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LETTER

I welcome the opportunity to respond to Dr. Nordenström's letter in order to correct some inadvertent erroroneous comments on my part and to more clearly define the differences and similarities between our two positions. Dr. Nordenström and I share the belief that electrical forces within the body have important physiological functions, and I admire his long-standing devotion to investigate and promote this concept. We differ primarily on the mechanisms involved and the effects produced. I based my comments on several attempts over the past few years to read and understand his book (1), on hearing him speak on several occasions, and on a conversation we held at the First Symposium of the Society of Bioelectricity in Boston, in 1983.

First, I wish to correct the errors I have made in regard to his technique. I am in error in attributing to him the use of stainless steel as the treatment electrode; clearly, he used platinum. I am also in error in attributing to him the use of a surface electrode as the cathode; clearly, he used implanted electrodes for this purpose. In both instances I had hurriedly misread portions of his book, under the pressure of publication deadlines, and had inadvertently confused his technique of wet diathermy for lung tumors with his DC techniques for treatment of the same lesions. I sincerely regret these errors of substance and apologize to Dr. Nordenström for any distress he may have suffered.

My statement that the therapy on some occasions appeared to result in increased growth of untreated tumor nodules is based on the afore-mentioned conversation during which Dr. Nordenström, other Symposium participants, and I discussed some additional radiographs. I was particularly interested in this prospect, having earlier reported increases in tumor growth with low-level DC such as would be found outside of the zone of direct toxic effects surrounding the anode in his treatment technique. It is my recollection that one, and possibly more, such possible instances were discussed but that some confusion arose as to whether the area in question was part of the original tumor or a separate metastasis. I note that this reservation on my part is not dependent on either the anodal material or the placement of the cathode.

In response to this and the other statements contained in Dr. Nordenström's letter and, hopefully, to clarify both our positions, I offer the following analysis of our respective positions.

In summary, Dr. Nordenström makes at least the following claims:

1. To have discovered a "mechanism for energy conservation in tissue over biologically closed electrical circuits (BCEC)" (ref. 1, p. 1).
2. That "artificial activation of BCEC systems offers the possibility of enhancing healing" (Ref. 1, p. 9).
3. That spontaneous healing of cancers may be similarly produced (Ref. 1, p. 9).
4. That his technique of DC electrical administration, based on his concept of BCEC energy conservation, is successful in a significant percentage of cancer patients (Ref. 1, p. 9).

Since his cancer treatment technique is based directly on his basic concepts and findings, a critical review of their validity is necessary in order to understand his position and the data that he believes support it.

As I understand Dr. Nordenström's basic concept, he postulates that necrotic tissue, within injured areas, provides electrical energy (via pH shifts and redox potentials) that is transmitted away from the area of necrosis by units he terms "ionars" and "ergonars," with the former consisting of ionic species and the latter of non-ionized molecules capable of providing energy. The electrical energy thus generated by the necrotic area is transported over structures postulated to form BCECs. He defines this term as follows: "[BCEC] is here used as a general term for structures with the capacity to channelize the exchange of energy in a selective way over long as well as short distances" (Ref. 1, p. 149).

He proposes that a number of such BCECs exist, with one specifically, the vascular interstitial closed circuit (VICC), as the healing mechanism for both simple injuries and tumors. "This type of BCEC has two conducting main branches and an intersected regulating mechanism in the capillary walls. One branch is formed by the electrically insulating walls of 'large' vessels surrounding their conductive component, the blood plasma. The other branch is formed by the conducting interstitial fluid and the insulating tissue matrix of cell membranes. The red blood cell membranes also possess a resistive function in the blood. These cell membranes therefore represent a movable part of the matrix of the VICC, variable with the hematocrit" (Ref. 1, p. 148).

In this view, the current of injury is the result of the pH shifts and other electrical events produced within necrotic tissue and transmitted to the surrounding tissue via his postulated BCEC mechanism where the electrical energy produces a number of biological processes that constitute healing. Simple injuries heal successfully via this mechanism because they are of a "nonprogressive" nature and do not increase in extent, so that this postulated healing mechanism can proceed. He postulates that the same mechanism occurs in malignant tumors but is inadequate because the injury is of a "progressive" nature, in that tumor growth rate exceeds the natural healing process resulting from the action of the VICC.

