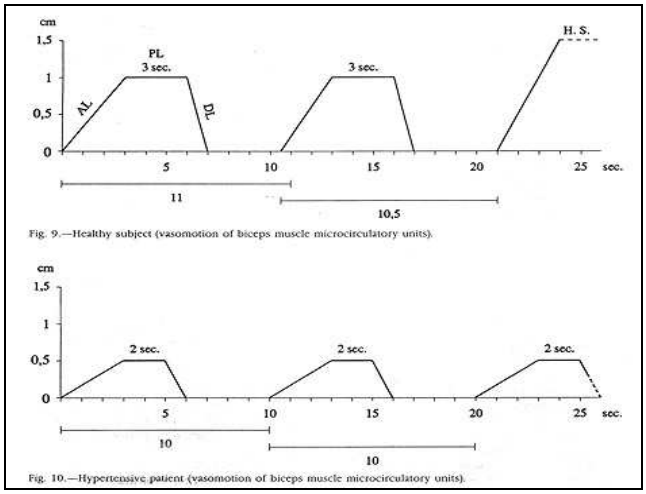


Fig. 3

Figure shows microvessel fluctuations in healthy individual and in hypertensive patient.

Finally, in hyperfunctioning tissue, e.g. the bone-marrow during infective disorders of whatever nature, small-mean digital pressure upon the middle line of breast bone, brings about low ureteral reflex oscillations, characterized by PL of 5 or more sec, intensity as well as periods practically identical each other (Fig. 4). Intensity and PL of every oscillation are directly correlated: more high the intensity, more prolonged appears PL and consequently more efficacious is the flow-motion of related nutritional capillaries.

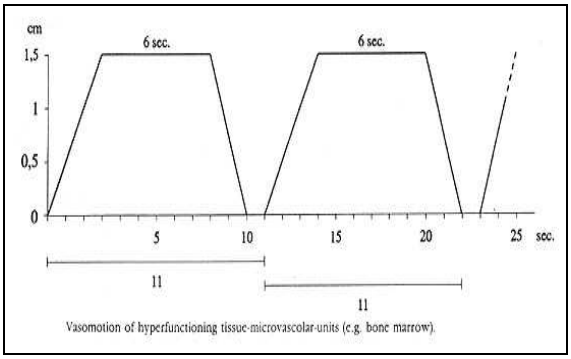


Fig. 4

This clinical evidence underlines the inner consistence of Quantum Biophysical Semeiotics.

In addition, superimposing the parameters of three subsequent oscillations of low ureteral reflex, in accordance with the length of single period, we realize really interesting figures. In healthy people the obtained area shows a "strange" shape, like a "strange" attractor (Fig. 5: fractal dimension (fD) >3,[1-4] that corresponds to the space occupied by a fractal structure.

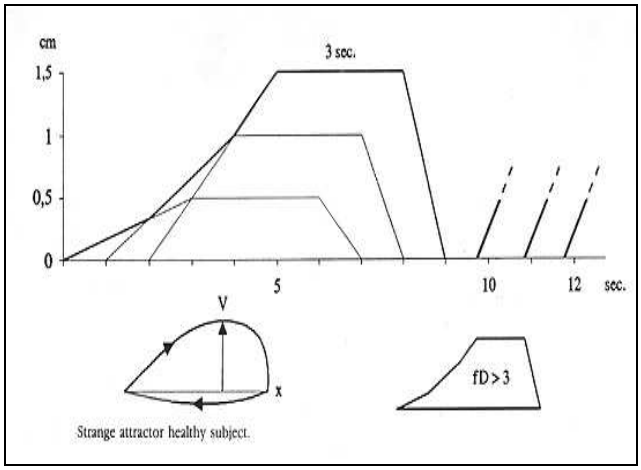


Fig. 5

Strange attractor: healthy subject.

On the contrary, under pathological condition, e.g. essential hypertension as far as biceps muscle microcirculatory bed is concerned, the area obtained in this manner appears quite small, resembling an attractor at fixed point (Fig. 6).

