Some remarks on the infectivity of cancer : being an address delivered at a meeting of the East Yorks Division of the British Medical Association at Hull on November 15th, 1907 / by A.T. Brand.

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EX-PRESIDENT, EAST YORKS AND NORTH LINCS BRANCH, BRITISH MEDICAL ASSOCIATION; FELLOW OF THE ROYAL SOCIETY OF MEDICINE.

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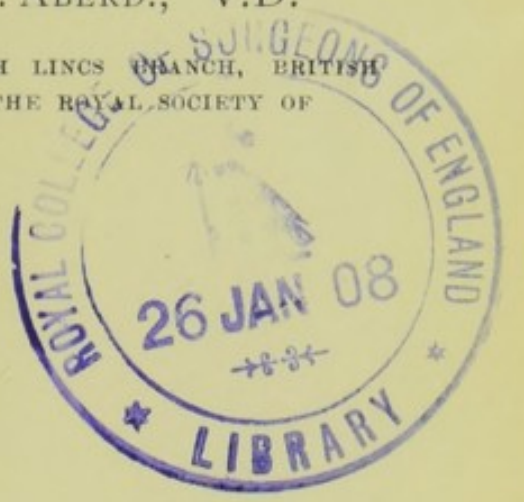

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Some Remarks ON THE INFECTIVITY OF CANCER.*

MR. PRESIDENT AND GENTLEMEN,—The problem, "What is Cancer?" is hoary with antiquity, yet, nevertheless, it is of perennial interest. On two previous occasions I have had the honour of addressing you upon this subject; once on its "Etiology,"[1] and again on its origin by "Exogenesis."[2] To-night I desire to direct your attention to certain points to which I have not previously referred, and to others already mentioned, but which I wish to enlarge upon and emphasise. That the importance of the problem is vital will be admitted by all, for, although many other diseases are just as incurable, and exact even a greater tale of victims than cancer does, there is no disease which is so universally dreaded, or causes more mental distress, in addition to physical suffering. This importance, moreover, becomes still greater when it is realised that the disease is becoming more and more widely diffused—that it is unquestionably increasing.

THE INCREASE OF CANCER.

An appeal to statistics leaves it in doubt whether the percentage ratio is or is not increasing, although the consensus of expert opinion is in favour of increase. No doubt the percentage ratio is affected by the greater accuracy in diagnosis and by the fact that the average duration of life is markedly increased, but it must not be overlooked that many deaths have been certified as due to malignant disease

* The superior figures refer to the bibliography at the end.

which have not been confirmed by *sectio cadaveris*. Even, however, if the percentage ratio is not increasing but remains stationary, it is still evident that cases of cancer must increase in number, *pari passu* with the increase in population. When, therefore, the population of a given place doubles itself, as it does in x years (Vienna, e.g., has doubled itself in 25 years), then the number of cases of cancer must likewise, at the end of this period, be double what it was at the beginning.

Dr. S. Monckton Copeman states[3] in the Guthrie lecture, delivered in 1907 at Westminster Hospital, presumably from reliable data, that of individuals at present living above the age of 35 years, 1 in 8 women and 1 in 12 men will eventually die from cancer. This means that cancer will decimate those of an age above 35 years—truly an appalling prospect!

I regret that I am able to corroborate this estimate of Dr. Copeman from statistics supplied by my own practice. During the last five years there have been 389 deaths certified, of which 44 have been due to cancer (17 males and 27 females), and this yields an annual average of 11·3 per cent. of deaths due to malignant disease. The actual figures are :—

Due to Cancer.

1903	66 deaths	5 (4 females, 1 male)	7·5 per cent.
1904	78 „	11 (6 females, 5 males)	14·1 „
1905	99 „	8 (5 females, 3 males)	8·0 „
1906	72 „	7 (6 females, 1 male)	9·7 „
1907	74 „	13 (6 females, 7 males)	17·56 „

Age.

Between 40 and 50 years...	2	Between 80 and 90 years...	5
„ 50 „ 60 „ ...	11	Above 90 years	1
„ 60 „ 70 „ ...	12		—
„ 70 „ 80 „ ...	13	Total	44

Youngest, 48 years; oldest, 94 years.

Region.

Internal (mouth—rectum)	24
Breast	9
Genito-urinary	6
Intracranial	1
Face and groin	4
Total	44

Under observation, 5.

Cancer Hypotheses.

Since the *causa causans* of cancer has not yet been demonstrated, it is not remarkable that many causes should have been suggested and many hypotheses propounded. Indeed, such causes and hypotheses are countless, and while their attempted recapitulation would doubtless be of great interest such would be but vain iteration. Suffice it to say that all these alleged causes and suggested hypotheses crystallise out into two classes: (1) *intrinsic*, of which the number is "legion"; and (2) *extrinsic*, of which there is but one. *Autogenesis* or *Exogenesis?* "that is the question." No doubt the calm, philosophic, and scientific attitude to maintain upon a subject which cannot be proved to demonstration is that of "the open mind"; but even the calmest, unless he is a disinterested Gallio, must find it hard to remain in a state of passive imperturbability when so much is at stake. Hence it is that there are warm advocates of both these views. The exponents of exogenesis believe that the evidence in favour of the extrinsic origin of cancer is overwhelming, and that this hypothesis will satisfactorily account for the incidence of cancer in every case, and they acknowledge only one possible cause—viz., parasitism. The believers in autogenesis, on the other hand, chiefly maintain a negative attitude, denying the possibility of an extrinsic cause, but fail to formulate any practicable hypothesis which will explain the origin of the disease in every case. They suggest theory after theory, continually shifting their ground, and nohow can they suggest satisfactorily why cancer should arise, apparently *de novo*, in any single case.