He equates corona-like structures and concentric zones of various density observed radiographically around malignant lesions in the lung to attempts to heal the lesion by action of the VICC. He states, "The biokinetic mechanisms behind the development of these structures—can be traced back to a common process of spontaneous healing.' This tendency of 'healing' is evidently insufficient for the development of a 'true healing' of a carcinoma" (Ref. 1, p. 265).

His therapeutic technique is based on this concept of a common mechanism of healing applicable to both spontaneous, traumatic injuries and tumors. In his clinical

technique, Dr. Nordenström inserts the anode into the center of a tumor mass and applies an average of 10 V DC between it and a cathode implanted in tissue at a distance usually approximately two and a half times the diameter of the tumor (statement at the 1983 meeting). The technique results in gas liberation and production of a zone of tissue destruction within the tumor. Clearly, he recognizes the direct toxic effect on all tissues in the immediate vicinity of the anode of the voltages used. However, it is evidently his intent to produce this necrosis not as a direct therapy destroying the tumor, but because his basic thesis holds that this necrotic area will produce specific electrical phenomena which will subsequently "heal" the surrounding, undestroyed portion of the tumor.

"Seen in the light of BCEC mechanisms, the therapeutic problem now is how best to support spontaneous tendencies toward healing of a growing tumor, when its foci of internal injury release energy only intermittently and often weakly. The energy released in spontaneous injury may be sufficient to include ionic exchange by diffusion and migration over a BCEC, e.g., in healing ordinary wounds and fractures. Such conditions should perhaps be called *nonprogressive injuries*" (Ref. 1, p. 272).

"The possibility is worth serious consideration that most of the energy necessary for ionic transports in healing a non progressive injury may be provided by the injury itself. In this view, infectious injuries or locally degrading injuries in cancers may be called *progressive injuries*. The critical point is that the healing induced in progressive injuries either temporarily or permanently lags behind the advancing primary pathologic process. Logically, extensive local destruction might release enough energy for the healing of progressive injuries" (Ref. 1, p. 272).

Therefore, he intends the application of his DC therapy to produce an increased focus of necrotic tissue within the tumor, which, acting via the postulated VICC, will subsequently "heal" those portions of the tumor remaining undestroyed. However, in addition to the DC electrical technique producing a central focus of necrosis, he also postulates a beneficial effect on the tumor of the administered DC itself.

"The present method is based on the assumption that the primary destruction of the tissue around the anode is supplemented by the ability of direct current to produce specific biological healing reactions in surrounding tissues" (Ref. 1, p. 281).

His DC therapy is therefore based on two actions of the administered DC: the direct destruction of tumor tissue in the vicinity of the anode and an antitumor effect of the administered DC outside of this zone. I am unable to reconcile the above statement with that in his letter," A 'drop below the level of electrolysis' in current density around an electrode is *per se* of no interest."

In support of his concept of the VICC and the effects of DC electrical parameters on living tissues, Dr. Nordenström describes many laboratory experiments.

In Chapter VI of Ref. 1, he reports numerous measurements of DC electrical potentials in normal and pathological conditions with tumor potentials all below 10 mV, with normal tissues only occasionally exceeding this level.

Chapter VII reports long-term pH measurements (40 days) on degrading human blood.

Chapter IX reports on extensive experiments involving electro-osmotic transport of water with administered DC potentials ranging from 10 to 40 V.

In Chapter X, Dr. Nordenström reports duplication of the corona structures and zones of various density he observed radiographically in lung lesions. These experiments involved a variety of particles and substances in solution with administered DC in the kV range.

Chapter XII reports his attempts to define the circuitry of the BCEC, by numerous tissue resensitivity measurements and tracing selected pathways for DC currents at applied voltages between 0.1 and 40 V in living tissues. He reports the production of: contraction of small arterioles, red cell diapedesis, and local intravascular accumulation of granulocytes (pp. 138–141).

In all the above experiments (Chapters VII–XII) the administered DC voltages required to produce the effect were considerably in excess of any naturally occurring DC potentials he reported in Chapter VI. With the exception of granulocyte accumulation, it is difficult for me to equate these reported effects to any naturally occurring phenomenon observed in healing of spontaneous injury or tumor, and the majority represent effects due to levels of electrolysis that would be directly toxic to tissues.

