

The Plant Kingdom Featured Significantly in the History of Cancer

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Abstract

A decade elapsed between 1947, when the author sat for a degree in Botany, and 1957, when he did likewise in Medicine. The latter year was fruitful in that during it he wrote his first paper which it was based on 1000 cases of lung cancer. This included the expressive plant kingdom phrase, "suitable nidus" with reference to the survival of transported human cancer cells. Therefore, it is instructive to now document in the prestigious Journal of Plant Studies how the long history of cancer was nicely interwoven with the plant kingdom. In particular, size was described with ready references to apple, apricot, cherry, chestnut, cocoa-nut, currant, filbert, garden pea, grape stone, hazel-nut, hemp, hemp-seed, millet, mustard seed, nut, oat, orange, pea, pear, split pea, thistle-down and wall nut. Moreover, branching and grafting appeared. So did fungus which is no longer in use. More importantly, seed and soil were brought in readily cancer cells being said to find roots both at the starting point and at the resting place. Moreover, prevention of cancer was compared with not allowing blight to become pestilential. Thus, surgical treatment was recommended in terms of early complete uprooting. In all probability, just as a Japanese group demonstrated that mimosine, an allelochemical amino acid, inhibited "the growth of lettuce protoplasts at the stage of colony formation," even so there is the human similitude named personally as the "Erythrocyte Associated Necrosis Factor" which is likely to turn out to be the micromolecule capable of being used in the war against human cancer colony formation. In conclusion, therefore, recondite researches in the translational laboratories should soon lead to that breakthrough which could conduce to cancer cure.

Keywords: Plant; Seed; Soil; Cancer; Comparisons; Target therapy

Introduction

The decade between 1947 and 1957 marked the author's taking of degree examinations in Botany and Medicine respectively. During the latter year, the documentation of 1000 cases of lung cancer appeared [1]. By chance, the word, "nidus," crept into that publication. Now, Merriam-Webster's Collegiate Dictionary defined it as a place in a plant "where something originates, develops, or is located." Moreover, since 2 out of the 38 references were dated to between 1896 and 1897, my interest in the historical parameters of cancer research so flowered that, within the next year, two historical papers of mine appeared [2,3]. Therefore, this paper emphasizes that the historical highlights of cancer concepts significantly incorporated botanical briefs.

Historical Texts

The plant kingdom shares pride of place with the animal kingdom in the writings of the medical masters of yester years. For example, Bence Jones was encyclopedic, incorporating ideas on "a single cell, or possibly even a nucleus, or a granule, or a particle of matter." On his part, Theodor Billroth [4] brought in another vegetable matter by wondering whether a "tumor could be as independent as a thistle-down." It was left to Coats of Glasgow to appreciate that "the actual cells of the tumor are carried off and deposited at a distance," this being the litmus statement as regards the "metastasis" i.e., the "spread" of cancer.

Cancer can start in any part of the human body. In this context, Marsh [5] agreed with the famous Sir James Paget that there are two factors concerning the origin of cancer, namely, "there is the general tendency, the seed, and there is the fitting condition of the part, the appropriate soil" or, as Erichsen [6] put it, "there are certain constitutions that afford a far more fertile soil for the development of that local poison, and in which it grows and spreads."

"Spreads" is dangerously what often takes place from the original site to a different situation. In this context, Campbell de Morgan reasoned that the facts were in favor of "dissemination and grafting rather than by

new original formation." Incidentally, the concept of grafting was also entertained by Snow [7], who noted that circulating elements of cancer are "deposited as grafts in other locations." Indeed, Savory [8] lamented that the "experiments on the grafting or inoculation of tumours" failed. Furthermore, he sensed that the failure was due to the crudeness of the subsisting researches.

Researches on cancer were significantly described with the plant family in mind. Thus, in his textbook, Beale [9] was sure of the distinction between different growths including the fibrous ones. Indeed, it should be recalled that he used the determination of the presence of starch in urine at microscopy to show that malingering had occurred in a puzzling case. Actually, microscopy was mustering strong. Thus, Müller [10] was clear: "The minute microscopic elements of morbid growths are, in addition to capillary vessels, fibres, granular cells both with and without nuclei." Then, he defined "granule" as "spheroidal or elliptical body." Moreover, he appreciated that human tissues are "composed of cells, which have precisely the same structure as those of vegetables." On his part, Ormerod [11] described lesions that were "very exactly resembling the awned seed of some grasses."

Grasses grew with another distinct plant called the fungus. Regarding this type, Carswell [12] mentioned that Hey and Wardrop called it *fungus haematodes* while Cooper named it *fungoid disease*. In the woman ill with breast cancer, which bled, Morgagni [13] considered it to be due to "Fungus." This was his diagnosis also in a man with a

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jaw mass, and in another man with an involved tongue. According to Warren, the other names were fungoides, fungoid disease and fungus haematodes. In particular, Budd [14] knew it as a disease which “grows more rapidly, becomes sooner and more widely disseminated, and sprouts into exuberant medullary or fungoid masses.” Incidentally, Hodgkin [15], because of his tidy and systematic mind, was unhappy about such nomenclatures. Indeed, he was so perturbed as to say that “we find the terms encephaloid tumours, cerebriiform cancer, medullary sarcoma, spungoid inflammation, fungus hematodes, and fungoid disease.” Therefore, as he continued, “I am rather inclined to prefer the last of these terms.”