Again, the supporters of exogenesis hold that if cancer has an intrinsic origin—e.g., "running to seed"—it would not only be very much more prevalent than it is, but that few, if any, could escape from it. They also hold that an extrinsic origin would satisfactorily account for the proportion of individuals attacked, and believe that the widespread occurrence of the disease among vertebrates indicates the omnipresence of a specific parasite, and that those who are attacked are simply those whose vulnerability, from whatever cause, has permitted its access to the host and favoured its development. The opponents of exogenesis urge that the extrinsic origin of cancer is impossible because it is not entirely analogous to any known infectious disease. The reply to this is that it is most unreasonable and illogical to

presume that pathological processes can be in any way limited or even influenced by analogy; and, furthermore, that analogy is quite incapable of proving anything. At the most, analogy can suggest mere probability, and is, after all, only a very convenient method of comparison between processes which resemble one another.

The following may be cited as a concrete example of the futility of trusting to analogy to establish a conclusion. When Farmer, Moore, and Walker announced their interesting discovery that the karyokinesis of the cells forming a malignant neoplasm is heterotype in character, and that the karyokinesis of the cells of normal reproductive tissue is also heterotype, the director of the Imperial Cancer Research Institute [4] hastened to emit the extraordinary declaration, *ex cathedrâ*, that "malignant new growths were virtually reproductive tissue arising in abnormal situations"!

Now, which hypothesis is most probably right—autogenesis or exogenesis? It is difficult, and even impracticable, to discuss the former, since the various intrinsic hypotheses are too numerous and too elusive, while their very multiplicity testifies to their inadequacy; but exogenesis, having only one string to its bow—viz., parasitism—can be considered. If further information regarding these numerous intrinsic hypotheses and suggested causes of cancer is desired, I would refer you to a work recently written by Dr. Jacob Wolff of Jena, entitled "Die Lehre von der Krebskrankheit von den aeltesten Zeiten bis Gegenwart" ("The History of Cancer from Ancient Times to the Present"). It was published in 1907 by Gustav Fischer and consists of 747 octavo pages.

Since cancer is admittedly a specific disease which runs a definite course of attack, extension by dissemination similar to that of many other diseases, such as tubercle, syphilis, malignant endocarditis, &c., constitutional intoxication, and ending only in death, believers in exogenesis cannot admit the possibility of any somatic cell spontaneously developing specific malevolent action. They are constrained to believe that a specific disease can no more originate without the presence of a specific morbific agent than that parthenogenesis can occur in the vertebrata. This specific agent, they consider, cannot be other than an extrinsic parasite, either a microphyte or a microzoön.

Parasitism.

It may truly be said of parasitism what Shakespeare [5] says of Cleopatra, by the mouth of Enobarbus, "Age cannot wither her, nor custom stale her infinite variety." The universality of parasitism is quaintly but concisely expressed in the quotation from Professor Russell Lowell :—

> "Great fleas have little fleas
> Upon their backs to bite 'em ;
> And little fleas have lesser fleas,
> And so *ad infinitum*."

What is true of the pulex irritans is equally true of all creation. The diseases which we already know to be caused by parasites are very numerous, and so many more are becoming suspected of a like origin that presently one will be driven to conclude that all the ills to which flesh is heir, excepting accidents, are due to parasitism. Organic chemistry has been defined as "The continued history of carbon." It appears that we shall soon be justified in defining all disease (apart from accidents) as "The continued history of parasitism."

Is Cancer Infectious?

If cancer is caused by a parasite it comes under the designation of "infectious." *Is cancer infectious?* Before answering this question, which is the theme of this essay, it were well to define what I mean by the terms "infection" and "infectivity." "Infection" is a comprehensive term and may be defined as the transmission of a disease from one individual to another, directly or indirectly, by the agency of a specific micro-organism, either a bacterium or a protozoön. *I believe cancer to be thus transmissible.* Infection varies greatly in degree, and cancer is evidently not infectious to the same extent as many other diseases—e.g., variola. It is probably acquired much as enterica is by introduction through the mouth; or as syphilis is, by contact; or as tetanus is, by access of the germ to any vulnerable part; or it may be through the agency of an intermediate host, as is the case in malaria or trypanosomiasis.

It has long been maintained, and many concrete instances have been quoted to prove, that cancer is transmissible by

direct contact, as in "cancer-à deux," of which "coition-cancer" is an example. Such transmission, however, has been generally denied and accounted for by fortuitous coincidence; but as transmission by implantation from one lower animal to another of the same species has been successful, and freely admitted to be so by all, the transmission in the case of "cancer-à-deux" has had reluctantly to be admitted as at least possible. This transmission has been designated "transplantation" and not admitted to be the successful and genuine inoculation of a specific disease. Now, if the "transplanted" cancerous tissue resembled a skin graft, always remaining local and forming no tumour, or if it merely continued to grow locally by proliferation without the usual metastatic dissemination and constitutional intoxication, and never caused death, then the term "transplantation" might be justified; but when the characteristic evolution of malignant disease follows, terminating the life of the invaded host, one can only regard the case as one of genuine inoculation of a specific disease by a specific agent—i.e., that it is the result of true "infection."