In Chapter XIV, Dr. Nordenström reports the results of experiments designed to simulate the action of the VICC by administration of DC electrical currents to dog mesentery and omentum with voltages between 100 mV and 10 V. He reports observing; diapedesis of red cells (p. 174), vascular pockets and ischemic dystrophy (p. 176), acid-base shifts (p. 178), gas production (p. 179), loss of pigmentation, crenation and vacuolization of red cells (pp. 181–186), accumulation of granulocytes (pp. 187–188), and local accumulation of charged chemical compounds (Evans blue) (pp. 191–192). Similar experiments on dog lungs, reported in the same chapter, produced blockage of blood vessels and development of "tumor-like" masses (p. 193), accumulation of leukocytes (p. 194), and dry black gangrenous appearance at anodal sites (p. 194).

Later, in Chapter XVI, Dr. Nordenström states, "The exposure of cells to direct current can lead to considerable cellular transformations (Chapter XIV). The development of fibroblasts may therefore be explained as a result of such electrogenic transformation of cells, (p. 240).

I can find no evidence for any cellular transformations or the development of fibroblasts in the experiments reported in Chapter XIV and listed above. I believe that Dr. Nordenström's claims for cellular transformations (as quoted from Chapter XVI directly above) resulting from DC electrical fields are unsubstantiated by any of his data.

Further, none of the effects reported (Chapters VII–XIV) appear to be related to physiological or cellular events usually considered to be associated with healing. The majority of his experiments were performed at highly nonphysiological levels of electrical current (e.g., Ref. 1, p. 216) and far from the levels of direct current normally present in injured tissues or tumors (as reported in Chapter VI).

I am also unable to find evidence that Dr. Nordenström exposed tumor tissues, *in vitro* or *in vivo* in animals, to DC fields at levels he proposes would be produced by his proposed VICC, or which would be present outside of the zone of necrosis in his DC treatment techniques. He presents no quantifiable evidence for a "healing" effect on malignant cells, such as reversion to normal cells, cessation of tumor cell growth, or any other desired alterations resulting from his DC treatment technique. I can find no objective evidence for Dr. Nordenström's concept that the mechanism that produces healing of injuries may also "heal" malignant tumors. It is my opinion that Dr. Nordenström's basic theses concerning BCEC and VICC, their existence or functions, as well as postulated "healing" effects of DC electrical fields on malignant tumors remain unproven.

One cannot contest the direct, nonspecific, toxic effect of products evolved by Faradic reactions of DC electrical current in the vicinity of the anode on any tissue.

If this effect is produced in a solitary tumor nodule in such a fashion that all malignant cells are destroyed, one can expect to have obtained a cure. However, I hold that this cure would in no way involve the action of DC fields below the level at which such cellular destruction is caused. I firmly believe that the question remains open as to the effects of the current outside of this zone, derived either from the administered direct electrical current itself or, subsequently, from the increased zone of tissue necrosis, *per* his postulated BCEC, on residual or neighboring tumor tissues. I cannot understand Dr. Nordenström's objection to my position that such electrical parameters may stimulate existing tumor growth when he himself has postulated that such parameters may stimulate the induction of cancer." It is suggested that activated BCEC systems, under certain circumstance, represent a common factor in carcinogenesis" (Ref. 1, p. 10).

I have reported evidence that the current of injury is the result of the activity of an organized DC electrical system and not dependent on the presence of necrotic tissue (2–4). Appropriate simulations of the current of injury in regenerating animals have been shown to stimulate regeneration in frogs (5) and rats (6,7) and to stimulate bone growth in mammals (8), with the latter enjoying some clinical application. In regard to the effects of such DC parameters on malignant cells, I have reported significant increases in the growth rate of human fibrosarcoma cells exposed *in vitro* to low levels of current in both a positive or negative environment (9).

