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Contributors

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CONTRIBUTION

TO THE

ÆTIOLOGY OF CANCER,

PRESIDENTIAL ADDRESS

DELIVERED BY

ALEX. THEODORE BRAND, M.D., C.M.

DRIFFIELD

MEDICAL OFFICER DRIFFIELD COTTAGE HOSPITAL

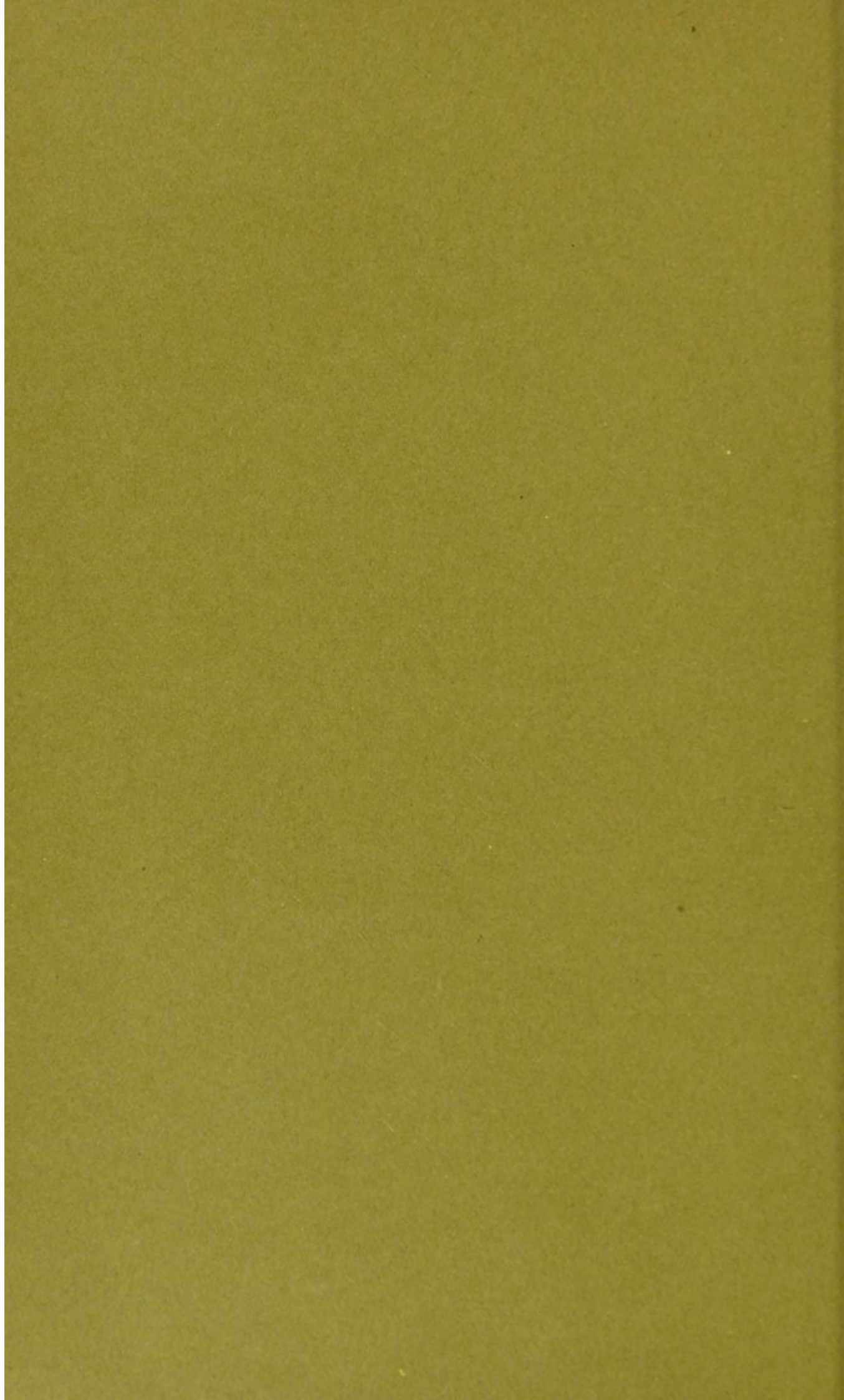
BEFORE THE EAST YORKS AND NORTH LINCOLN BRANCH,
BRITISH MEDICAL ASSOCIATION

AT HULL, THE 28TH MAY, 1902



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A CONTRIBUTION TO THE ÆTIOLOGY OF CANCER.¹

BEFORE inflicting upon you what can only by a euphemism be termed a "Presidential Address," I desire to thank you very sincerely for the great honour you have conferred upon me, by electing me to the Presidency of this branch for the coming year, an honour which, I assure you, I appreciate very highly.

When I think of the long line of illustrious men who have preceded me in this chair, the knowledge of my unfitness for the honourable position presses heavily upon me, and the fear haunts me that you also will share this knowledge long before my term of office has expired. I therefore crave your kind indulgence for my shortcomings, and your assistance in the discharge of my duties.

The choice of a subject on which to address so erudite and critical an audience is, I should imagine, ordinarily difficult enough, and I have found it especially so, for, as a general practitioner, and a country one at that, I can offer you no record of brilliant surgical successes, or original operations, nor can I present to you an interesting series of recondite medical problems successfully solved.

In a minor way, certainly, I suppose I may be entitled to be considered somewhat of a Specialist, since, as a disciple of the immortal Jenner, I practise, extensively and successfully, the prophylactic treatment of Variola; but on this subject I have nothing unusually interesting to submit.