In connexion with the successful inoculation of cancer in the lower animals of the same species, and also as bearing on the question of "cancer houses and rooms," an interesting communication was made by Dr. Gaylord of Buffalo entitled, "Evidences that Infected Cages are the Source of Spontaneous Cancer developing among small Caged Animals."[6] I regret that the time at my disposal is too short to permit of reference to this paper at length, but I am sure you will find it well worthy of perusal. Dr. Gaylord first refers to the endemic occurrence of cancer of the thyroid in brook trout hatcheries in Germany, recorded by Pick. Pick states that his investigations show that certain hatcheries are entirely free from this affection and that where the fish are affected the disease is confined to individual tanks or pools in which the fish are kept; that wild fish introduced into those ponds to replenish the stock acquire the disease, and this, to his mind, eliminates heredity as a factor in the development of the disease. The nature of the affection is true carcinoma, and he concludes that this endemic occurrence of cancer among trout in certain tanks only indicates that the water of these tanks contains the agent which is the cause of the disease. Dr. Gaylord then proceeds to narrate many instances of cancer occurring in rats which developed the disease after occupation of cages previously occupied by other rats suffering from cancer. These instances are quoted by several observers, both medical and

lay, in the latter case by the man who supplied rats to the laboratory for experimental purposes. It was found that when the infected cages were thoroughly disinfected no further infection occurred.

Auto-inoculation of Cancer.

To my mind, the strongest argument which can be adduced in favour of the exogenesis of cancer is one of its most distinguishing characteristics—viz., its undeviating method of growth and dissemination by proliferation and metastasis and auto-inoculation. Although cancer is unquestionably purely local at the outset, unfortunately it does not long remain so. Indeed, it would be completely under the control of the surgeon's knife and would lose all its terrors were it not for the fatal metastases which are invariably formed and that with a startling rapidity which is not sufficiently realised.

Mr. C. B. Lockwood[7] has drawn attention to this rapid extension of the disease in a communication entitled, "Carcinoma of the Breast and its Spread into the Lymphatics." He points out that in malignant growths of organs which have no capsule—e.g., the mamma, tongue, or pharynx—hardly any interval of time exists between the onset of the disease and its spread into the lymphatics. He says, "In the smallest carcinoma of the breast that I have seen the neighbouring lymphatics were already cancerous." It is this inevitable and rapid metastasis which is responsible for the equally inevitable failure of the great majority of operations for the removal of malignant neoplasms.

Mr. H. T. Butlin,[8] in his recent address in surgery at the annual meeting of the British Medical Association in 1907, on "The Contagion of Cancer in Human Beings and Auto-inoculation," says: "The key to the problem of communicability of cancer in human beings must surely lie in the study of auto-inoculation. If auto-inoculation can be proved on such evidence as would be admitted in a court of law there is a *primâ facie* case for contagion." He then goes on to say: "If the proof of auto-inoculation falls through from the lack of sufficient evidence it is no longer worth while to pursue the study of contagion from individual to individual." Granted, but auto-inoculation of cancer requires no proof. Unfortunately for mankind it is indisputable; it is a marked and only too self-evident characteristic feature of the malady. Every metastasis is a true auto-inoculation. So,

also, is every so-called "recurrence." There is obviously no such process as recurrence. That which has been removed cannot recur, but what has been *left behind* continues to grow. Worse still, what has been set free from divided lymphatics and the tumour itself by the surgeon's knife, and what that infected knife has itself inoculated in and about the wound infallibly grows also. Mr. Butlin's conception of "auto-inoculation" appears to be a very limited one, applying only to the inoculation of an adjacent healthy surface by an affected one. Although it is well known that this auto-inoculation of adjacent structures not infrequently happens its absence or presence is merely of academic interest. Its presence is confirmatory, but its absence cannot in the slightest degree invalidate the obvious fact that auto-inoculation is one of the most marked characteristics of cancer. Mr. Butlin's "key" is therefore ready to his hand, for the condition he considers necessary to establish a *primâ facie* case for contagion is, only too clearly, already in evidence.

Mr. Butlin further says: "Experiment has proved that successfully implanted carcinoma invariably presents, both in the graft and its metastases, the characters of the carcinoma from which it was implanted"; also that, "no transformation has yet been observed of one variety into another variety." Then, as a corollary to this, he adds, "all cases of reputed contagion of cancer, in which the disease is not of the same variety, must be unhesitatingly rejected." With regard to his first point, that grafts and their metastases always present the same characters as the parent carcinoma, it could not possibly be otherwise. It is another characteristic of cancer that "breeds true," and every metastasis, wherever situated, is an actual fragment, or graft, of the original neoplasm, and a cancerous graft implanted successfully in another individual is, to all intents and purposes, a metastasis of the tumour supplying the graft. Consequently, all implanted carcinoma grafts and their metastases must be of the same variety as the original growth. As regards the second point, Mr. Butlin must be unaware of the recent experiments of Ehrlich and Apolant[9] which have demonstrated beyond doubt that even a carcinoma can, under given conditions, lead to the development of a sarcoma in connective tissue immediately adjacent to it. If, then, a carcinoma can give origin to a sarcoma, it is obviously even more probable for one variety of carcinoma to originate another variety of carcinoma. It does not, therefore, appear necessary, after all, to reject the cases of reputed contagion in which the disease is not of the same variety.