I must note that in no case have I reported the *induction* of cancer by such electrical currents as Dr. Nordenström claims, in his letter. Further, for him to state that "the 'stimulation of tumor growth' is again an unproven assumption" is incorrect. To the best of my knowledge, my observation (9) has not been refuted. As a result, I view with caution the exposure of malignant cell populations to seemingly innocuous levels of DC electrical current either anodal or cathodal.

In brief, I believe that the laboratory experiments Dr. Nordenström reports at length in his book do not provide a credible, scientific basis for his use of DC electricity on tumors in human patients, and it is my contention that the successfully treated cases he reports may well be due solely to the direct cytotoxic effect in the immediate vicinity of the anode and not to any specific antitumor effects of DC parameters outside of this area of effect.

Analysis of Dr. Nordenström's clinical case reports provides some tentative substantiation for this opinion. He reported in his book (1) the results of his treatment on a total of 33 specific tumor treatment sites in the lung with tumor regression observed in 12, indeterminate results in seven, and tumor progression in 14. I believe that it is not clinically feasible to determine, in cases of observed tumor progression, whether the growth rate is the same as that prior to therapy or enhanced above that rate. Resolution of this requires *in vitro* or *in vivo* animal experimentation.

In reviewing the tumor types versus the treatment outcomes, I find that all the tumors in which regression was observed were not primary in the lung but were metastatic from the ovary (2), breast (2), uterus (2), and pelvis (1). In cases where he reported progression of the tumor, there were metastatic (cervix, esophagus, and uterus) and four were primary tumors of the lung: adenocarcinoma (1), squamous cell carcinoma (2), and small cell bronchogenic carcinoma (1). I find it particularly interesting that primary lung tumors appeared not to respond to the therapy while metastatic tumors derived from the female reproductive system, with two exceptions, did. However, there were three metastatic tumors in which two metastases from the same primary differed in their response. One osteosarcoma metastasis regressed while another

progressed. Similar results are reported in an adenocarcinoma of the ovary and an adenocarcinoma of the rectum. The data are insufficient to establish any statistically significant relationship between treatment outcomes and either types of tumor or primary versus metastatic tumors.

However, there does appear to be a relationship between tumor size and treatment outcome. Rough calculations of tumor volumes indicate that tumors in which regression was reported ranged from 1980 to 93,600 mm^3, with an average of 20,653 mm^3, while tumors that progressed during treatment ranged from 1000 to 316,875 mm^3, with an average of 65,390 mm^3, approximately three times as large as tumors showing regression. While the number of tumors is again too small to draw a firm judgment, these data may lend support to my contention that the successful outcomes are probably due to simple, direct cytotoxic effects in smaller tumor masses, and that Dr. Nordenström's postulated effects of the DC outside of this zone remain unsubstantiated. Unfortunately, Dr. Nordenström was unable to verify the posttreatment status of the majority of treated tumors by biopsy. However, in one instance (patient 18, a primary lung tumor) autopsy 3 weeks following treatment revealed viable cancer cells at the periphery of the zone of anodal destruction. Clearly, these cells were exposed to the DC electrical parameters claimed by Dr. Nordenström to produce "healing" in tumors.

My reservations regarding Dr. Nordenström's treatment are based on my observation of a markedly increased growth rate of only one type of malignant cell, fibrosarcoma, when exposed to such electrical factors (9). Dr. Nordenström has presented no firm evidence for his contention that similar DC electrical parameters exert a "healing" effect on any type of malignant cell. While I cannot claim that my observation extends to all types of malignant cells, I believe that, until it is proven otherwise, the possibility cannot be lightly dismissed. Further contentious discussion without an expansion of the present objective database will serve no useful purpose.

In summary, I believe that Dr. Nordenström has not presented clear, objective, or credible evidence to support his hypotheses of the existence or physiological functions of BCECs or VICCs, either in normal healing processes or in his postulated "healing" processes in tumors. I further believe that the successful treatments he reports in human tumors are probably the result of the direct toxic effects of electrolytic products from the levels of voltage he applies, and that there is no evidence for antitumor effect from DC fields below this level.

It may be possible to ultimately develop a system of DC administration, based on this direct cytotoxic effect alone, in which the administered fields are such that the total destruction of a tumor is reasonably assured. Such a therapeutic system could well be clinically useful for circumscribed, solitary tumor nodules located in surgically inaccessible areas.

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