Cervical cancer as a natural phenomenon

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Summary

Recognizing cervical cancer as a natural stochastic phenomenon, that is in the first stage of its self-organization into a new biological dissipative structure (initiation) and sustaining its development in the second stage (promotion), is a basic requirement in conquering cancer and preventing neoplastic disease, i.e., the third stage of neogenesis (progression). A dissipathogenic state inside an organism is the only common primary cause of neoplasia. Thus, medical thermodynamics clarifies why so many non-specific factors enable the origin of cervical cancer, that is, can cause cervical dissipathogenic states. This thermodynamical theory abolishes opposition and unites the heretofore cellular neoplastic theories by bringing them to an atomic level. Diagnosis and treatment of dissipathogenic processes implies true causal prophylaxis of cancer, therapy of which always has to encompass its environment.

Cancer; Self-organization; Dissipative structure; Thermodynamical branch

Introduction

Man, in feeling his greatness or, perhaps due to his conceit or vanity, resigns with difficulty from his relinquished, unfullfilled dreams. Centuries had passed before man, for example, ceased attempting to build perpetuum mobile. However, stubbornness is also inherent with false outlooks, insofar that man can't, or doesn't want, to understand relatively long-lasting secret phenomena; prehistoric examples of which are fire, solar eclipses, thunder and lightning from a clear sky and, more contemporarily, the essence of cancer or life. Amazingly, with appropriate progress in knowledge, some of these phenomena, in general, still startle in their simplicity, causing further impedance in their acceptance. The aim of this paper is to show that cancer is such a simple, natural phenomenon. Accepting it's thermodynamic interpretation is not only easy to comprehend for all, but extremely useful from a medical point of view.

Cancer as a biological phenomenon and disease is characterized by many well-recognized facts, the enormous amount and variety of which do not fit neatly

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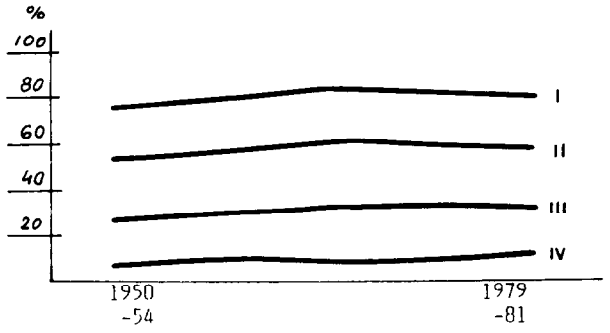

Fig. 1. Five-year survival of carcinoma of the uterine cervix.

into the framework of any heretofore well-known neoplastic theories. What is more, the past several decades of observing the best known neoplasm, that being the carcinoma of the uterine cervix (Fig. 1) shows a commonly unbelievable lack of therapeutic progress [1]. This fact has to force us to radically revise our methods of conduct as well as to modernize old interpretations regarding well-known data concerning cervical neoplasia.

Thirty years of clinical observation is a sufficient amount of time to acknowledge that the heretofore methods of treating cervical cancer – as well as many other forms of neoplasia – have reached their apogee in the second half of this century. Today, women die from cervical cancer as quickly as they did in 1950, that is, 150 years after medicine's reliance on R. Virchow's cellular theory and after several decades of surgical and radiotherapeutic treatment. It's worth adding that the mortality from cancer is greatest in the period of the first three years following its diagnosis [1].

Perfecting therapeutic methods of the past several years barely makes up the deficiency which women experienced in their health. For example, over the period between 1953–86, the proportion of young women ($\leqslant$ 35 years) with cervical cancer increased from under 9% in the 1950s and 1960s to about 25% in the 1970s and 1980s along with pelvic lymph-node metastases [2]. After the standardization of rates of age, parity, smoking, social class, number of previous normal cervical smears and history of sexually transmitted diseases of 47 000 women followed since 1968, it was stated that those who had used oral contraceptives had a significantly higher incidence of cervical cancer than women who had never previously used them [3]. The incidence increased with prolonged duration of use. Cervical cancer accounted for four-fifths of the invasiveness and deaths from genital cancer in users when compared to those that had never used contraceptive pills.

