Review article

Controversy Concerning Constitutional Cancer: Historical Review

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Abstract

Objective: The general pathology of cancer was long in turmoil over the two extremes of constitutionalism and localism. Therefore, my mini-Library of historical works was searched so as to obtain a good idea as to the ultimate development.

Methods: Many different literatures on the subject matter were reviewed and used.

Results: Two major issues were delineated. The constitutional theory saw cancer being a whole body affair with some local manifestations whereas the localists believed in a focal origin which may go on to manifest widely. Naturally, there was the midway group called the dualists who managed to hold both concepts

Conclusion: The controversy that reigned in the history of these concepts are deemed to be worthy of documentation. By 1900, the localists gained the upper hand principally on the principle of embolism.

Keywords: *Cancer, Constitutionalists, Dualists, Localists, Embolism, History*

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Introduction

The essential contribution of the 18th century to general pathology was the turn from the theory of humoralistic *diathesis* to that of solidistic *localism* (1). In the important field of cancer, this occurred after considerable controversy. The definition "diathesis" is in terms of constitutional predisposition, i.e., of an intrinsic condition of the body which renders it, as a whole, liable to certain diseases, and "localism" in terms of focal predisposition, i.e., of an innate condition of the part, which predisposes it, as a part, to succumb to disease (2). These two forms of predisposition led to the doctrines of constitutionalism and localism. Indeed, it was controversial whether constitutional factors or local factors led to the development of cancer.

Historical Texts

The problem as it was seen was whether cancer is a "primitively constitutional" disease or a disease with a "primitive focus" (3). This was appreciated as a fine distinction for 1833 (4). So did another author in 1881 thus: "Now, of course no one can doubt that malignant diseases are in their later stages constitutional, and that the blood itself becomes tainted. But the question is, on which class of influence does the very commencement of cancer depend" (5)?

All along, it was recognized by the old masters themselves that the two theories were controversial. When reference was made to them in 1793, it was to the effect that "different and contrary opinions" were prevailing concerning them (6). By 1818, it was acknowledged thus: "I do not enter into the difficult and abstruse question, as to the cancerous diathesis, and consequently, whether the cancer is a disease only local, or produced by a specific cancerous virus, dispersed through the whole frame" (7). Again, it was put in 1832 as follows: "It is still also a disputed point, whether cancer be a local or constitutional disease" (8). And by 1842, the revelation was that "very vague and unsettled notions on this point are still prevalent in the profession" (9).

In the epochal paper with which Hodgkin's disease was put on the clinical map, there was a grasp of the changing times back in 1865:

The generally accepted doctrine has been, that an affection like the present must be constitutional; but modern research would quite approve of a theory which should make it commence in one part of the lymphatic system, and from this, as a source of contamination, be propagated through the body (10).

By 1871 we find Henry Arnott of London ranging over the debate with an international eye:

There are two leading views of the nature of cancer which may be briefly characterized as that which regards it as an affection *purely constitutional*, and that which ascribes to it a *purely local* character. Of

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these two views the latter is by far the more recent; but although it has been warmly adopted by some few English surgeons …. It cannot be said to be generally welcomed on this side of the channel, though long held by some of the leading pathologists of Germany (11).

In an address delivered in 1878, John Simon referred to constitutionalism as "the older cancer-theory of our times – the theory which was in full bloom some twenty years ago, and is even now not quite extinct" (12). Ten years later, the *Lancet*, on surveying the arena, observed that "the older controversy between localists and constitutionalists has practically died out" (13).

Who were the constitutionalists? What were their arguments? These are the questions whose answers demand the first consideration. One of the celebrated constitutionalists was John Abernethy who argued in 1816 that the growth which appears in a cancer operation scar is "in consequence of the diseased propensities of the constitution, rather than that it has lain dormant so long, and is now awakened" (14). In those days, the constitutionalists were saying that recurrence was due to the recharging of the operation field with tainted matter pervading the body itself, the original tumor being presumed to have been completely removed surgically (15).

The presence of tumor nodules in subcutaneous tissues interested John Macfarlane in 1832. In his view, their origin "is to be ascribed to constitutional and not to local causes," for he reasoned that they form in parts where "it is impossible that the diseased action could have been communicated through the medium of the absorbents" (16).

Henoch also hung his argument on transportation. In fact, he opposed Budd's concept of secondary liver cancer as transported cancer "on the ground of its being unsupported by direct observation" (17). By 1846 Walshe was writing that "malignant tumours are local manifestations of some specific morbid states of the blood" (18). He was of the opinion that malignant tumors possess "distinctive characters" and that the benign tumors, lacking these characters, are the only tumors which deserve to be called local diseases.