There is one dread Disease, however, which is equally familiar to us all, whatever position we may occupy in the

¹ An abstract of this address is published in the *British Medical Journal* for 26th July, 1902.

medical world, which may be very aptly described by the term that Robert Burns applied to toothache, *viz.*, the "Hell of all Diseases," whose true nature we are as yet ignorant of, which is, without doubt, increasingly prevalent, and which is inevitably fatal.

It is almost unnecessary to say that I refer to Cancer, a subject of absorbing interest, and to this I wish to direct your attention. I regret that the time at my disposal is so short that it is impossible to treat this subject with the fulness its importance merits, therefore what I shall be able to bring before you this afternoon can be only sketchy and imperfect. At the outset I may state that under the generic term of "cancer" I include all that is clinically described as "malignant".

This mysterious disease, which is alike the scourge of mankind and the reproach of medicine, has, for decades of centuries, eluded and defied all efforts made for the elucidation of its nature and cause.

There is ever a fascination about a mystery, and the discovery of the cause of Cancer has long been to the young and enthusiastic Medico what the invention of a practicable perpetual motion machine is, or used to be, to the budding Engineer, or what the discovery of the *elixir vitæ*, or the philosopher's stone was to the Alchemist of the past; and it is devoutly to be hoped that the Medico will meet with better success in his quest than the others have done.

Since, unfortunately, no one, so far, has been successful in the search for the cause of Cancer, and as no one has discovered a reliable empiric remedy for it, there has been engendered in the Medical Profession a mental attitude of the most profound pessimism, amounting indeed to absolute fatalism, and this, if possible, obtains even more strongly with the Laity.

Defeat must not, however, be permitted to paralyse our energies, it should rather be a stimulus to renewed efforts.

We must recognise no such word as "impossible" and, without doubt, one day, success will be assured.

If success has not been attained it has not been for want of endeavouring to solve this problem.

Numberless specific causes have been suggested, and many theories have been evolved, but the very number and variety of these simply go to prove that the true cause has still to be discovered.

ALLEGED SPECIFIC CAUSES.

Among many other alleged specific causes Cancer has been ascribed to over-indulgence in tea, in sugar, to the consumption of the succulent but harmless tomato, to excessive flesh-eating, and to excessive consumption of common salt.

Well, Cancer was in existence long before tea and sugar became articles of diet, and thousands die of Cancer who never heard of the existence of a tomato.

With regard to excessive flesh-eating, this would, doubtless, give rise to an excess of uric acid in the blood, which is alleged to cause many of the ills to which poor mortals are heirs, and among others to Cancer; but when we find Cancer occurring freely in the Hindoos, who eat flesh sparingly if at all, and also when it occurs in such strict vegetarians as the horse and cow, we fail to see an exclusive causal relation to Cancer on the part of flesh-eating, excessive or otherwise.

Of these alleged causes common salt alone is a vital necessity to the organism, and all warm-blooded animals partake of it to the necessary degree, without exception.

Braithwaite alleges that pigs alone of domesticated animals do not have salt given to them, and that, in consequence, they are not subject to cancer.

Pigs do appear to enjoy immunity from cancer to a

notable extent, but, whatever the reason may be,¹ it is certainly not abstention from salt. The Pig consumes quite as much salt as the Dog, in which Cancer is, *e.g.*, quite common. The source of the salt is, obviously, the food given, which is specially rich in salt, *e.g.*, skimmed milk and the *olla podrida* of the swill-tub.

It is altogether unreasonable to suggest that a specific disease, such as Cancer is, can possibly be caused by excessive consumption of flesh, as alleged by Mitchell Banks, or by excessive consumption of salt, as alleged by Braithwaite. It is not unreasonable, however, to assume that the tissues may be so irritated by this consumption as to be rendered more vulnerable, so that a condition precedent is established, but this must be the limit of their evil influence.

The confounding of *post* and *propter* constitutes a common fallacy, and it is equally illogical to suggest, as the cause of Cancer, that which is not universally applicable.

THEORIES.

Of the many Theories advanced I shall very briefly pass in review a few of the best known and most important.

The first I shall mention is Cohnheim's which attributes malignant tumours to awakened growth of Embryonic Rudiments.

I believe no one has ever seen any such rudiments, and if they, perchance, do exist I presume something must awaken them; and it is reasonable to suppose that this something may be the *x* cause of Cancer.

¹ The "optimum" temperature for the growth of pathogenic bacteria in Man is 98°-99° Fh., and a temperature lower or higher is less and less favourable in proportion to the amount of deviation from the "optimum," and the virulence of the toxins secreted becomes correspondingly reduced.

Now, the normal temperature of the Pig being 103°-105° Fh., it is not unreasonable to assume that this temperature is sufficiently unfavourable to the growth of the Cancer bacterium to account for its unsuccessful culture in the Pig, and hence the immunity of this animal from Cancer.

Another theory is that of Thiersch who maintained that epithelioma is due to a war between columns of epithelial cells growing downwards and loops of blood-vessels growing upwards, until they meet and interlock in deadly combat. This may, and no doubt does, more or less accurately describe what goes on in an epithelial growth, but it does not suggest the *casus belli*, which is the cause of malignancy we are in search of.

Then Hansemann thought that Karyokinesis was concerned in the causation of Cancer. Here again we have only a description of what goes on in the nuclei of the developing cells of malignant tumours.

Karyokinesis takes place in the nuclei of normal cells as well as in pathological ones, and if the method of mitosis differs according to the kind of cell, it is only what might be expected, but it does not suggest a cause to account for this difference, and therefore does not explain the originating cause of Cancer.

It is interesting to find, in connection with this karyokinetic process, that some observers, noticing the rapid evolutions going on in the nuclei of developing tumour cells, have been deceived into believing such cells to be actual microzoa; while others have mistaken wandering leucocytes, etc., for coccidia, and so still another theory has been evolved *viz.*, the Parasitic Theory of Cancer.