Although the Papanicolau diagnostic test for detecting cervical cancer has been shown to be effective in reducing the morbidity and mortality rates from invasive cervical cancer in appropriately screened populations, there is no evidence that this test has succeeded anywhere in complete eradication of this theoretically preventable disease [4]. From epidemiological studies we learn that over the past 100 years the improved sanitary methods for disposing sewage, purifying water and preparing food had a more profound impact on public health, infectious disease and individ-

ual longevity than any other contemporary advances in medical sciences. That is why we must pay more attention to the environmental prophylaxis and therapy of cervical cancer.

Cervical cancer as a stochastic process

The linear course of all survival curves on four stages of cervical disease (Fig. 1) singularly proves that statistical data assembled by gynecologists and oncologists around the world are sufficiently extensive so as to eliminate local intensification of specific factors that condition cervical neoplasia. Cancer is above all a stochastic phenomenon, as best exemplified by currently known facts which, even with the best of medical experience, we can anticipate only with a greater or lesser probability. In 1842, Domenico Rigoni-Stern first grasped its statistical feature by pointing out its high frequent occurrence among married and widowed women and the rarity of the disease in virginal women.

Most cervical cancers are of the squamous variety; however, up to 10% are adenocarcinomas. Two existing opinions about unicellular as opposed to the multicellular (multicentric) field of origin of intra-epithelial neoplasia express only a different probability of arising in well-defined and pre-destined fields that are well demarcated from each other. Similarly, there are two different pathways of intraepithelial neoplasia through atypical squamous metaplasia in the transformation zone or, less commonly (16–23%), atypical basal hyperplasia in original squamous epithelium. It is worth recalling that the metaplastic process predominantly leads to normal epithelium.

The stochastic character of neogenesis could also be properly illustrated by the simultaneous occurrence of different, always well-demarcated from each other, forms of CIN. In 233 pre-invasive cervical lesions, E. Burghardt and A.F. Ostor [5] found a single type of epithelial cell in only 143 cases (61.4%: carcinoma in situ 30.9%; mild dysplasia: 15.9%; or severe dysplasia: 14.6%). The above-mentioned cell types were observed in the cervix of 10 cases (4.3%) and two of them in the remaining ones (severe dysplasia and CIS: 21.4%; mild dysplasia and CIS: 7.7%; mild and severe dysplasia: 5.1%). Moreover, when dysplasia and CIS coexisted on the lip of the cervix, the former was nearly always situated peripheral to the latter, using the external os as a reference point. Finally, they found that the distribution of immature squamous metaplasia and severe cell hyperplasia was very similar to that of CIS. We observed similar behavior of these cells in vaginal smears of infertile patients undergoing immnopotentialization [6,7].

It can take as long as several years or only as short a time as several months for pre-cancer to develop into cancer in which many genetic, neurohormonal, immunological, psycho-emotional and environmental factors take part in the progression (mostly) or regression (rarely) of this change (Fig. 2).

Also, age of coitarche, number of sexual partners, even including an early age of their partner's first intercourse, early first pregnancy, smoking, use of oral contraceptives, occupation and social class of both partners predispose, with a certain probability, to the origin of cancer which acts as if it lacked it's own history. It originates ostensibly in an arbitrary place and time, whereas the type(s) of cell

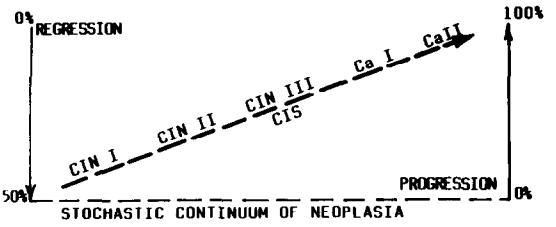

Fig. 2. Stochastic regression or progression of cervical neoplasia.

comprising the cancer are not to be anticipated; the only exception being that they differ from the cells of the host, the only organism in which they can multiply and replicate.

Understanding the stochastic character of neoplasia holds true in our experiences with the many causes of neogenesis, as is best exemplified by the multitude of theories attempting to identify a certain causative factor as primary or fundamental. Each of these factors though can in turn cause tissue damage or death, liberating other complaints or more specific diseases which, in the case of bacteria, viruses or parasites, stirs no doubt as to their primary causative role in disease. Recognition of specific causes of tuberculosis, venereal disease or other infectious diseases was related to a deterministic point of view for over 100 years as an unappreciated understanding of the organism's state of health and its environment. It was postulated that a similar external factor would be discovered in the case of malignancy. We presently know that such a deterministic relationship does not exist between cancerogenic factors and cancer, allowing us to acknowledge that they are nonspecific and, hence, not primary causative factors of cancer as well as the various diseases caused by it.