Farther on I shall endeavour to show that any one variety of malignant neoplasm may originate any other variety. The reason for Mr. Butlin's rejection of these cases is entirely consistent with his belief, which is that, although he considers cancer to be a parasitic disease, he is not apparently able to admit the logical sequitur that a specific parasitic disease must be necessarily caused by a specific extrinsic parasite. In the Bradshaw lecture[10] delivered by him in 1905 Mr. Butlin maintains that "cancer is a parasitic disease," but that the "carcinoma cell" itself is the parasite and "acts as an independent organism like many a protozoon."

Is the Cancer Cell Itself the Parasite?

Imprimis, there is no such entity as a special "carcinoma cell." Professor D. J. Hamilton[11] of the University of Aberdeen says, with reference to carcinomata: "The old notion that there was a special cell indicative of cancer is erroneous. The only point which is typical about the cells of the tumour is that they are always epithelial; they have no constant morphological features beyond this." The elements of any malignant neoplasm are simply ordinary somatic cells which have undergone abnormal, exuberant proliferation under a specific stimulus. Transmitted by the lymphatics and blood-vessels, or implanted deliberately by artificial means, these cells certainly *appear* to act like independent parasites, but they act in this manner not voluntarily but only by virtue of the intracellular malignant stimulus which is clearly the micro-parasite.

It is impossible for the "carcinoma cell" to be the true parasite.

Let it be supposed for a moment that the "carcinoma cell" could be the parasite, then—1. There must have been an original neoplasm for it to come from. How, then, did this original growth arise? Certainly not from any pre-existing "carcinoma cell," since "*ex nihilo nihil fit.*" 2. All cases of cancer would also of necessity be due to direct contact. 3. All cases of cancer would be of only one variety—viz., the same variety as the original neoplasm from which the "carcinoma cell" emanated. Now, we know that comparatively few cases of cancer are due to direct contact; so few, indeed, that they are not generally accepted as genuine, and the "cell parasite" would account for them only. The great majority of malignant neoplasms

arise apparently spontaneously and sporadically; also it is a characteristic of cancer that its variety is very great. It is obvious that the origin of cancer and its great variety must be explained in some other way than by the direct implantation of a "carcinoma cell" or by the preposterous suggestion that any somatic cell by any intrinsic stimulus can possibly develop *de novo* a *specific* disease such as cancer. We may as well be asked to believe that tuberculosis, for example, can be originated by the agency of an intrinsic stimulus. I beg to submit that the living implanted cell which may be the starting point of any malignant neoplasm must have been derived from a pre-existing neoplasm, and that its malignant influence is due to an intracellular micro-parasite endowed with extraordinary and most malevolent powers. It is this intracellular entity which is the "*deus ex machinâ*" or, as it might be more appropriately designated, the "*diabolus ex machinâ*," of Mr. Butlin's "carcinoma-cell parasite," and this micro-parasite can, and does, exist independently of any cell. It alone is responsible for the original of all neoplasmata.

With regard to his "carcinoma cell," Mr. Butlin states [12] that it exhibits a singular tenacity of life, for such cells have been kept for many days at a temperature below 27° F. or have been placed in sterilised glass flasks and sent across the sea by post and yet have in each case been inoculated with as good a result as if they had just been transplanted from one individual to another. Later, however, he adds that all experiments made with the object of cultivating the "carcinoma cell" outside the body of the host have resulted in failure, and that Ballance and Shattock have reported that they have been unsuccessful even in keeping these cells alive outside the host. These statements are contradictory. It is impossible for living cells of any kind, malignant or otherwise, to retain their vitality for any length of time after removal from their natural environment. Everyone knows that any cells can, by sterilisation, be preserved from decomposition for an indefinite time, but this preservation is not synonymous with vitality. How, then, can these conflicting statements be reconciled, and how was it that these dislocated "carcinoma cells" were successful in inoculating fresh hosts as alleged? Their success was clearly due to the vitality of the intracellular parasite itself and not of the encapsuling cells. The vitality of the intracellular parasite is of paramount importance for the perpetuation of its species and is very great, whereas the vitality of the dislocated "carcinoma cells" is of very brief duration and of

only secondary importance. Although the cell itself is dead it can still originate a neoplasm by virtue of the living intracellular parasite, but the resulting neoplasm is, as I shall presently show, of a different type from that originated by a living cell.

Classification of Neoplasmata.

All neoplasms may be divided, clinically, into: (1) benign; and (2) malignant.

The *benign* are, for the most part, simply local hypertrophies of normal tissue and remain so unless they become infected like any other normal tissue, in favourable circumstances, and they do not form metastases. These benign tumours do not require any specific stimulus to originate them, simple stimulus of a mechanical nature being quite sufficient in many cases for the purpose. They are comparable to the pearl of an oyster which is simply the deposit of a normal substance around a foreign body.

Malignant neoplasms are divided into: (1) epitheliomata; and (2) sarcomata. Epitheliomata arise from epithelium, originally derived from the epiblast and hypoblast. They disseminate themselves chiefly by the lymphatics but also, to some extent, by the blood-vessels. Sarcomata arise from connective tissue, originally derived from the mesoblast. They, on the other hand, chiefly utilise the blood-vessels for propagation but they also utilise the lymphatics. Malignant neoplasms cannot arise without the agency of a definite specific stimulus. These two great classes are further subdivided into very many varieties as regards structure but in all other essentials they are practically the same in each case. This great variety is, simply and entirely, due to the anatomical diversity of the tissues in which they occur and their environment. As Professor Hamilton [11] points out, all such subdivisions as osteoid, villous, colloid, chondroid, encephaloid, &c., are "useless and misleading."