Regarding the poor results of surgical treatment, Sir Everard Home in 1805 stated that "too many medical men ... Have come to the conclusion, that such failures have arisen from the whole constitution being contaminated, and therefore that the local appearance was only the consequences of a diseased state of the whole mass of blood" (19). The bodily effects of cancer so struck Johannes Miller that he defined such growths not only as those "which are constitutional from their very commencement" but also as those "which, when once they have infected the constitution, if extirpated, invariably return, and conduct the persons who are affected by them to inevitable destruction" (20). Likewise John Collins Warren was pessimistic in respect of "fungoid cancer." "The disease," he bemoaned, "is constitutional and malignant; of course it is incurable in any stage" (21). As he also stated, "Wherever it may occur, it is usually dependent on a constitutional cause, and is a local symptom of constitutional disease."

Sir James Paget, a confirmed constitutionalist, gave a number of reasons in the Morton Lecture for 1887 (22). "If we had to reckon cancer as a local disease," he argued, "we should have to look for a different remedy for it in each locality." Moreover, he doubted that any part of the body could, of itself, become cancerous, saying that such an eventuality "would be to assume more than can be matched in all the range of sure pathology or of natural history."

Before we meet the localists, it is well to consider those 19th century workers who sat, as it were, on the fence. These workers, the dualists, held to both constitutionalist and localist theories! Sir Astley Cooper was one of them (23). So was Stillé who in 1847 spoke of cancer spreading "partly by the absorption of cancer cells, and partly through the influence of the constitutional diathesis" (24). In the next decade, Wood hedged thus:

The propagation may be owing either to a sympathetic irritation, acting upon a cancerous predisposition, or, what appears more probable, to a transplantation of the cancerous germs through the medium of the absorbents … It is possible, however, that the result may be owing rather to a general carcinomatous diathesis, than the mere progagation of the disease from a single point (25).

By 1864, George Macleod (26) was telling students at the Anderson's University of Glasgow that cancers were "local manifestations of some specific morbid states of the blood". As he saw it, the disease was "a constitutional as well as a local affection."

A dualist turn of mind is deducible from the question posed by Wagstaffe in 1876. He asked, "It seems to me that the occurrence of what appears to be primary cancer at so short an interval in both breasts affords support to the constitutional view of its origin, but why does this not happen oftener, if so" (27)?

Turning to the localists proper, let us begin with their 18th century representatives. As far back as 1748, John Freke was teaching that cancer "is frequently local, and then extirpation will cure it" (28). Early operation was also recommended by Percival Pott in the epochal paper with which he spotlighted chimney sweeper's cancer as "the disease brought on them by their occupation, and in all probability local" (29).

Lecturing around 1786, John Hunter himself had warned his students to bear in mind that cancerous disease "does not affect distant parts, like those

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which really affect the constitution" (30). In 1792 Hugh Munro (31) had declared that scirrhous cancer is always, at first, a local disease. His contemporary, John Pearson (6), commented thus:

But if we may judge of men's opinions by their practice, it seems probable that the greater part of surgeons consider the cancer as a local complaint; since they generally advice it to be removed, when its situation is favourable for an operation. It is also an indisputable fact, that the cancer is often solitary; that it may remain in a quiescent state for many years; that a cancerous ulcer of the lip, or breast, may be removed at a remote period from its first appearance, and the patient never suffer from the disease in any other part of the body.

As the above passage shows, the central argument of the early localists was that cancer starts at a particular locus and remains localized for some time (32). When it "has acquired its largest bulk" or "has acquired the power of contamination" (19), other parts then become involved (33). In other words, such parts are not affected "until a certain maturity of the local disease" (34).

Perhaps, the strongest point made by the localists was the fact of surgical cure (35). In 1829 Benjamin Travers even took into account "all the mistakes of pathology" before accepting "instances of the early and complete removal of the disease" (36).

George Thin considered that, "as the wound resulting from an operation in the part heals well, it follows that the materies morbid is localized" (37). It was, in fact, the focal origin of cancer which raises the hope placed on surgery. When tumor appears again in or near the old operation field, the localist saw this event not as evidence of an all pervading disease but as evidence of the regrowth of tumor tissue incompletely removed during the original operation. In fact, Theodor Billroth concluded that such lymph node recurrence points to the fact that "the earliest commencement of the lymphatic disease escaped our observation, rather than that it did not exist" at the time of previous surgery (38).

The clinical observation of the circle-like nature of cancerous disease also reinforced the localist arguments. Thus, Samuel Young stated that "it would appear obvious that the progress of the cancerous sore is effected by circle after circle, taking on the same disposition from the previously altered structures" (39). In 1885, Herbert Snow stated that "malignant disease of whatever from is, at the commencement, strictly a local disease, starting at one point, next extending around that point as from a focus, but then proceeding to locate itself at distant centres, along a definite track, which can usually be predicted" (40).

The precision of the scrotal focus in chimney sweeper's cancer so impressed Percival Pott that he used this phenomenon to support the localist school. As he put it, the locality of this trade-associated cancer should "be fairly presumed from its always seizing the same part" (29).