For example, the specific factor most consistently implicated in the etiology of cervical neoplasia was viral infection: in the 1970s with herpesviruses and in the 1980s with papillomaviruses. The peak age of genital herpesvirus detection is approximately ten years earlier than that of CIS, but over 60% of the infected women will not develop CIN. Since 1969 we know that chromosomal abnormalities are associated with 30% of cells with dysplasia, 40% with CIS and 60% with invasive carcinoma [8]. Again the stochastic feature of neogenesis was proved. A monumental list of onco-, proto-onco- and anti-oncogenes has been assembled, but these genes together with many other molecular components are now also implicated in the control of normal growth. On the other hand, the immune or neuroendocrine system may be of crucial importance in the development and persistence of gynecologic malignancy; however, cancer appears and develops only when the whole body's defense-repair mechanisms fails or is simply reduced either prior to, or as a direct result of, cancerogenesis.

Cancer as a self-organizing biological dissipative structure

Carcinogenic stimuli may have two stochastic effects: one on the target cells to generate neoplasia and the other on the environmental cells and mechanisms, e.g., for the immune system to cause immuno-suppression, thus allowing tumor survival.

Fortunately, mathematics and physics came to our aid towards the end of the 20th century, describing more closely not only stochastic phenomena but, above all, the so-called self-organizing dissipative structures so common in Nature [9,10]. The actual familiarization with these structures and their conditional origin, and development in physics, chemistry and sociology brought not only an understanding of the essence of neoplastic disease (that which is common to all neoplasms without exception) but mostly, allowed identification of a causative factor of their origin, specifically, as self-organization in multi-cellular organisms [11–15]. From a medical thermodynamic point of view neoplasms are natural and not only possible, but sometimes indispensible phenomena.

The survival charts with regard to cervical cancer (Fig. 1) pertain to disease caused by neoplasms in the 3rd stage of their development where treatment of those affected is significantly delayed (Fig. 3). Hence, recognizing cervical cancer as a natural phenomenon, that is, in the 1st stage of its self-organization (initiation) and sustaining its propagation in the 2nd stage (promotion) is a basic requirement in conquering cancer and preventing neoplastic disease, that is, the 3rd stage of neogenesis (progression). Then, we only need to become acquainted with certain well-known facts in a thermodynamic interpretation [16].

Taking as our starting point any cell of the body, we label it a *system* as if every part of nature were taken into consideration. We automatically label the rest of the organism as the *environment*. Analogously, we label a zygote as a system in the mother's organism, which is, the zygote's environment.

Every system has its fundamental properties as, for example, it always reacts as a whole unit while its ability to do external work depends on its internal state (Fig. 4).

In order to exist, a biological system must exchange matter and energy with its environment. It is further development is most effective when its comprised parts and the relations between them are at equilibrium; therefore, we conclude that the system finds itself in a state of equilibrium.

It is well known that if the system diverges itself from this state due to internal and external factors (i.e., finds itself in a state near-equilibrium) it will hence always react in such a manner so as to return to its state at equilibrium. In so-called states far-from equilibrium, the systems' external work limits itself more and more exclusively to ensuring survival of the system as a whole, so as to guarantee it's stability.

Each system can find itself in states of 'near' and 'far-from' equilibrium, and the collection of such stable states we call its *thermodynamic branch*. At the beginning of this branch deterministic processes dominate followed by stochastic ones dependent

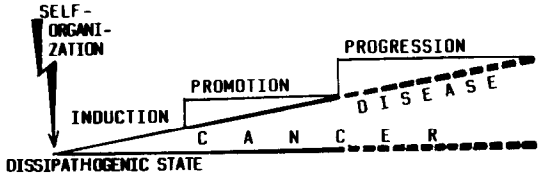

Fig. 3. Cancer as biological phenomenon and disease.

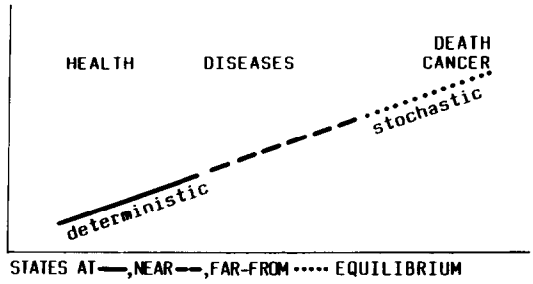

Fig. 4. Thermodynamic branch of human life.

upon statistical laws. The branch ends at the so-called *bifurcation point*, beyond which the system cannot exist nor function in its present spatial-dynamic structure (Fig. 5). It can, sometimes even must, self-organize itself into such a new structure which contains not only to usurp matter and energy from the environment, but must simultaneously dispense more matter and energy than it had up till that point.