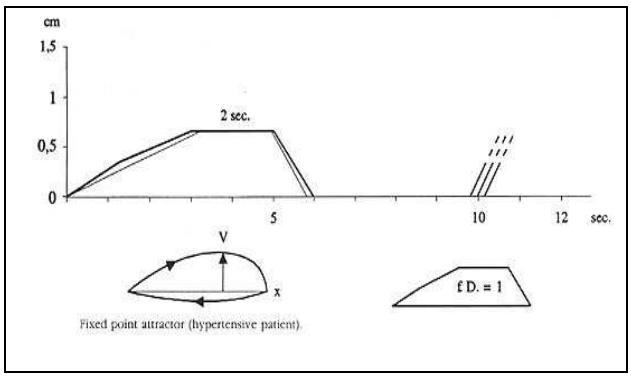


Fig. 6

Fixed point attractor: hypertensive patient

Finally, the area corresponding to hyperfunctioning microcirculatory units results the largest one, due exclusively to its large Euclidean perimeter; its shape, however, resembles clearly a deformed circle, corresponding to a “closed loop” attractor (Fig. 7).

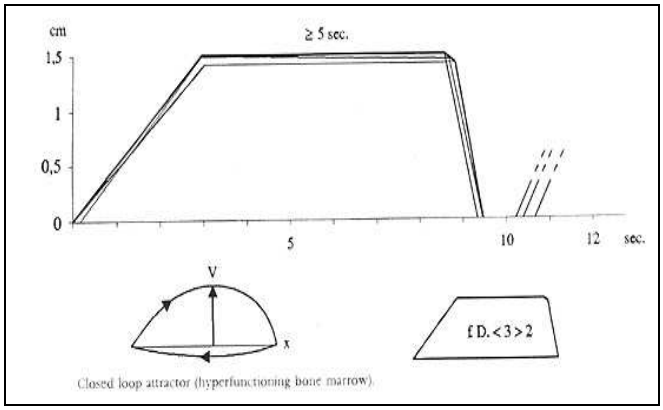


Fig. 7

Closed loop attractor in hyperfunctioning bone-marrow.

From the above remarks, it results that morphological accurate analysis of vasomotion, by means of **Quantum Biophysical Semeiotics**, in physiological as well as in pathological conditions, represents an original, reliable and useful tool in both daily practice and research, as allows us to state a long, well established experience.

Allegra's Syndrome: type II and III, Pathological, Dissociated Microcirculatory Activation.

In health, at rest, both vasomotility and vasomotion parameter values are identical, so that the blood-flow along the diverse AVA types is not abundant: middle third ureter oscillates slightly, showing an intensity about 0,5 cm.; tissue oxygenation is normal, thus pH is about 7,4.
Really, physicians observe more easily these data with the aid of gastric aspecific Reflex parameter values, showing a latency time during "small intense" digital pressure applied upon, for instance, the phemoral artery at groin level: 8 sec. (NN = 8 sec.), reflex duration > 3 sec. < 4 sec., i.e., normal value, since Microcirculatory Functional Reserve is physiological, and finally reflex disappearing time before the following oscillation is > 3 sec. < 4 sec.: fractal Dimension = 3,81.
During microcirculatory activation, e.g., under stress tests, physician can gather really interesting data about the type of such a activation, illustrated in Tab.1

MICROCIRCULATORY ACTIVATION.

Type I , "associated", physiological, e.g., in working parenchyma: both vasomotility and vasomotion are activated in the same manner, showing identical parameter values. AVA are slightingly open. Tissue pH about 7,4.

Type II, "dissociated", intermediate, e.g., in localised diseased organ in initial stage: at rest, vasomotility is more or less activated, but vasomotion shows normal fluctuation, as at rest, indicating the beginning of every disorder. AVA appear more open than under physiological condition: > 0,5 cm. to 1 cm. Tissue pH is still about 7,4 especially at rest.

Type III, "dissociated", pathological, wherein *vasomotility* is intensively activated, while *vasomotion* shows a decreasing activity, i.e., below the normal one. As a consequence, AVA are pathologically open and hyper-functioning :more than 1 cm.: AVA hyperstomie. Tissue Acidosis.