Again, there is a Theory which attributes Cancer to the Spermatic Influence of Cells, whatever this may mean.

Here the cells of a tumour, having increased in number, are said to exert such an influence upon the surrounding healthy cells of the connective tissue, that the latter are stimulated likewise to increase in number, not, however, in their own proper structure, but transformed into the same type as the exciting tumour cells. Once more we have to ask, "What is the originating cause of the primary tumour

which in turn exerts such a malign influence upon the surrounding connective tissue cell?" It is, doubtless, the *x* cause of Cancer.

The last theory I shall mention is that suggested by Creighton, *viz.*, that Cancer is due to the Unconscious Evil Memory, or Bad Habit of the Tissues. He says Cancer is "the peculiar Nemesis of secretion or other epithelial action gone wrong, of long-standing catarrhs, repeated congestions, or habitual irritations of epithelial surfaces, or the peculiar liabilities of women in respect to the early obsolescence of their primary and secondary sexual structures and functions."

This is simply a statement of the condition precedent. Irritation, *per se*, can never cause a specific disease such as Cancer, though it can and does most materially assist the true cause.

Most of these theories seem to me to have been built up by dreamers at the ocular end of a microscope in histological laboratories, and there they may very well be permitted to remain as museum specimens, for all the practical value they are to any one.

No doubt they are interesting, but at the most they are only descriptive of pathological processes, or suggestive of probable contributory factorship. Nowhere do they suggest the originating cause of a specific disease.

One recent writer, who, in common with the authors of these theories, appears to believe in the autogenesis of Cancer, *i.e.*, that the cause of Cancer is to be found within the organism, gives it as his opinion that the cause of Malignancy will only be explained when we know more of the cause of the development of foetal organs.

Alas! if we have to wait so long; for when we know that we shall know everything, even to the cause and origin of life itself, and that, I presume, will be when

we are all behind the Veil, where Cancer, and all other mundane evils, shall have ceased to interest us !

INFECTION THEORY.

What I conceive to be one great barrier to the discovery of the cause of Cancer is the apparently universal feeling that this cause is desperately recondite and complex ; whereas it may, and probably will, be found to be excessively simple with nothing especially mysterious about it.

If we are to make any headway in the elucidation of Cancer, we must discard all dreamy theories, and form a good working hypothesis, and it is the practical man, not the dreamer, who will succeed. The clinician and the experimental pathologist must combine and work upon such a hypothesis, and only abandon it when it has been proved conclusively to be untenable, and not merely because it is said to be impracticable.

Now, there is a Hypothesis which suggests that the cause of Cancer exists apart from the organism, *viz.*, the Infection Theory.

It has been stated of this Theory that the negative evidence is abundant, and what little positive evidence exists will not bear criticism. Now, to say that a disease cannot be infectious because the infective agent cannot be found, or because it is not strictly analogous to another disease, known to be infectious, is pure *petitio principii*.

Infectious Diseases present the widest diversity in their nature and behaviour, *e.g.*, in their length of incubation, their mode of attack, their eruptive characteristics, their sites of selection, their duration, the tendency of some to pass, and the inevitably fatal ending of others.

What can be more striking than the difference between the fulminating rapidity of action of malignant Bubonic Plague, Cholera or Yellow Fever, and the very leisurely

advance of Leprosy; or the difference between the rose rash of Enterica and the loathsome eruption of confluent Variola?

The very Microbes themselves display a variety not to be surpassed by a garden of flowers.

I have no doubt whatever that in time it will be found that very many diseases, of whose origin we at present know nothing, will be demonstrated to be due to Microbes and their toxins.

For example, that most mysterious disease, so rapidly fatal, Landry's Paralysis, in the absence, in many cases, of all pathological signs in the spinal cord, together with the enlargement of the spleen, is shrewdly suspected of being caused by the toxin of some microbe as yet unknown.

Again, who, twenty years ago, would have suspected that Tetanus is caused by the toxin of a bacillus?

From what I have read and observed, the belief has been forced upon me that the cause of Cancer comes from without the organism, and that the Infection Theory is an excellent working hypothesis.

It is the only hypothesis, to my mind, that meets the case fully. It can explain everything in connection with Cancer,—its origin, its growth, its undoubted and ever-extending increase, and its behaviour generally.

It should, therefore, be the aim of us all to investigate the subject on this hypothesis, and satisfy ourselves of its truth or falsity.

We should, farther, hope, all the more fervently, that this hypothesis shall be established, when we realise that, if Cancer originates within the organism, whether from the misbehaviour of laggard embryonic rudiments, or any other peculiar misconduct of our tissues, we are confronted by the grim truth that no treatment can ever be hoped to be successful on any lines; for, if there is one thing more

certain than another, so far as I can see, it is the utter hopelessness of any specific antidote to Cancer fortuitously forthcoming.

Many alleged specific remedies have been announced from time to time, and many methods of treatment have been promulgated, but one and all have proved utterly futile.

Recently a sensational statement regarding the efficacy of violet leaves in Cancer went the round of the lay newspapers; and cases of Cancer have actually been treated, in an orthodox hospital, with the remedies of that gigantic fraud and archquack, Count Mattei.

Now, no one will deny that man's capacity for self-deception is enormous, or that the credulity of mankind is unbounded, but, when we are asked to believe that boiled violet leaves, externally applied, effected a cure of cancer of the larynx, or that *aqua simplex*, of doubtful purity, can heal a fungating mamma, or render patent a stenosed pylorus, even unquestioning faith must pause, appalled!