In accordance with thermodynamical laws, the sum of production of entropy by the system and its environment must be positive. If a new structure produces less entropy than needed in order to survive, it must increase its environmental chaos; the measurement of which is actually entropy. Fulfilling this condition is not an easy task and, hence, cells finding themselves in such a *dissipathogenic state* (i.e., at the bifurcation point of their thermodynamic branch) generally die. Only one in a million is able to re-organize itself to begin a new thermodynamic branch as an actual cancer cell, giving off itself a new multicellular biological organism (tumor, system). If a dissipathogenic state assumes tissue as well, then neogenesis may begin in more than one point. This explains the possibility of the simultaneous occurrence of various neoplastic cells in a cancer.

The self-organization of dissipative structures is a natural phenomenon and, consequently, dissipathogenic states inside an organism are in itself sufficient enough reason for malignancy to arise. This is the only actual common causative factor of neoplasia.

Neoplastic initiation exhibits self-organization into new dissipative structures of the organism's parts that are threatened by death, whereas attributing to them immortal characteristics as essential cellular properties able to undergo neoplastic

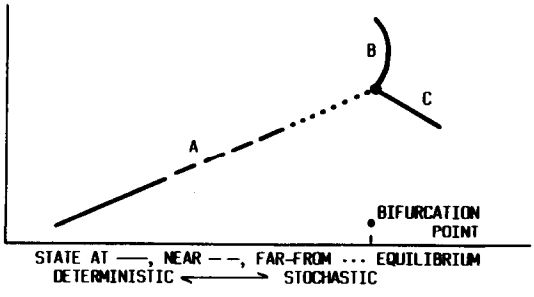

Fig. 5. Thermodynamic branches of systems A, B and C.

transformation is simply exhibited only as a statistically conditioned occurrence. Similarly, promotion applies to the inability of a certain factor to create a dissipathogenic state but only supporting a system's state far-from equilibrium.

We can accept any subcellular structure as a system to be considered. This is valid inasmuch spatial-dynamic changes on this level can be observed with the help of NMR before they assume cellular dimensions accessible to other forms of technology. Thanks to NMR, we can describe an organism's dissipathogenic state and, so begin the actual elimination of the true cause of neogenesis [17–22].

Environmental therapy of cancer

We know from thermodynamics that the internal state of all systems is dependent upon many factors, especially those that are environmental. This clarifies why so many non-specific factors can condition the origin of cervical cancer, that is, can cause cervical dissipathogenic states which we well know are precancerous states. We also understand why we can't foresee from the perspective of time, if at all, that they will transform to malignancy.

The most essential property of a neoplasm is its own unrepeatable identity, differing from the cells and tissues in and from which it self-organizes. We always observe distinct borders with the host's cells, implying possession of their own thermodynamic branches. Even while the tumors appear to be the same histologically, there is a marked difference in growth potential among them. All developing cancer cells are reliant upon the biological environment. Due to the unrepeatability of the individual character of each person, man's malignancies are also unrepeatable in their identity.

Diagnosing pre-cancerous and cancerous states can be accomplished using a multitude of methods depending upon clinical experience and access to the required technology. It is independent from the type of theory acknowledged, which has rather a fundamental significance in prophylaxis and treatment. The thermodynamical theory of neogenesis introduces new methods directed above all by the normalization of the immediate environment of potentially arising and existing tumors.

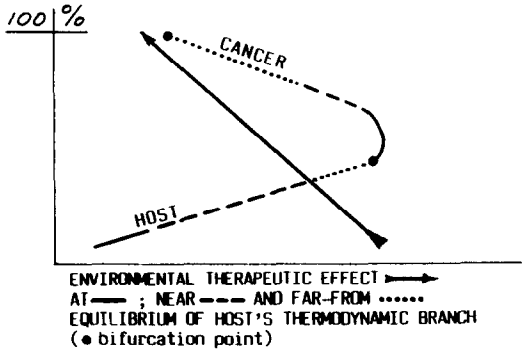

Fig. 6. Environmental therapy of cancer.