With regard to their method of origin in the tissues, malignant neoplasms are of two distinct types: (1) primary; and (2) secondary. The primary are those formed by the proliferation of the cells of the *local* tissue invaded by the parasite itself. When the parasite is in a *free* state or encapsuled in a *dead* cell thrown off from the surface of a neoplasm (which practically amounts to the same thing, for a cell devoid of vitality is obviously incapable of proliferating and so originating a tumour composed of its own

elements), and when it gains access to the host, then the resulting neoplasm will consist of the proliferated elements of the *local* tissue cells *invaded*. Thus the free parasite emanating from a glandular-celled carcinoma may originate a squamous-celled carcinoma in another individual if it invades such tissue, or the free parasite from a squamous-celled carcinoma—of, e.g., the tongue—may give rise to a columnar-cell carcinoma of the stomach or rectum, or to a spheroidal-celled carcinoma of the mamma, or to any other variety of carcinoma, according to the structure of the tissue invaded. The great majority of malignant neoplasms which arise, apparently *de novo*, are of this primary type. They are originated directly by the parasite itself and indirectly by the tumour from which the parasite is set free. Thus the great variety of cancer is accounted for and to the free parasite are we indebted for the original neoplasm.

The secondary are formed of *alien* cells by the proliferation of the directly implanted infective tissue cells themselves, acting under the stimulus of intracellular malignant influence, the micro-parasite. When the parasite is encapsuled in a *living* cell and this cell gains access to any host the resulting neoplasm will be of the same variety as the *invading* cell, being formed by its proliferation in its new situation and not by the proliferation of the cells of the local tissue invaded, as in the primary type. All that the *invaded* tissue cells do is to provide ordinary nutriment for the proliferating *invading* cells. Thus, the parasite-bearing *living* cell from, e.g., a columnar-celled carcinoma will originate another columnar-celled neoplasm by its own proliferation, quite irrespective of the structure or situation of the tissue invaded. Such infection is immediate and direct as regards the implanted cell and indirect as regards the inclosed parasite. All metastatic growths and all auto-inoculations are of this secondary type For example, the metastasis from a neoplasm of the rectum established in the liver or lungs consists of proliferated rectal epithelial cells. All cases of "cancer-à-deux" and all cases of deliberately implanted cancerous growths are also of this type. So great are the activity and vitality of these malignant parasite-bearing cells that even one such left behind after an operation for the removal of a malignant neoplasm is able to reproduce it. Thus, the infection of invaded tissues by a parasite-bearing living cell, with subsequent proliferation of the latter, corresponds to what occurs after an unsuccessful operation. Now we see that Mr. Butlin's "carcinoma cell" parasite could only originate this secondary type of neoplasm

while the origin of the enormous majority of malignant new growths is left unaccounted for by his hypothesis ; but the primary type of origin accounts for this majority and supplies the original neoplasm from which the living cell, apparently acting as an independent parasite, emanates. It also accounts for the great variety of malignant neoplasms, a variety only limited by the anatomical diversity of tissues.

All this demonstrates how *true* a parasite the micro-organism responsible for cancer is. In the secondary type we find it comfortably ensconced in a living cell which it compels to slave for it, when implanted in any situation, stimulating it to proliferate and so provide accommodation for its numerous progeny. It exerts no personal influence whatever on the surrounding local tissue cells, which are generous enough to furnish the invaders with food supplies. It is only when death of the host occurs, or if perchance a cell dies and becomes detached from the colony, that its tyranny ceases for a time. Now it must make personal exertion and endeavour to find a fresh victim in the cell of the nearest available living tissue. Having succeeded in gaining a footing it proceeds to induce the selected invaded cell to commence work by proliferating, and the process progresses as before except that this time it is the cells of the local tissue which have both to increase in number and find their own food. This is the primary type.

In all other parasitic diseases the micro-organism of causation remains free and active personally, but the cancer parasite is the *truest* parasite of them all, for it never exists free if it can avoid it, but clings to its cell-host with indomitable pertinacity.

The Parasite of Cancer.

Although its presence is proved by induction, as is also the existence of, for example, the micro-parasite of variola, the parasitic agent of cancer is, as the Germans say, "*noch nicht konstatirt*" (it has not yet been conclusively demonstrated). Doyen of Paris believes that the bacterium known as "micrococcus neoformans" is the germ responsible for cancer. This belief appears to be corroborated by the researches of Dr. C. Jacobs and Dr. Victor Geets, the result of which was communicated by them to the Royal Belgian Academy of Medicine at Brussels in January, 1906 [13] These observers report that it is practicable to immunise the human organism by means of a series of inoculations of the micrococcus

neoformans vaccine, provided that these are properly controlled by examination of the opsonic power of the blood. They cultivated the micro-organism from 90 per cent. of tumours examined and succeeded in producing localised, or generalised, neoplasmic lesions in 30 per cent. of the cases, by inoculating young and vigorous cultures of the micro-organism into mice and white rats. They prepare the vaccine in exactly the same manner as Koch prepares his tuberculin T.R. and treat their patients in a similar way to the vaccine treatment of tuberculosis. They allege that in some cases they obtain cures, but point out, however, that as tuberculin does not cure all cases of tuberculosis, cancer vaccine, too, cannot cure all cases of cancer. Success or failure depends entirely upon the reserve of vital energy and capacity for reaction which each patient possesses, and these differ in each case. Other observers—e.g., Wright—have failed to confirm these results and they are, I believe, now discredited.