If, on the other hand, the cause of Cancer comes from without, there is every hope that this disease will eventually be overcome, yielding to prophylaxis and specific treatment.

I admit that the weak point in this hypothesis is its extreme simplicity.

It cannot be expected to commend itself to those who are fascinated with such complex and involved mysteries, more mouth-filling than anything else, as Karyokinetic Evolutions, Spermatie Influence of Cells, awakened growth of Embryonic Rudiments, Unconscious Memory of the Tissues, *et hoc genus omne*; but the simple theory of Infection has this to recommend it, that it is eminently practicable, while the others are utterly impracticable.

Of course the acceptance of the Infection Theory involves the acceptance of the existence of an infective micro-organism, whether microzöon or microphyte, not yet discovered;

but this need not stand in the way of its acceptance, since no one questions the fact that Variola, Pertussis, Scarlatina, or Morbilli, etc., are infectious and 'due to the influence of micro-organisms, although no germs have, so far, in these cases, been isolated.

Nor need we look to the microscopists, who have already run amok among imaginary coccidia, normal or pathological cells undergoing karyokinesis, or pseudopodiferous amœbiform leucocytes engaged in diapedesis or in patriotic phagocytosis,—it is not to them that we must look for help, but to the practical observer and the experimental pathologist.

Is it too much to hope that, when the latter have established the Infection Hypothesis, the histologists may at length discover the special microbe, or microbes, of Cancer? It is true that Scheuerlen and Doyen have reported the presence, in cancerous tumours, of microbes which they believe to be the active agents in their origin but, so far, causal nexus has not yet been conclusively established.

HISTORICAL.

That Cancer is infectious has long been a belief. In the middle of the seventeenth century, Zacutus Lusitanus stated his belief that Cancer is contagious, and cited cases. In 1672 Nicolaus Tulpius, the famous anatomist, whose portrait must be familiar to most of us from the picture painted by Rembrandt, was so sure of it that he stated that "an ulcerated cancer is just as contagious as an inflammation of the Eyes". Juncker, in 1731, said that successful engrafting necessitated that the infective material should fall on a suitable place where there was already a breach of the surface. In 1773 the Academy of Medicine at Lyons discussed the subject.

EVIDENCE MUST BE CIRCUMSTANTIAL.

In the absence of a demonstrated microbe, to try to prove this hypothesis of Infection, one must fall back upon inductive methods.

The evidence in favour of Infection must, necessarily, be circumstantial; but such evidence need not be less valuable on that account.

The planet Neptune was not, primarily, discovered by the telescope. It was not until its exact situation had been indicated by the purely inductive reasoning of Adams and Le Verrier that it was, at length, actually seen by the telescope. These men based their hypothesis upon circumstantial evidence alone, and this evidence was the aberrant behaviour of another planet, Uranus, in its orbit.

EVIDENCE OF THE EXOGENESIS OF CANCER.

In stating the evidence in favour of the external origin of Cancer, one might begin with the general statement that the cause must come from without, because the cause of, practically, all disease exists outside the body, for it is extremely problematical if any disease can possibly arise, of itself, within the organism.

This general statement, however, will not materially help to establish the Infection Hypothesis, and so recourse must be had to more particular evidence.

To my mind, the great, central, fundamental and most convincing argument in favour of this Hypothesis is the incontrovertible fact that Cancer, once generated, spreads locally by infecting its immediate environment, and that it is disseminated metastatically by the blood current and lymph streams, the latter infecting glands *en route*.

Each metastatic mass and infected gland becomes a fresh focus of further infection and dissemination. This alone

should, I think, effectually dispose of Cohnheim's theory of awakened growth of embryonic rudiments.

Another very suggestive fact is that, while Cancer is at the outset a purely local disease, it becomes eventually constitutional, one of the indications of such being the gradual establishment of a so-called "cachexia". This term "cachexia," I should imagine, simply means that the victim of cancer has become saturated with the toxin of the bacterium causing his disease.

That this toxin is slow in accumulating seems fortunate in view of the preparation of an antitoxin. There would be ample time for the free and, let us hope, successful exhibition of such a serum.

METASTASIS.

With regard to the secondary metastatic foci of Cancer, it is peculiarly characteristic of this disease that each new focus consists, histologically, of epithelial elements identical with the cells of the original primarily infected growth.

There is here no "mimicry" as has been alleged. There is undoubted reproduction of the original pathological tissue itself, showing most clearly that actual cells from the primary growth have been transported along the blood and lymph channels to be deposited at fresh sites, and, being charged with the infective material, they form new and active colonies.

In other diseases where metastasis occurs, such as Tubercle, Actinomycosis, Syphilis, and Pyæmia, although the disease germs are transported by the blood and lymph, the cell elements themselves are not so transported; but this difference from Cancer does not militate in the very slightest degree against the infection theory of cancer-causation.

It is only another example of the infinite variety to be found in germ-caused disease.

SELECTIVE SITES.

While primary Cancer can be originated in, practically, any tissue, it has an almost exclusive selective affinity for Epithelial surfaces generally, and for the Mucous Membrane in particular. Its favourite sites are at places which are directly and easily accessible to infective germs. We find 55 per cent. of these sites in the alimentary canal, which would suggest that the infective agent is ingested.

The remaining favourite sites are in the organs concerned in the reproduction of the species, and the nutrition of the young.

These sites are not only suggestive of infection from without, but also of the probability that the micro-organism is a microphyte and not a microzöon; for, wherever Cancer grows luxuriantly and rapidly, we find present the chief desiderata for the growth of pathogenic bacteria, *viz.*, moisture, an eminently suitable nutrient medium, a constant temperature most favourable to the growth of pathogenic bacteria, and exclusion of light and air.