Terms like root and tuber came into the picture nicely. For instance, Velpeau [16] pointed out that the removal of cancer cannot but be incomplete unless done “at one sweep,” i.e., total removal of “the whole of the tumour in the breast, and the roots which it sent out.” Walshe [17] was picturesque thus: “Primary lung cancer may infiltrate the tissue; or spread from the root of the organ in irregularly tuberous form; or hang in pedunculated masses from the surface of the lung; or festoon its free margin with rows of fringed processes.” Finlay [18] held that “the main portion seemed to be in the neighbourhood of the root of the lung; but whether it originated in the lung, pleura, or glands could not be determined.” In the second case of West [19], there were more details as follows: “At the root of the lungs surrounding the bronchi and vessels, and compressing them, was found a mass of new growth, which extended by branching rays about half way through the substance of the lung.” Concerning the thyroid tumor, Carrington [20] found its swelling “around the root of the neck,” there being also “numerous discrete white nodules, varying in size from millet to a hemp seed.” Earlier, Kidd and later, Griffiths [21] used “neck root.” In addition to these descriptions, what also came up was “juice.”

Juice as an element was the undoing of even Virchow [22], although he was acknowledged as “The Father of Cellular Pathology.” Thus, he did not think primarily in terms of “cells” but of “morbid juices.” For instance, concerning breast cancer spreading to the liver, he thought that “it seems pretty probable that juices are taken up, which occasion a further propagation.” Moreover, Carl Rokitsky [23] taught in terms of “cancer-cells, or of cancer blastema, of a lax, soft, semi-fluid character.” In fact, juices were also mentioned by Ie Dran et al. [4,13,24-30] whose own choice words were “a copious milky juice.” Interestingly, Todd [31] experimented with a specimen and wrote: “On pressure a lactescent cancerous juice exudes.” Then, he continued, “If macerated in water or a weak solution of chlorine, the cancerous matter is dissolved, leaving a marginal fibrous tissue behind.” Next, as for Burrows [32], he described the sputum of the lung cancer patient as having “the singular currant-juice” appearance.

Appearance may be quite deceptive. This altruism was made use of by Sir Astley Cooper [33]. Thus, concerning breast cancer, he stated that the lesion “is not all the disease; there are roots which extend to a considerable distance.” Then, he warned thus:

When you dissect a scirrhus tumour, you see a number of roots proceeding to a considerable distance, and if you remove the tumour only, and not the roots, there will be little advantage from the operation; no glandular structure, nor any of the roots should be allowed to remain.

Remain to be guarded against even in those days was the indiscriminate use of the word, “root,” by quacks. This was how Sir Spencer Wells [34] saw it. In this context, Young [35] had berated even a surgical colleague thus:

We find him talking more like a magician than a surgeon; and,

by throwing obscurity upon the disease itself, in every possible way (descanting on “its roots,” and “seeds,” and “the state of the juice”), would seem to infer, by such mysterious phrases, that his remedy, in short, was nothing more nor less than a charm.

Charm was not at issue but whether there was an independent life of the cancer-cell. As Dickinson [36] explained, “these bodies are taken up by the absorbents and deposited as seeds in the glands and organs traversed.” However, he did wonder whether it was “fluid poison that is conveyed.”

Conveyed cancer cells came into the farm-yard picture beautifully as regards the descriptions of their manifestations to the naked eye. For example, Carswell [12] noted that the tumors were “varying from the size of a hemp-seed to that of the cherry,” while he used orange elsewhere, this tree being favored also by Curgeven [37] and Turner [38]. Furthermore, Murchison [39] repeatedly illustrated with the pea.