Tab. 1

At this point, it is easy to understand the real nature and diagnostic significance of Allegra's Syndrome. For instance, in the virus hepatitis, even initial, firstly is present type 2, intermediate, dissociated, and secondly type III, pathologically dissociated, microcirculatory activation.
In case of Inherited Real Risk, e.g., of type 2 Diabetes Mellitus, small stimulation of VI thoracic dermatomere (= the skin immediately below the costal arch, along middle clavicular line) shows type II, dissociated, intermediate microcirculatory activation, but in overt DM, even in the II-III Quantum-Biophysical Semeiotic Stages (45- 51), we observe worsening type III dissociated microcirculatory activation.
Analogously, in case of Inherited Real Risk of prostatic cancer, in initial stage, physician observes type II dissociated microcirculatory activation in the precise site of cancer can occur, demonstrating the diagnostic importance of microcirculatory changes (53).
Allegra's Syndrome proved to be particularly useful in studying and structuring Quantum-Biophysical Semeiotic Microcirculatory Theory of Arteriosclerosis (1-4).

According to Microcirculatory QBS Theory of Atherosclerosis, based on experimental evidences, and illustrated in previous papers (1-4), 120 subjects with IRR of CVD allowed me to define the pathogenesis of atherosclerosis in the first decade of life, in subjects with atherosclerotic constitution and IRR of CVD, due to the clinical investigation of the arterial wall in vivo, when the composition of the blood is generally still normal: Antognetti's Sign negative (1-4).

In these subjects, from the birth till the end of first year of life (table 2), we can diagnose vasa vasorum with IRR of CVD, a slight dissociated microcirculatory activation type II, worsening during efforts and Allegra's Syndrome, while pH shows at rest normal physiological values (first pre-clinical stage of ATS). Later one, till the fifth year of life, the type II dissociated microcirculatory activation worsens, even at rest, pH decreases, while poly-diamines, Fibroblast Stimulating Factor and hyaluronic acid fragments significantly increase.
As a consequence, VV proliferate abundantly in the HP zone since birth, so that physicians observe intense in toto ureteral, Choledochus anf aspecific gastric Reflexes, indicating VV higher density, according to Hildebrandt et al. (54). In addition, some other cells, beside endothelial cells, e.g., smooth muscle cells, whose proliferation and migration stimulation bring about artery intimal thickening (second pre-clinical stage of ATS).
From the age of five years till the age of ten ones, in the above mentioned subjects, there is type III dissociated microcirculatory activation, the pH continues to decrease, and thus damages worsen in local endothels and tissue. All these facts, due to venous hypertension in capillary and venules, subsequent to VV microcirculatory remodeling (See later on), bring about cellular infiltrations, initial plaque formation and subsequent artery lumen narrowing, but exclusively where intense CAEMH is present (third pre-clinical stage of ATS).

Stage I, at Birth → 1st Year.	Vasa vasorum with Inherited Real Risk of CVD. Type II, "slight", dissociated Microcirculatory Activation, worsening during efforts, Allegra's Syndrome: at Rest: pH NN.
Stage II, after 1st Year → 5th Year	Type II "intense", dissociated Microcirculatory Activation, even at Rest → pH ↓ → Poly-diamines and Jaluronic Acid Fragments↑ → Cell Proliferation-Migration Stimulation → Artery Intimal Thikening.
Stage III, after 5th Year → 10th Year	Type III dissociated Microcirculatory Activation → pH ↓ → local Endothel and Tissue Damage → cellular Infiltration and initial Plaque Formation → subsequent artery Lumen Narrowing

Tab. 2

The three stages of atherosclerosis in the first decade of life (explanation in the text).

Two Experimental Evidences corroborating the Key Role of Vasa Vasorum heritable Impairment in Atherosclerosis Patho-Physioloy, according to Microcirculatory QBS Theory of Atheroscleoris

As previously referred (1-4), the Microcirculatory QBS Theory of Atherosclerosis is based on three fundamental bases: intense, localised CAEM in both Vasa Vasorum cells and parietal vessel cells, Mitochondrial Eteroplasmy, and arterial Wall Acidity, well limited at birth, where CVD Inherited Real Risk is present.
As regards the heritable flow-motion alteration, i.e., shear stress lowering, and blood-flow turbulence, and particularly tmvu. venous blood pressure increasing, brought about by "anastomoses lasting hyperstomy", caused by newborn-pathological type I, subtype b),

Endoarteriolar Blocking Devices, microvessel remodelling is based on (48), the following two experimental evidences, easy to perform, corroborate our theory (1-4).

The Venous Stasis of Tissue Microvascular Unit (TMVU) brings about histangic damage.