Roswal Park, Gaylord,[14] and others in America believe that cancer is caused by an organism of the same nature as the plasmodiophora brassicæ. Their observations seem to prove that minute plasmodiophoræ are present in carcinomatous tumours and that they can be grown from such tumours through a definite stage in their life cycle. In summarising their results and conclusions Dr. W. Ford Robertson and Mr. Henry Wade[14] state that they had been able to recognise in carcinomatous tumours bodies which, in their form and in their reaction to the platinum and silver-gold methods, are identical with the plasmodiophora brassicæ but from $\frac{1}{10}$th to $\frac{1}{20}$th of the size. They had succeeded in growing from three carcinomata an organism which accurately represented the post-spore or pre-amœboid stage of a plasmodiophora. If plasmodiophoræ were present in carcinomatous tumours it was hardly open to doubt that they had the same relation to the morbid growth as the plasmodiophora brassicæ had to "club-root," that was to say, that they were the determining etiological factor.

In a later communication (August, 1907) Dr. Ford Robertson[15] claims that he has obtained much new evidence which he considers confirmatory of this view, evidence derived from cultural and histological observations of the occurrence of special intranuclear bodies of the nature of those previously described, to show that structures morphologically identical with the spirochæta microgyrata can be demonstrated in human carcinomata. Gaylord and Calkins[15] have also described a special spirochæta in primary and

transplanted carcinoma of the breast in mice. The confirmed discovery that spirochæta pallida is the etiological factor in syphilis is analogically suggestive of a spirochætan cause of cancer. Much undoubtedly remains to be done, however, before the elusive parasite can be demonstrated to the satisfaction of all; but these discoveries tend to show that the net is gradually, but surely, closing around it.

I offer the suggestion that the examination of fresh, living, carcinoma cells on the warm stage of the microscope would result in much additional and valuable information; also that the employment of high power microscopy would be a great aid to investigation. The objective of a microscope reaches the limit of its useful development in the direction of increasing magnifying power as soon as, by reason of the shortening of the focal length, the diameter of the object glass, in its principal plane, is reduced to something not much less than the diameter of the pupil. Added power, however, to any required extent can be obtained by high power oculars, but the image thus obtained is rendered defective by the blurring of the image from dust and obstructions in and on the lenses, and by the observer's eyelashes, tears, and muscæ volitantes; but, quite recently, the image has been rendered perfectly clear and very high magnifying power obtained by the skill and ingenuity of an expert in microscopy. In February, 1905, at a meeting of the Royal Institution of Great Britain, Mr. John W. Gordon[16] described a device by which a magnification of 7000 diameters could be obtained as well as a perfectly clear field of view. Mr. Gordon substitutes for the eyepiece a compound microscope with a half-inch objective and an ocular magnifying eight times. A ground-glass screen is held in the image plane of the principal microscope, and this screen is made to revolve and also at the same time to oscillate eccentrically. The screen abolishes the intrinsic images of dust and foreign matter and the eccentric rotary motion renders the screen invisible.

Quite as important as high magnification of the image is good field illumination. Dr. Siedentopf[18] has devised a system of dark field illumination, applicable to objectives of the widest possible aperture, which renders visible objects so minute and clustered so close to one another that by no other known contrivance can they be rendered separably visible at all. I must not further occupy time in describing this system of illumination and would refer those interested to the Proceedings of the Royal Institution of Great Britain, Vol. XVIII.

There is another desideratum of the greatest importance in the histological investigation of cancer which, I fear, is more likely to be sought for than found, and that is a specific staining reagent which will act on cancerous tissue in an analogous manner to the selective action of iodine upon the diseased areas in amyloid disease which renders them clearly distinct even to the naked eye. It is true that there is such a selective stain, but it acts only in one species of malignant neoplasm. I allude to the staining by melanin in melanotic cancer. Its presence makes it possible not only to detect every particle of original and metastatic growth in this variety, both macroscopically and microscopically, but it also permits optical demonstration of the method of dissemination by the blood-vessels and lymphatics. This has been most ably demonstrated by Mr. W. Sampson Handley [17] in his Hunterian lecture on the Pathology of Melanotic Growths in Relation to their Operative Treatment.

The Condition Precedent.

Since perfectly healthy tissues are probably immune from, or invulnerable to, the attack of the cancer parasite, there must be causes predisposing to the acquisition of the disease, and these go to form what I have called the "condition precedent." This condition is induced by whatever lowers or impairs the power of resistance of the body to infection. In the case of cancer the chief factor in producing this vulnerability is degeneration of tissue from any cause, but more especially that due to obsolescence of organs, senescence, and senility, for cancer is, *par excellence*, the disease of advanced age, though by no means confined to it. This is obviously due to the fact that in those of middle and advanced age decay is in marked and increasing excess over repair (the reverse being the case in youth), and the tissues are less equal to the strain of resisting the attack of the aggressive parasite, especially when this degeneration exists in conjunction with the other predisposing factors of this condition, which are chronic disease, continued irritation, traumatism, and congenital susceptibility. In my opinion, it is the failure to realise the invulnerability of young and healthy subjects which is one of the causes of so many unsuccessful inoculation experiments. I have discussed this point fully in another paper.[2]

Channels and Mode of Infection.