One could hardly imagine a better culture chamber for bacterial growth than the alimentary canal or uterus.

Conversely, we find that Cancer has not been observed in the Invertebrata, very rarely in the cold-blooded Vertebrata. It is chiefly found in Man and domesticated mammalia. It is very rare in wild mammals. Bland-Sutton states that he found a mammary adenoma in a phalanger, and that this single case represents the extent of his knowledge concerning adenomata and carcinomata in wild mammals. This statement is emphasised by the fact that he was in close attendance in the prosector's room of the Zoological Society's Gardens for eight years, during which time he was particularly on the look-out for tumours of all kinds.

RÔLE OF IRRITATION.

The infectiousness of Cancer, like that of Leprosy and Tubercle, does not, fortunately, seem to be very great, otherwise the increase would be much greater than it is, and it is evident that something else is necessary besides a culture chamber.

The nutrient material is not an inert substance like gelatin or bouillon, but is living tissue, capable of repelling the attacks of invading bacteria, so long as there is no breach in its continuity.

When, however, this occurs, either by accident or from long-continued irritation, vulnerability is induced, especially if at the same time the general health is impaired. In all probability Cancer does not arise in sound and healthy tissues. We generally find that it has arisen in situations where this breach of continuity has occurred.

For example, we get the Lip irritated by an unglazed pipe-stem; the Tongue by ragged teeth or whatever induces chronic superficial glossitis, or injured accidentally as by the prick of a bone, etc.; the Œsophagus injured in a similar way or by scalding liquids; the Stomach by chronic dyspepsia or ulceration; the Intestines injured by foreign bodies such as pins, tacks, bones, etc.; the Rectum by the same or by scybala, etc.; the Anus by fissures, fistula, eczema, etc.

Again, in the case of the Breast we find the nipple terribly irritated, excoriated, and fissured by lactation, while the gland itself may be injured by the blows and rough handling of impatient infants, or by accident. Paget's eczema of the nipple, like leukoplakia of the tongue, has probably no direct relationship to Cancer, but these affections prepare so excellent a nidus for the infective agent, and are so conveniently situated for its reception, that they have come to be termed "pre-cancerous".

The lactiferous ducts also are very large in calibre and very easily accessible.

The uterine cervix is rendered vulnerable in the parous woman, where it is stellate with the fissures of parturition, and, both in her case and in that of the nulliparous or unmarried woman, the cervix is frequently eroded by acrid discharges.

From the Uterus to the Ovary, scarred all over by the rupture of numberless follicles, the transition is easy and the way open.

No doubt the loose and open arrangement of the nether garments of the majority of women would, naturally, favour access to the generative organs of the infective micro-organism, especially if its *habitat* is the soil.

Thus we find that Cancer arises generally in sites rendered vulnerable by injury, or irritation, or degenerative change, and this vulnerability is greater, *a fortiori*, in the middle-aged and old, in whom the resisting power is still further reduced from the fact that, in them, decay is in excess of the power to repair.

CANCERODERMS.

The majority of infectious diseases have cutaneous affections accompanying them peculiar to each, which are commonly known as eruptions.

Now, if a well-marked characteristic cutaneous manifestation accompanied Cancer in most, if not all, cases, we should have another point in common between Cancer and diseases well known to be directly caused by an infective germ.

Have we any such canceroderm (if I may coin a term analogous to syphiloderm) ?

When a student, a quarter of a century ago, the first operation at which I assisted was the excision of a cancerous

mamma, and it was performed by my old friend and teacher, that able and accomplished surgeon, Dr. Ogilvie Will of the Aberdeen Royal Infirmary. While chloroform was being administered, my attention was particularly drawn to the skin over the woman's chest, which had, scattered over it, a number of bright scarlet, shining, punctate spots, unaltered by pressure and varying in size from a pin's head to a split pea. I pointed them out to Dr. Will, and on asking what they were, he told me that he had observed such spots before in cases of mammary cancer.

These spots made a deep impression on my mind and I have looked for them ever since in such cases, and have rarely or never failed to find them, sometimes few and small, at other times larger and more numerous, but almost invariably present.

Since then I have always considered them as naturally accompanying cancer of the breast, and I have occasionally pointed them out to other surgeons doing the same operation, but without succeeding in arousing any special interest in them. Until recently I had not looked for them in cases of Cancer other than mammary. A few days ago however I found them in a case of pelvic cancer, and in another case of cancer of rectum and liver.

When the probability of Cancer being due to direct infection from without was gradually, but irresistibly, forced upon me, the question arose in my mind whether these spots are characteristic of Cancer to such an extent as to entitle them to be considered pathognomonic, or whether they are merely fortuitous concomitants.

I have not observed a sufficient number of cases to form a decisive opinion, but I feel that my views have been greatly strengthened by what I read the other day in an article giving a *précis* of a paper published in the *Münchene medicinische Wochenschrift* of December last.

This article is contributed by Leser, who says that he finds a small angiomatous growth frequently occurring in the skin of patients suffering from Cancer, and that he has not seen any literary notice of it in such a connection.

Freund and Hollander have recounted the existence of such growths in the skin, but they lay little stress on the occurrence.

In many cases of Cancer, Leser found that a number of raised spots were present, chiefly on the skin of the trunk. The spots vary in size from that of the head of a pin to that of a lentil. They are bluish-red, or bright red in colour, and do not fade on pressure. They are angiomatous in structure.

To ascertain the clinical significance of these spots, Leser and his assistant, Müller, investigated in fifty cases of Cancer:—

1. Whether these spots usually accompanied Cancer.
2. Whether they occur in either healthy subjects, or in patients suffering from diseases other than cancerous.
3. Whether their appearance is of diagnostic value.