Mean-intense digital pressure applied on common femoral vein at groin region, after about 2 seconds, causes microvessel fluctuation cessation – vasomotility in systole, whereas vasomotion in diatole. After another 1 sec., the physician observes increased vasomotility, statistically significant, as a result of Veno-Vasomotor Reflex activation.

Due to such a increased vasomotility, Venous Stasis worsens, because the subsequent increased flow-motion provides only a minimal amount of blood to nutritional capillaries, while - as a result of the obstacle opposed by newborn-pathological EBD - the most abundant blood flows through the AVA, showing pathological persisting hyperstomy phenomenon, thus raising the jet present stasis in capillary-venular microvessels, as it demonstrates the further increase of lower ureteral reflex diameter.

At this moment, the duration of the finger pulp-gastric aspecific reflex appears lasting more than normally, i.e., 4 – 5 - 6 sec., paralleling the Microcirculatory Functional Reserve impairment. The Latency Time is normal (NN = 8 sec.) till the reflex duration reaches the value of 6 sec. After this value, the Latency Time shows an initial reduction, due to increased, critical, histangic acidosis.
As a result of these events, tissue acidosis occurs and quickly worsens, reviled by the pathological data of glycocalyx evaluation, as well as the widening of the interstitial space due to imbalance of GAG (especially, Jaluronic Acid) bound/free water, as it demonstrates ureteral and choledocus dilation.

This experimental evidence shows, from the clinical view-point, that venous stasis in TMVU causes the acidosic suffering of local tissue, bringing about alteration of the structure and function of the cell membrane, glycocalyx, inyerstitial amorphous fundamental substance, emphasizing the n-DNA and mit-DNA damage.

A) To demonstrate the important role played by venous hypertension in both post-capillary venous and capillaries, physician has to use the mean-intense digital pressure, applied upon common phemoral vein at groin of individual lowing down in supine position, associated to small pressure on foot finger pulp, aiming to cause vasomotily and vasomotion of local tissue microcirculatory units, according to a synergistic model.
Soon there after, the lower ureteral segment diameter increases significantly, paralleling dilation of related venous post-capillaries, as well as capillaries of foot pulp finger. Immediately, due to venous-arteriolar reflex, i.e., venous-vasomotor reflex, vasomotility increases in a significant manner, aiming to remove waste material, and especially H+.
Interestingly, at this point, the foot pulp-aspecific gastric reflex shows a reduced latency time due to intense local acidosis, emphasizing the inner and outer coherence of QBS theory..
To summarise, this experimental evidence demonstrates, from the clinical view-point, that the venous stasis at capillary-venules tract, and subsequent hypertension on capillary endothels in biological systems, cause locally metabolic damage due to the acidity.

The Vasa Vasorum Impairment causes Acidosis of arterial Wall.

Digital pressure of mean intensity upon the common femoral artery is followed by the arrest of local VV fluctuations, present when the stimulation is small. This event is associated with the lengthening of arteria-gastric aspecific reflex, and soon thereafter with the decrease of the latency time of this reflex, paralleling the acidosis of vessel-wall related segment.
The QBS assessment of Compliance of this artery tract, appears to be significantly impaired both at rest and particularly during Adiponectin, Insulin, and Atropine tests.

To summarize, the small, localised impairment of Vasa Vasorum, due to VV. heritable remodeling, brings about acidosis of the three artery layers of local segment, i.e., Intima, Media and Adventitia, as demonstrate diverse stress tests with substances (Insulin, Atropine, and Adiponectin) that act respectively on endothelium, arterial smooth muscle cells and both.

B) According to Microcirculatory Theory (1-4), Vasa Vasorum, when involved by microcirculatory remodelling, bring about nutritional damage not only to adventitia and media, because of reducing blood supply, but also to intima, due to impaired removing waste material, as I have demonstrated in earlier experiment.
Small-intense digital pressure, applied upon common femoral artery at groin, lasting for 15-30 seconds, causes the disappearance of VV vasomotility and vasomotion.
As a consequence, in this precise zone, on the one hand, adventitia and media are not provided by blood, while intima is suffering because of its waste material is not removed completely.
At this point, physician observes a significant lowering of femoral artery-aspecific gastric reflex (NN = 8 sec.), as well as compliance intensity, reduced to a halve of normal values.

In conclusion, the impairment of Vasa Vasorum, due to their inherited remodelling, bring about the suffering of artery wall tree layers, although by different action mechanism.

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