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FROM THE FILES

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NUMERATION OF BIOMARKERS: REGARDING FOR FORMATION OF SOME INDEXES

A discussion by Christian Duraffourd on 16 April, 1999

Introduction

Biomarkers testify at every moment to the metabolic activities which relate to life itself, to its basic functioning, to the vigilance and constant efforts of the organism to face each event, to respond to each request. The fluctuations of the constants which manifest the adapted reactions of our organism to each of these solicitations take place within two types of references.

BASAL AND ADAPTATION STATES

The first marks out the basal metabolic state, a common expression of the structural functioning specific to each person. Its evaluation requires either specific conditions for collecting the humoral environments (schedule, rest, meals, etc.) or a permanent adjustment of the ranges separating the lower limits from the upper limits. Intended to establish, in an artificial way, the border between two states: that of good health and that of disease, the normal values indicate only the visible result of the global metabolic activity.

The second determines ***the zones of tolerance outside the basal state*** (emphasis by author) and in the face of stimulations of all kinds likely to lead to recognized modifications in the levels of circulating metabolites. Schedule, rest, meals, orthostatism, decubitus, stimuli of all kinds, listed, recognized, diagnostically exploited are all factors authorizing a new adjustment of the ranges of values. The following are also sources of accepted or tolerated differences: age, sex, period of the menstrual cycle, sports activity, certain pathologies, and certain

treatments. Paradoxically, and although they clearly testify to variable modalities in physiological activity from one individual to another, these variances have never been studied in an attempt to understand, explain and exploit their effects. Fundamental differences. Yet it is in the particular way of each individual to maintain, against all odds, this biophysiological constancy in which resides the crux of pathogenicity of each organic structure, of each terrain.

By pathogenicity, we must clearly understand the notion of a source of disease and therefore the responsibility for our difficulties in functioning and in permanently maintaining this level of balance. This implies that all the biochemical parameters, measurable in the serum, remain within the so-called normal range, which have been methodically defined. These parameters bear witness to the effect resulting from the multiplication of the organism's reactogenic resources in the face of its own chromosomal weaknesses. Understanding the permanent solicitation of disorders of which each individual is the object constitutes without any doubt the surest means of access to a true etiology and consequently to a real prevention.

Highlighting the permanent consequences of endogenous deviations from the functional exploitation of our genetic heritage constitutes the means of screening for pathogenic risks, their imminence and their chronology. It constitutes one of the most reliable means of controlling evolution, be it spontaneous or under applied therapies.

The successive evaluation of the thresholds of progression in the distortion of the factors involved makes it possible to establish the zones of particular fragility, of potential breaking points under the effect of supernumerary aggression. It makes it possible to predict the location of this rupture in the face of a non-specific, massively supra liminal aggressive event. It also makes it possible to recognize the location of preferential target organs, places of weakness where the threshold of fragility is particularly low and can at any time break the precarious balance that characterizes it under the action of a specific aggressor.

These notions of threshold and potential are fundamental to understanding any notion of functionality.

BIOMARKERS AND NORMAL RANGES

…Like medicine, (the science of) biomarkers is entirely oriented towards pathology. Routing disease in its beginnings or at its initial origin is certainly laudable, and nevertheless an obligatory objective. Can we still nowadays be satisfied with this binary limitation of the consideration of the meaning of biomarkers as indicating health or disease? The cost of disease is too high for us not to focus on early detection by focusing on identifying the biological regulatory modifications that inexorably lead to disorders. The clinical encounter can be a valuable means if the physician is attentive to all the details of the expression and evolution of each person's behavior. It requires time, attention, deepening and synthesis of all the conscious and unconscious signs that can be detected after a complete consultation. In the eyes of the majority (of physicians), it retains a subjective and intuitive character which limits its probative value. (In contrast), The numerical, quantified expression of simple measurements has an *a priori* objectivity to facilitate the transmission of methods and techniques of field study and its corollary, which is functionality.

Two important notions are at the origin of the current use of biomarkers to determine the terrain, evaluate its functional movements, understand, manage and correct its activity. The first, already mentioned, is the permanent or eventual fluctuation of any measurable biological parameter. The second is, in the same individual, the constancy of the level of the structural parameters within the reference ranges and outside of all pathological reasons.