Of these fifty cases in only one (cancer of the cesophagus), were these angiomata absent. In one case the number of spots was seventy-six and the average number was fifteen.

They decided that the first query must be answered in the affirmative. To settle the second point they examined 300 cases of surgical and medical diseases, and found the angiomata only in subjects of advanced age in a few cases, and probably in these cases Cancer could not definitely be excluded.

Leser therefore concludes that they do not appear in healthy subjects, or in persons suffering from other diseases in early or middle life, and never, even in old age, in large numbers.

Further, when found in large numbers in young or

middle-aged people, there is every reason to suspect Cancer.

The detection of a number of small angiomas of the skin of apparently healthy subjects may point to a commencing cancer.

The abdomen seems to be the favourite site of the spots in internal cancer, and in other cases the skin superficial to, or in the vicinity of, the seat of the disease appears to be chiefly affected.

These spots do not appear to have any direct relationship to the cancerous growth itself, nor are they influenced by changes in the vessels of the growth.

Leser points out how important it would be, should this prove to be a reliable sign, in making an early diagnosis of Cancer, and distinguishing between benign and malignant tumours in cases of doubt.

The only literary notice I have been able to find of angiomas in connection with Cancer was furnished me by the kind courtesy of Mr. Malcolm Morris. He referred me to a tract published in 1872 by the late Mr. Campbell de Morgan, of Middlesex Hospital, entitled, "*The Origin of Cancer*".

In this tract (page 16), De Morgan says:—"There is another circumstance in connection with the recurrence of Cancer after operation which, to my mind, is very significant. I have noticed, and it has been verified by the observations of many others, that concurrently with, or following on the development of, cancer, small outgrowths of warty, or vascular, or dermoid structure are frequent. Now, one would imagine that, if there were a cancer poison in the blood, these, or one of them, would become the seat of the disease; but it is never the case."

Again on (page 23), referring to a case under his care, he says: "From the large size of the breast the discharge,

which was very profuse and sanious, lodged on its upper surface and trickled down the axillary fold. In these situations there sprang up a number of small pinkish excrescences which looked something like crops of minute vascular warts. They were attached to the superficial layers of the skin only. They were found, too, only in situations where the discharge could lie, and, while in these they became more and more numerous so as to coalesce in the end and form elevated patches, not one appeared above the level of the ulcer. Even after many months these little growths had hardly extended to the deep layers of the skin. I have no doubt that the lodgment of the cancerous discharge on her irritable skin had allowed of the implantation and superficial growth of cancer germs." These angiomas were called by the Middlesex Hospital staff "De Morgan's Spots," or "*plaques de Morgan*".

Personally, I have not observed these angiomas to follow operation, but found them already in evidence in cases of Cancer coming under my care for advice and treatment.

Whether these angiomas, found in connection with Cancer, are genuine canceroderms is a point of great interest, and I hope that these spots will be looked for, now that attention has been directed to them. There is, unfortunately, only too abundant material for making observations, and if such are systematically made it should not be a difficult matter to confirm or discredit this sign.

AUTO-INOCULATION.

Of authentic cases of auto-inoculation of Cancer the number recorded is very considerable, and many must no doubt be familiar to you all.

Recently Ebert collected twenty-three cases of contact cancer, such as lip to lip, tongue to gum, one labium majus

to another, etc., and mentions the case of a woman who inoculated the corner of her eye from a cancer on the back of her hand.

"CANCER À DEUX."

In the *Deutsche medicinische Wochenschrift*, of June last, Behla gives a number of instances of "*cancer à deux*," quoting the names of the observers.

Thus Boas mentions the case of a daughter who inoculated herself with rectal cancer by using the same enema syringe her mother had used during her fatal illness, which was of the same nature.

Tross reports a very interesting and most significant case.

A man developed a carcinoma of the glans penis presenting a structure histologically identical with the cervical carcinoma from which his wife suffered.

Other thirty cases of a similar nature were reported.

Guelliot also has collected twenty-eight such cases.

In my own practice a woman suffering from, and who died from, cancer of the breast, was nursed assiduously during her illness by an apparently healthy woman of about forty-five years of age. This woman developed cancer of the stomach and died from it within twelve months of the death of the woman she had nursed. This nurse was practically in constant attendance upon the case of mammary cancer, and, not being a particularly cleanly person, it is more than probable that she had eaten her food with hands unwashed after dressing the ulcerated sore, or handling the soiled dressings.

ACCIDENTAL INOCULATION IN CONNECTION WITH OPERATION.

Smith cites the case of a London hospital surgeon who developed cancer of the tongue after having accidentally

got into his mouth some of the discharge from a cancerous breast.

Budd mentions the case of a French hospital surgeon who died of Cancer eight months after having injured himself during an operation on a cancerous patient.

Guermonprez reports the case of a gynæcologist who developed cancer of the finger at a point where an acne pustule existed, infected during an operation for scraping a cancerous uterus.

Bland-Sutton says that it has been demonstrated beyond possibility of cavil that in women, who have had their ovaries removed for adenomata, it has been found that tumours have subsequently grown in the abdominal cicatrix; such tumours showing, under the microscope, the structure of ovarian adenoma. Since these tumours have been unassociated with any recurrence in the pelvis or secondary nodules in the peritoneum or viscera, the conclusion is irresistible that they were due to infection of the edges of the abdominal incision in the course of the operation of ovariectomy.

Sippel has published a case of Cancer inoculated along each one of the suture tracks made after extirpating a cancerous ovary.

No doubt the same local soiling of the edges of skin incisions in operations for Cancer, *e.g.* of the mamma, takes place, and this probably accounts for the presence of recurrence in the form of cancerous nodules so common in the cicatrices of breast cases.