This is because malignancies arise in a strictly defined and conditioned vicinity, and only as a new biological dissipative structure, that permits its existence and allows further development. What for the malignancy is a state at equilibrium, the beginning of its thermodynamical branch, is in fact a state far-from-equilibrium inside the host's dissipathogenic body area (Fig. 6). Therefore, it suffices to return the tumor's vicinity to states near or at the host's equilibrium (even without medical intervention) which means finding itself in a state far-from-equilibrium and generally dying at its own bifurcation point. This is, for example, regression of neoplasia clinically proven in treatment of cervical intraepithelial neoplasia in infertile women with Gynatren immunopotentialization [6,21,24].

The results of the last observation [7], identical with previous ones [6], showed a statistically significant disappearance of CIN in 72% of cases within 28 days (CIN I from 27 to 7 cases; CIN II from 10 to 3; and CIN III from 2 to 1; $chi^2 = 26$, $p < 0.001$).

Cancer disease

Neoplasms cause diseases of a second generation. As natural phenomenon in their two initial stages they fulfill a general natural function of informing and regulating. Informing through the most general signals which are dissipathogenic exchanges of matter and energy in some part of the organism which were not eliminated by local defense-repair mechanisms and mobilizing in turn general-systemic mechanisms leads to a quicker disappearance of damaged cells and tissues. Cancer exhibits itself as a regulator of cell and tissue life and, if not noticed in time and left untreated, it eliminates specific individuals of the human race.

This is frequently observed; however, most alarming to us, is the speed of death wrought upon young people or the relative quick progress of systemic destruction through incomparable advancing local changes. It has been shown that, even in patients dying of cervical carcinoma, 50% have no gross disease beyond the pelvis at the time of death. This only demonstrates the lack of suitable appreciation for energetical changes which are less spectacular than morphological ones.

Man, as every thermodynamic system, reacts as a whole even if it merely appears that disease changes apply only to the uterine cervix. If we treat infertile females under 35 years of age with Gynatren vaccination, then the disappearance of cytological and colposcopic signs of inflammation and the appearance of *Lactobacillus* rods is slower (statistically significant) in those women with CIN as compared to those without this pathology [6,21,23,24].

Dissipathogenic or already dissipative states arising in locally disturbed areas are, on the whole, immediately destroyed by the body's defense mechanisms. This is especially true of neoplasms as they are foreign biological structures to the organism. All the same, neoplasia can survive only in an organism distanced from its' own equilibrium, i.e., in an already diseased person. The developing and increasing chaos in the host's organisms furthers it from a state at physiological equilibrium. If it does not surrender to localization – a process which can take place over many years – it will lead to the well-known signs of neoplastic disease. For that reason this last process is lethal, since it is inflicted upon, a priori, a diseased organism.

Conclusions

Cancer can appear only at dissipathogenic points of the organism known as *puncta minoris resistentiae*. Diagnosis and treatment of dissipathogenic processes imply true causal prophylaxis of cancer, therapy of which must also always encompass its environment. Accepting neoplasia as natural phenomena leads to the following basic prophylactic and therapeutic benefits:

1. The elimination of cancer's secrets against the malignant diseases is the most important element of human self-defense. It eliminates the anxiety of its inscrutability, incurability, infectivity and heredity as well as provides successful personal and medical help as early as the precancerous states.
2. Prophylaxis takes on a totally different dimension, since each person's health is more dependent on the state of his family and ecological environment than the best and most accessible contemporary medical assistance. Therefore, therapeutics must take greater advantage of natural advances because cancer is a natural phenomena just as thunder and lightning from a clear sky. Man did not eliminate the dangers from lightning itself though he did learn to protect himself from it.
3. Human life in accordance with Nature's laws best defends and eases the fight with cancer insofar from conception, each person has his own unrepeatable thermodynamic branch of life. For many reasons therefore, as much as this is possible, medicine should teach each person how to preserve and retain its organism's state at equilibrium for as long possible so as not to present conditions for self-organization and further development of neoplasia.
4. The thermodynamic theory of neoplasia abolishes opposition and unites the heretofore cellular theories bringing them to an atomic level. It is worth recalling that Democrates' theory of the atom is the most perfect of the oldest existing scientific theories which in a singular way clarifies a tremendous amount of phenomena. Similarly, contemporary thermodynamics have provided us with a new dimension in medicine.

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