I have elsewhere[12] fully considered the channels of infection and it remains to consider how one becomes exposed, unknowingly, to the risk of attack by the parasite. This evil agent appears to be practically omnipresent, as so many other pathogenic micro-organisms are, such as the bacillus tuberculosis, the bacillus tetani, and the malevolent legion of micrococci, and it is ever ready to act aggressively as opportunity arises and circumstances favour. One hardly appreciates how very close the relationship is, if only indirectly, with our neighbours, including those suffering from cancer. All our food, both cooked and uncooked, passes through the hands of many individuals, and the only safeguard, cleanliness, on their part is practically beyond our control. As evidence of this I give you an instance from personal experience. A widespread epidemic of enteric fever which occurred in a village near Driffield, in which I had several patients, was easily traced to an imported case which was nursed by a woman who supplied milk to all those attacked. This woman, though altruistic, was a most uncleanly person and made it her practice to milk her cows without even washing her hands, and that immediately after attending to the discharges and soiled linen of her patient. Much vegetable food, e.g., salads and fruit, is eaten uncooked. Each strawberry, for example, we eat is gathered by the unwashed hands of the gatherer. Strawberries also lie very near the ground, as do lettuces, &c., and are readily accessible to domestic animals, such as the dog and cat, which also suffer from external cancer as well as from intestinal worms. There is an article published in The Lancet of July 16th, 1904, entitled "Fruit and Filth,"[13] which will well repay anyone's perusal, provided the reader is not too greatly under the dominance of his nerves, or has not too lively an imagination, for anyone who reads that article is not likely to touch strawberries again unless he picks them himself from plants above suspicion of defilement.

Far be from me the desire to harrow your feelings too deeply, but how, let me ask, is one to know that the common house-fly, which crawls all over our bread and butter, or other article of food, was not, immediately before, disporting itself on the surface of a cancerous wound? Flies are well known to carry tubercle and typhoid bacilli, as well as other pathogenic micro-organisms, on their feet, and in the stomach, and it is also well known that they have infected

food and drink with these germs, with disastrous results. I would refer you to a very able and suggestive communication published in THE LANCET of July 27th, 1907, under the title of "The Carriage of Infection by Flies."[19] This article gives the result of experiments made by Dr. R M. Buchanan, bacteriologist to the corporation of Glasgow, with the object of demonstrating this fact. I wrote to Dr. Buchanan to inquire if he had made any experiments as to the cancerous contamination of food by flies and received the following reply: "I have not yet tried the experiment you suggest with reference to cancer, but hope to do so as soon as I can obtain material. The same problem presented itself to me in connexion with the death of a friend some years ago from intestinal cancer."

One's own footgear must bring much dust, laden with all kinds of pathogenic micro-organisms and, on occasion, dust from a cancer sufferer's room, into one's house, and it may easily find its way to one's food, &c. In this connexion the Eastern custom of leaving the outside shoes at the entrance of the house has, truly, much to commend it. Another risk to which we are exposed is eating the flesh of animals which have been suffering from malignant disease when killed. In December, 1904, according to press cuttings in my possession, a man was fined £50 and £7 costs at the Guildhall, London, for sending meat to Smithfield which on examination was found to be sarcomatous. It cannot be assumed that this is a solitary instance, only it happened to be discovered. Cooking is said to minimise risk, but underdone meat is not unpopular.

I once knew a dentist who suffered from cancer of the prostate, from which he eventually died, and who followed his occupation during his illness. One of the physical signs of his malady was a urethral discharge, which necessitated frequent manual attention. I have no reason to doubt that he occasionally washed his hands! In my own practice[1] a patient suffering from a fungating cancer of the mamma was nursed by a woman who frequently had occasion to remove soiled dressings and who was not particularly cleanly in her habits, and did not always wash her hands before meals. Within a year of her patient's death the nurse developed cancer of the stomach and died. This may have been a coincidence but I believe it to have been a case of indirect infection, a neoplasmic disease of the primary type.

I have thus indicated a few possibilities; some may be considered far-fetched, still they are possibilities, and unpleasant ones; doubtless many more will occur to yourselves.

Prophylaxis.

From the foregoing it is obvious that the only reliable prophylactic against cancer as well as other filth diseases, and it is an efficient one, is cleanliness in its widest sense. Earth burial, with all its hideous possibilities, should be superseded by cremation of all who die from infectious disease, and especially from cancer. Cremation would deal with the disease at its source. All soiled dressings and discharges from cancerous subjects should be destroyed by fire and all rooms inhabited by them should be most thoroughly disinfected both during the illness and after death. No food should be prepared or consumed with unwashed hands.

New Facts about Cancer.

Within recent years several new facts have been discovered about cancer. 1. The mitosis of the cells of malignant neoplasms has been found to be heterotype in character, whereas the mitosis of all somatic cells with one exception, and of the cells of benign tumours, is homotype. The mitosis of normal reproductive tissue is also heterotype. 2. It has been discovered that cancer is not restricted to the higher vertebrata, e.g., man and the domesticated animals, as was at one time supposed, but that it occurs in all vertebrata, with the possible exception of certain reptilia. The malignant growths occurring in other vertebrata are identical with those found in man, clinically, pathologically, anatomically, and microscopically. 3 The transmissibility of malignant new growths from one lower animal to another of the same species has been demonstrated.