Again, we find often that an extensive operation for Cancer is followed by such rapid recurrence, and such increased energy of growth, that it is evident operation has hastened matters and caused a much worse state of things than non-interference would have done.

Bland-Sutton explains this by suggesting that in the

operation the infected blood and lymph vessels, gorged with cancerous material, are divided, and the cancer cells let loose over the damaged tissues, which they infect, and so lead to a still more extensive outbreak of local cancer.

EXPERIMENTAL INOCULATION.

Cancer has also been successfully inoculated experimentally, chiefly, however, in the lower animals.

Langenbeck made a watery emulsion of a soft cancer, mixed it with blood serum, and injected it into the femoral vein of a dog.

Two months later, on *sectio*, nodules were found in the upper lobes of both lungs, and a vascular mass in the middle lobe of the right lung which proved to be cancerous, and was found to be of the same structure as the original growth.

Follin and Lebert used injections made from a cancerous axillary lymphatic gland and, within fifteen days, found in the animal several cancerous nodules in the lungs and liver.

Gonjon has produced melano-sarcoma in small animals within fifteen days after inoculation.

These are but a few examples of many I could quote.

It is most important that much more should be done in experimental inoculation, and it is even more necessary that such experiments should be made on the *genus homo*.

Bosc alludes to three cases of inoculation from man to man, done both intentionally and successfully, but is discreetly silent about details.

Fortunately there is fairly abundant material for this purpose, although it is at present recklessly wasted annually by the common hangman !

Capital punishment, as at present administered, is so barbarous, so illogical and so entirely non-deterrent, as well as being nothing other than cold-blooded, judicial, murder,

that it might very well be discontinued, and the material, now lost to science, be made available for research in the pathological laboratory. The one thing to fear, however, would be that this committal to the laboratory instead of the scaffold, would be too deterrent, and, murder becoming a lost art, the material would run short of scientific requirements !

There is a precedent for this source of material for research, inasmuch as inoculation for small-pox was performed experimentally upon six condemned criminals, in 1722, by permission of the government of George I.

No doubt there would be a great outcry from the shrieking sisterhood of both sexes ; but they should, of course, be simply ignored, for science must be permitted to pursue the calm and even tenor of her way, undisturbed and undeterred by the vapourings of irresponsible cranks.

In making experimental inoculations two points strike me as likely to help materially towards a successful result if duly observed, *viz.*, that the part to be inoculated should be suitably irritated for a sufficient time, and that the infective material should be taken from an actively enlarging lymphatic gland or metastatic focus, since here we may expect to find the germ in its greatest activity, and free from the effete material of the primary growth, as well as from other germs.

I cannot but think that one is justified, even at the present time, in saying that, since auto-inoculation and accidental inoculation are so common, and experimental inoculation has been so successful, there should be no longer any doubt that Cancer is, in truth, a contagious disease.

CANCER DISTRICTS.

With regard to locality, we find that Cancer is more prevalent in some places than others, so much so that the former have been designated " Cancer Fields ".

We find the highest death rate from Cancer in districts which lie low, and are liable to seasonal floodings, and characterised by alluvium and subsoils of the various clays. The favourite districts in the North and East Ridings of Yorkshire lie principally along the banks of the Ouse, the Derwent, and the Humber. I believe the Derwent region is locally called "The Cancer Valley".

On the other hand, Cancer is least prevalent in elevated districts, where there is a good fall for drainage, freedom from floods, and characterised by porous subsoil, and the oldest palæozoic rocks, especially the limestones.

Thus we find Cancer most rampant where sewage is most difficult to be got rid of, and where it is most likely to be deposited and remain after floodings or high tides, on a non-porous soil.

This permits of and fosters the prolific growth of micro-organisms; and the frequent occurrence of shallow surface wells in such districts suggests an easy and extensive contamination of drinking water.

It is not difficult, therefore, to realise how Cancer may be spread in such localities, and the frequency of its occurrence in the alimentary system favours this view.

CANCER HOUSES AND ROOMS.

As might be expected, we also find in these districts certain houses, and even certain rooms in houses, which seem to be cancer-haunted.

The authentic cases recorded are numerous, but as too much time would be necessary for detailing them I shall quote only one or two instances.

In a house near London a room was occupied by three women in succession who all died of Cancer at fairly short intervals. Each of these women appeared to be in perfect health when she in turn came to occupy this room, and had

lived in other rooms in the same house; but within a year of occupying this room they developed Cancer. There was no relationship between them.

No further cases of Cancer occurred in this house after the room was thoroughly disinfected, and the bedding burnt.

There is in Driffield a row of three notorious houses, or rather hovels, all under one roof, without drainage and with doubtful water supply, where I have attended cases of Cancer in each, and in one of these houses more than one case. At present I have a case of cancer of the breast in one of these houses.

There is also a narrow street in Driffield, undrained and also with doubtful water supply, where Cancer is especially common.

It was in one of the houses in this street that the two cases occurred which I mentioned under the subject of "*cancer à deux*".

Such circumstances as these appear to me to strongly suggest that Cancer is infective, and also that locality is a factor in its transmission.

GEOGRAPHICAL DISTRIBUTION.

Cancer seems to be chiefly a disease of temperate regions, avoiding the extremes of temperature such as exist in Greenland or Iceland and the Tropics. Although the extremest cold has no destructive effect upon bacteria or their spores, it certainly keeps them dormant and this would explain the paucity of cases of Cancer in cold climates.

It is not so easy to account for the alleged infrequency of Cancer in the tropics, but it is probably more apparent than real, and may be due to less accurate supervision of disease in these regions. Besides, as a matter of fact, Cancer is very common in many parts of India and China.