Pea was the descriptive plant of both Seymour [40] and Fox [41]. Much earlier, Sharp [42] had chosen hazel-nut. So did Arnott [43], while Hutchinson [44] favored walnut. On his part, Campbell de Morgan preferred split pea. Bristowe [45] took notice of masses “generally from the size of filbert downwards, but in rare instances, assuming yet larger dimensions than this.” Dickinson [36] described the tumors as being “about the size of nuts.” Bayle [46] was precise as to size and location thus: “There was found a white scirrhus body as large as a nut, fixed upon the pancreas, without touching the liver.” Morgagni’s [13] description was precisely that of wall-nut. Wiseman [47] mentioned apricot-stone, and Warren considered filbert. So did Targett [48]. Wilks [49] brought in cases described as about the size of “an ordinary sized cocoa-nut,” and of “orange.” Smith described different lesions of “about the size of a garden pea,” and “about the size of a chestnut” as well as pear and orange. Richard Bright [50] saw “a tuber of the size of a chestnut” in the liver, part of it being “rather botryoidal,” i.e., like a bunch of grapes. Mentioned on the smaller size was the oat [51], while Legg [52] opted for the size variation “from a mustard seed to a small apple.” On the part of the eponymous giant, James Paget [53], note his vivid description: “The tumour growth was branched, like a stunted, leafless shrub, about two-thirds of an inch high.” Billroth [4] also noted branching, while Lack [54] painted the picture of an array of postoperative stitch site tumors “varying in size from a pea to a cherry stone.” His contemporary, Stiles [55], remarked that “They may be no larger than a grape stone, or they may reach the size of a filbert, or may even be larger.” Another contemporary, Lack [56], likened the size variation “from a pin’s head to a small pea,” while Beatson [57] included beans, peas, and even small shot! Little wonder that, in the midst of using so much of plant materials, Hutchinson [58] differed by going the way of the human element, namely, mentioning growth “the size of an adult fist” and in another case continuing with growth “as large as two or three fists” [44]. Much earlier, Adams had described “a globular tumour of the size of a man’s fist.” Continuing with the human side, there was a patient of Turner [59] who, on being questioned, said that she became quite blind overnight, but that, during the previous evening, she was able to see people moving about “like trees walking.” In other words, the various references made to plants were the routine conception.

Conception of the events led to the emergence of a vital question, namely, Do cancer cells grow elsewhere at random or according to observable principles? As shown above, the answer was sought by way of the experiences prevailing in farming. In sum, down to earth comparisons emerged. Thus, the old idea was that cancers behave as plants do and that like plants they require a suitable soil in which to

grow [35,60,61]. In fact, Billroth [4] was clear concerning the fate of cancer cells. They are, he felt “like the seeds of some of the lower plants (and) they find almost everywhere soil suited for their development.” Incidentally, it was Stephen Paget who mostly popularized the seed-soil concept, seeing that he wrote a lengthy review in the *Lancet*. However, as I pointed out [62], he did not include its historical development.

Development of the surgical treatment of cancer, be it noted, took notice of the above plant parameters. Thus, Pearson [63] pronounced that “when every altered fibre cannot be included within the incision, no operation ought to be attempted.” This was also the teaching of both Munro [64] and Burns [65]. Accordingly, lest the tumor buds afresh, nothing of it should be left behind [66,67]. Indeed, to achieve worthwhile surgical results, both Syme [68] and Moore [69] long ago urged the advisability not only of cutting wide of the tumor but also of excising the whole organ or part of the body. In this context, even the wound itself must be carefully attended to. Thus, as Lack [56] warned, the cancer cell should not be the “seed.... which was sown in the wound.” In other words, what was at stake was the integrity of the whole body.

Body of knowledge of cancer was, as illustrated above, evolving naturally over the centuries. Perhaps, the future can be prognosticated with the ancient experience of Leake [70]. In sum, he used “blight,” a disease or injury of plants, to argue that “the cancerous matter frequently fixes upon some other glandular type; so that what was at first only local, now becomes a universal disease, and like a pestilential blight, overspreads and lays waste the whole frame.” Consequently, may moderns take this hint from the plant kingdom with special reference to that planned health education which will ensure that cancer nipped is in the bud i.e., before it sprouts and overwhelms the entire bodily soil.

Discussion

Soil par excellence was discovered in the thoracic duct by me when I followed certain strategic stages. Firstly, using the mono-block formalin-fixation method for investigating lung cancer [71], I obtained a unique axial system, namely, the 45 cm long thoracic duct. It was easily dissected free in continuity. Secondly, serendipity led to its being coiled in Swiss-roll fashion, thus facilitating its being so easily processed as to be viewed on a single microscope slide [72]. Thirdly, lung cancer cells were seen in panoramic fashion as they were being transported from the upper abdomen, through the chest, and up to the neck at the moment of death. Finally, inspection revealed, in the processed human thoracic duct, the required two research subsets, namely, *lively* lung cancer cells and *dying* lung cancer cells, especially those which were commingled with red cells. In effect, for research, there are the cancer cells, the “seeds,” as well as the flowing lymph, the par excellence “soil.” Consequently, the importance of this particular seed-soil pabulum was identified [73]. This is as regards its own potentiality just as in the case of mimosine, an allelochemical amino acid which inhibited “the growth of lettuce in being categorized as a subsisting healing factor. Indeed, I have designated it as the “Erythrocyte Associated Necrosis Factor” (EANF). Incidentally, I have hypothesized that, if EANF, which is actually nature’s signaling factor, is harvested from the thoracic ducts of consenting patients, recondite replication of it should follow in translational laboratories [74]. In all probability, just as Mori et al. [75] demonstrated in the plant kingdom that mimosine, an allelochemical amino acid, inhibited “the growth of lettuce protoplasts at the stage of colony formation.” In essence, there is the human similitude. It is that erythrocyte associated necrosis factor is likely to turn out to be the micromolecule capable of turning the table in the war against human

cancer colony formation itself. In conclusion, therefore, resourceful researches should sooner than later lead to that scientific breakthrough which could conduce to cancer cure.

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