With regard to the first of those discoveries it was the resemblance between the mitosis of malignant cells and that of normal reproductive tissue cells which led to the enunciation [1] by the director of the Imperial Cancer Research Fund of the famous analogical fallacy that malignant new growths are merely reproductive tissue in abnormal situations. The heterotype character of the mitosis of malignant cells and the homotype character of somatic and benign tumour cells are, indeed, of academic interest but of little or no practical importance beyond affording a possible means of differential diagnosis in some doubtful cases which, however, would signally fail in the case of tumours of the reproductive tissues, since the mitosis is heterotype in either

case, whether benign or malignant. It has been suggested to me that the fact of the mitosis of malignant and generative tissue cells being heterotype in both cases was important as showing that generative tissue cells, like those of cancer, have the power of proliferation. Of course, this fact cannot prove any such power, since analogy can prove nothing, but can merely suggest ; still, if it could prove it it would not be necessary to corroborate the power of proliferation of generative cells, since the first infant one comes across is ample and convincing proof of that! At the same time there is a very suggestive parallel between the two proliferations. *Neither generative tissue nor other normal tissue cells can proliferate without a specific stimulus.* In the case of generative tissue the ovum only commences to proliferate when it has been invaded by the spermatozoon, which acts practically as an extrinsic specific protozoan parasite. The proliferation is enormous and rapid. The resulting tumour is benign, though some might consider it to be a malignant tumour in a normal situation! It is easily got rid of, and "recurrence" does not take place unless there is reinfection! In the case of somatic cells proliferation only commences when they are attacked by the cancer parasite. Mitosis becomes heterotype, proliferation goes on apace, and the tumour is malignant and impossible to eradicate. Nothing is known of the method of the influence of the cancer parasite on the somatic cell, any more than the influence of the spermatozoon on the ovum is understood, but it will be admitted that the one process is equally as marvellous as the other.

With regard to the second of these facts, among the vertebrata in which cancer has been discovered to exist are certain fishes, found both in rivers and in the ocean round our coasts. This fact has induced the director before mentioned to state[20] that "the wide zoological distribution of malignant new growths indicates that the cause of cancer is to be sought in a disturbance of those phenomena of reproduction and cell-life which are common to the forms in which it occurs." Thus he makes another statement of opinion which clearly indicates how little is the help towards solution that may be expected from intrinsic hypotheses and their advocates. To the "man with the open mind," however, it might probably occur, as it certainly does to me, that this wide distribution of cancer throughout the vertebrata, with the resulting great diversity in environment, food, and conditions of life generally, was suggestive of the omnipresence of a specific malevolent agent of great vitality ; that, with regard to the

fluvial and marine fishes found bearing cancerous growths, this fact might well suggest that the specific cause of cancer is water-borne and, like the bacillus typhosus, it is not injuriously affected by sea-water; and, finally, that since the neoplasms found in fish are identical in every way with those occurring in man, infection may well have arisen through the agency of parasite-bearing sewage polluting both the rivers and the ocean into which they flow.

Regarding the third discovery of the transmissibility of cancer from one individual to another of the same species, although this has had to be admitted, it is qualified by the assertion that such transmission is merely a transplantation of a graft of a malignant tumour and not the genuine inoculation of a specific disease. It would be more graceful to concede that since transmission between individuals of the same species is proved to be possible it may be eventually found that transmission between animals of different species, and even the development of one variety of malignant growth from another, is possible also.

An admission which may be looked for sooner or later is that a carcinoma of epithelial origin has been observed to give rise to a sarcoma in the adjacent connective tissue. Then will be confirmed the dictum that cancer is a specific infective disease and that one specific micro-organism is capable of originating every variety of malignant neoplasm, the variety depending upon, and only limited by, the anatomical diversity of the structure and the situation of the tissue invaded.

Deductive Evidence.

As it is necessary to apply the strictest canons of logic to the arguments brought forward in support of any hypothesis I beg to submit the following, which to my mind fulfils this postulate. Every specific disease is infectious to the individual. By this term, "infectious to the individual," I mean the gradual evolution of disease, more or less rapid, locally and constitutionally, over the body from the point of origin of the disease. Specific diseases infectious to the individual are very numerous and are caused by the agency of some extrinsic parasite, either a microphyte or a microzoon. These diseases are communicated to others, directly from individual to individual, or indirectly by inanimate objects, or through an intermediate host.

Now cancer is, emphatically, a specific disease, and it is intensely infectious to the individual ; therefore, the only logical conclusion that can be drawn is that cancer is both transmissible to others and that it is caused by an extrinsic agent. Except for the solitary fact that the elements of a malignant neoplasm—i.e., its cells—are themselves transported, in addition to the infective agent (which is the peculiar and characteristic idiosyncrasy of cancer), this disease very closely resembles in its origin and evolution a chronic infectious disease.

My argument may be condensed into two syllogisms—viz : 1. All diseases which are infectious to the individual are transmissible to others. Cancer is infectious to the individual. Therefore cancer is transmissible to others. 2. All diseases which are infectious to the individual have an external origin. Cancer is infectious to the individual. Therefore cancer has an external origin.

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