The locality of the action of cancer-causing agents struck George Budd in 1845. Because of this, he subscribed to the view "that cancer originates in depraved nutrition of the original nucleated cells of the part in which it first appears." "We are ignorant," he went on, "of the conditions which lead to this depraved nutrition, except in the comparatively few cases in which the disease can be traced to some direct injury, or to some palpable cause of irritation" (41).

Another localist argument was the microscopic mien of the parent primary and its daughter deposits. The lineage of the latter deposits was appreciated by Norman Moore who called them "the descendants of the first growth" (42). A reviewer examined their genealogy in 1872:

Microsopists have discovered an almost invariable similarity between primary cancers and their secondary growths, whether these be in lymphatic glands or in distant parts of the body; and this similarity has led them to believe – not that there is a special cachexia present, which is attended with growths of a special histological structure, although this may be held by some – but that secondary tumours are always the offspring of elements derived from the parent growth, and transmitted bodily therefrom, through the medium of the blood, or by some other available channel (43).

In a great debate on cancer at the Pathological Society of London in 1874, Walter Moxon did not mind his words:

I am sure I may appeal to the experience of many pathologists here when I say that we do find cases of cancer in the colon and in the rectum whose structure is really that of the Lieberkűhn follicles of the mucous membrane of the gut. Well, that would not have been wonderful, if, when we went to the liver, we found that the cancer exploding in the liver had taken the shape of liver tissue, just as when exploding in the rectum it had taken the shape of rectum tissue. The generalist (constitutionalist), if he thinks that there is any general state of cancer which comes out locally, according to the nature of the part, must expect to find rectum cancer in rectum and liver cancer in liver. But instead of that I have repeatedly seen rectum in liver. I do not hesitate to say so; I have seen Lieberkuhn follicles of exquisite construction in the liver itself (44).

How did the Lieberkuhn follicles come to be found in the liver? According to the localists, "propagation" was responsible. This was the apt word used by many of the old authorities (45-49) to indicate the process whereby cancer evolves from a purely local disease to one having body-wide dimensions. The recognition of this phenomenon,

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now called embolism, was perhaps the greatest contribution of localism to oncology.

Rudolph Virchow, the father of embolism, was interested in "the mode of propagation both in the immediate neighbourhood of the diseased part, and in remote organs" (50). So were other authorities, but how differently they expressed themselves! The other renditions included "transfer of the newly-formed morbid molecules to the different parts of the body" (51), "transportation of cancerous emboli - actual, detached fragments of living cancer cylinders – through the lymphatics or the veins" (52), and "spread by lymphatics both locally and to distant parts" (53).

A natural deduction from the localist theory of propagation, namely, that later nodules are smaller than earlier ones, went further to strengthen their theory. Thus, concerning lung cancer, Hasse of Zurich mentioned that other organs are affected "in subordinate degree, as regards both size and development" (54). Of course, gradation in size may not occur. Thus, there are cases "where the distinctions between the ages of the several morbid growths are indefinite" (55).

The fact of size gradation was observed at its best in the lymph nodes (56). "The glands which are found affected earliest in cases of carcinoma," affirmed John Galloway in his Glasgow doctoral thesis, "are undoubtedly those which receive the returning lymph from the affected organ first" (57). John Hughes Bennett of Edinburgh also noted the centrifugal nature of lymph node invasion (58).

The *first* event was the essential theme of the localists. Consider cancer cachexia which impressed the constitutionalists so much. Does it come first or last during the illness? John Zachariah Laurence considered this point in the Liston Prize Essay for 1854. As he concluded, "Authors, it would appear, have in their discussions, not sufficiently separated the two questions – the *existence* of a cachexia generally, and the *time* at which that cachexia makes its appearance" (59).

The success of the localist school went beyond explaining cachexia. It was able to make use of the full force of statistics. Good data were provided by Septimus Sibley in 1859 from the Middlesex Hospital:

In a large proportion of these cases, the secondary tumours were not very distant from the original cancer … In all these instances, the multiplication of the cancer appears to have depended on local, rather than constitutional causes; for if the system were much involved, the viscera would not be more likely to escape the ravages of the disease, than the parts near the original tumour (60).

Discussion

Cancer was long held to be a **constitutional** disease, i.e., a disease which, from its very commencement, attacked the whole body, although it may manifest itself in but one locality of the victim. The members of this school, the **constitutionalists**, began to be opposed during the 18th century by the **localists**. The latter taught that cancer commenced in one locality, grew there for an appreciable period, and then spread to the whole body. Of course, there was in between them the dualists who clung to both concepts.

Conclusion

For well over a century, controversy raged between the historical giants in the exciting fronts of both constitutionalism and localism. However, by 1900, as Senn noted regarding embolism (61), localism had gained complete ascendancy over constitutionalism. Nowadays, it is good to note that the researcher should take time to look back, e.g., the metastatic progression of breast coupled with "insights from 50 years of autopsies (62). Indeed, the famous Australian scientist, Burnet (63), advised that, in order to advance knowledge, one should know about the past!

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