THE EXAMPLE OF LEUKOCYTES

In pathology, its variation indicates:

1. a more or less important mobilization to face, in a process of combat, a "foreign" cell population that the body must annihilate and eliminate (microbial agent, most often cellular debris), *or*
2. a phenomenon of congestion calling for an immediate concentration of leukocytes and associating a release into the circulating blood of cells enclosed in the reservoir zones (e.g., peri-hepatic) and a reduction in the circulating blood volume (hemoconcentration) in ischemic phenomena, for example, *or*
3. an anomaly of bone marrow production, in excess (leukocytosis), in deficiency (aplasia)

In physiology, its variation meets in multiple circumstances escaping any randomness:

1. particular to the phase of life:
    a. **an initial rapid evolution** during the first days, months and years of life, during major events of hormonal transformation,
    b. **unique events** (puberty, genital pauses and their general repetitions)
    c. **repeated events** (menstrual cycles, cycles seasonal, cell cycles, tissue cycles),
    d. **single or repeated events** (pregnancy, amenorrhea, polymenorrhea)
2. **evolution of daily cycles and their chronology** (hormonal, neurovegetative, social, food)
3. **relational events of daily life** or in all its daily, weekly, monthly and annual automated rhythms and rites (acute or chronic manifest stress, single or repetitive), according to the alternations of rest and effort, according to their opportunity or habit characters.

The activation or deactivation of leukocytes, their mobilization and production to face various situations come under the same principle of functional adaptation of the subthreshold of minimal leukocyte activity. This threshold, defined by standard normal ranges, is surpassed during an increase in mobilization of leukocytes by a pathological situation which requires (a greater number of leukocytes). This context, outside the norm, is however only a visible manifestation of normality. It testifies to the physiological reaction to fight against a disease which involves the leukocytes and not to a physio-pathological reaction to a disease against which they are fighting.

The extension and misuse of this context of non-standard normality leads to abnormality, a pathogenic state, and ultimately to disease.

The maintenance of leukocyte recruitment, in a given situation, becomes a manifestation of a leukocyte pathology. It arises from phenomena of adaptation of the medullary system (of bone), according to modalities of intensity and duration that are inappropriate (pathological adaptability).

Linked to changes in the internal balance, the physiological variations of leukocytes are therefore subject to conditions. Their circulating rate is governed by a set of factors of which it testifies to the resulting effect. These factors are quite naturally (that is to say, as for any circulating element, whether metabolite or figurative) of three orders: production, concentration and consumption…

Some examples of the use of physiological variations in leukocytes:

- their **absolute value** testifies to their mobilization according to the needs of the body. It represents at all times
    - the result of the level of bone marrow production
    - the only representative of the hormone responsible for it

- the mobilization of reserve elements in the immediate and mediate adaptability phase, representative of the general adaptation factors.

Apart from its diagnostic interest, it only has a relative orientation value on the basic functional level judged on the intensity of the response with regard to the seriousness of the responsible condition. It also gives a first argument on the cause state or on the consequence state.

On the other hand, their **relative value** compared to another biomarker which corresponds to the same methods of adaptation and mobilization makes it possible at any time to consider the relative share of mobilization and the degree of production and its level of participation in the maintenance, term or adaptation and restoration; basic restore and reserve pool replenishment.

ERYTHROCYTES AND PLATELETS

The first testifies to these phenomena of adaptive regulation, obviously the other figurative elements of the blood. The first order of importance is red blood cells (c.f. Shen resides in the blood by Kellyn Adams in this issue of Living Systems). Their production is under the primary control of androgens.

The Genital (Androgen/Estrogen) Ratio, calculated from red blood cells (RBC in units $10^3/\mu l$) divided by the total number of white blood cells (WBC in units $10^6/\mu l$), is a very good indicator of the relative share of total androgens and estrogens in the functioning of the structural maintenance of our bodies: Genital Ratio = RBC / WBC. The normal range for women is 0.7-0.85, for men 0.8-0.95.

The second most important (after RBC's) are platelets. Their production is under the primary control of the pituitary: ACTH/FSH dyad. The sequestration of platelets depends on the production of androgens. Their liberation depends on the sympathetic beta system (adrenaline).

The ratio of platelets to leukocytes (allows us to derive the) leukocyte mobilization index, which measures the relative share of leukocyte mobilization in relation to their production. The ratio of platelets to red blood cells (allows us to derive the) platelet mobilization index, which measures the relative part of the mobilization of red blood cells in relation to their production. ❊

About the Author

Christian Duraffourd, MD (1943-2017) was the founder of the theory of Endobiogeny. He graduated from Paris V University in 1970 and began practicing general medicine in Paris, France. He co-authored numerous articles and books re-defining the notion of physiologic terrain and approaches to expanding the therapeutic arsenal of physicians. He introduced his approach to functional biology, *the Biology of Functions,* in 1980.