One reason why so little disease and so few cases of old age are seen among savage peoples, for example in Central

and South Africa, is the regular, unostentatious, and mysterious disappearance of such useless individuals, about whose fate no one exhibits any inconvenient curiosity!

Again one need not be surprised to find in the distant islands of the Pacific a healthy native population. They live much in the open air, in an atmosphere practically free from pathogenic germs, so long as contamination from without does not reach them; but the very disastrous results of imported disease, such as Small-pox, Measles, Syphilis, etc., are notorious, and one can easily believe that the advent of cancer-bearing individuals would be followed by the spread of this disease also.

ETHNOLOGICAL.

The freedom of certain peoples from Cancer does not appear to be due to individual immunity, but to the accident of locality and environment and the mode of life.

Under favourable conditions any one may become a victim to Cancer.

There is a popular belief that Jews as a race are remarkably exempt from Cancer, but this belief is quite erroneous as is shown by cancer statistics. One reason alleged for this belief is that Jews, generally speaking, have a great repugnance to being inmates of hospitals where Gentiles are in attendance, and, so, few cases are found in these institutions. Private practitioners do not find that Jews exhibit any special immunity from Cancer in general. The male Jew may, unquestionably, claim perfect immunity from one form of Cancer which his Gentile brother may suffer from, but, apart from this, he is equally vulnerable and liable!

MICROBES IN CANCER.

About fifteen years ago, Scheurlen isolated from cancers of the breast a bacillus which he claimed to be the active

agent in their causation. It grows readily in blood serum, and forms a red deposit on potato. It reproduces by spores which stain only by the Ehrlich method, in use for the tubercle bacillus, but the bacillus itself stains by ordinary methods. He has injected pure cultivations into the mammary glands of bitches with the effect of producing a hard tumour which he states is epithelial.

Doyen lately submitted a paper to the French Academy of Medicine, stating the constant presence of a new microbe in cancerous tumours, which he isolated and cultivated. He says it occurs in the form of motile diplococci, which can be cultivated in tubes of gelatin and gelose with the addition of a special bouillon.

This microbe is more easily found in the affected glands and secondary growths than in the primary tumour, and it is also found in the blood.

To the organism he has given the name "micrococcus neoformans".

In animals, he says, it determines an intense epithelial inflammation followed by formation of adenomata. The subcutaneous injection of sterilised cultures of the organism induces a local reaction in the cancerous growth which he compares to the action of tuberculin on tuberculous foci. The post-operative injection of this liquid has given results satisfactory to Doyen. I daresay we shall hear more of this microbe after further experimentation.

That these micro-organisms are different in structure is no reason for doubting their causal relationship to Cancer, for, as in suppuration several different microbes are concerned, so in malignant disease, which exhibits much greater variety than suppuration, we may, *a fortiori*, expect to find several different pathogenic bacteria involved.

HEREDITY.

With regard to Heredity in Cancer, the believer in the Infection Hypothesis cannot possibly accept the doctrine that an individual will develop Cancer in later life merely by virtue of his having had cancerous parentage.

It is imaginable that the children of cancerous parents may acquire more or less vulnerability congenitally, as in the analogous case of Tubercle; but it is most improbable that the disease itself can be transmitted. If it could be so transmitted we should expect to find it at or soon after birth as is the case in Syphilis.

It is interesting to find that even the warmest advocates of heredity in Cancer cannot trace cancerous parentage in more than 50 per cent. of cases of this disease.

The occurrence of Cancer in several members of a family, after the death of parents from that disease, cannot be accepted as evidence of Heredity; but, on the contrary, it can, and ought to, be accepted as evidence of Infection from an obvious source.

TREATMENT.

The question of treatment of Cancer hardly comes within the scope of my subject, but I am tempted to allude briefly to it.

With our present knowledge this is limited to simple removal of the tumour, if accessible, by the surgeon at the earliest possible moment, and no guarantee can be given by the surgeon that every particle has been removed, or that no recurrence will take place.

But, given an infectious origin, almost certainly bacterial, the lines on which scientific and successful treatment may be carried out become more clearly defined.

Syphilis was long treated empirically. The treatment is still the same but it is no longer empiric, for the bacillus of Lustgarten is overcome by two of the most powerful bactericides known.

We must find a bactericide which will prove of equal efficacy in the case of Cancer, or it may be that Serum-therapy will prove effectual. There is even now reason to hope for good results from the use of Electricity, whether in the form of Roentgen rays or currents of high potential, both of which are alleged (Cohn and Mendelssohn) to be inimical to bacteria.

As regards Prophylaxis, much may be hoped for from notification; improved sanitation, including disinfection of houses, cremation of bodies, destruction of dejecta, dressings, etc., by fire; the use of pure drinking water; scrupulous personal cleanliness, especially the avoidance of unwashed hands when food is taken, the use of the Turkish bath; exercise; moderation in diet; abstention from alcohol in excess; and general observance of the known laws of health.

I fear by this time that I have exhausted your patience, but I have come to the end of my Thesis.

It seems to me that, after all, my trying to hold a brief for the Infection Hypothesis of Cancer is a work of the purest supererogation, since it must be evident that it is hopeless to attempt to explain the causation of Cancer on any other ground.

No alleged cause can possibly be accepted which is not universally applicable, and Infection from without is the only suggested cause which will satisfactorily account for every case of Cancer.

To sum up, this is my case:—

From the evidence at my disposal, I deduce that Cancer

is a Specific Disease, that it is contagious and therefore infectious. That there is an infective agent is a logical *sequitur*.

Probability and analogy point to this agent being a microphyte and not a microzoon. That this microphyte is a facultative aerobic bacterium is suggested by the fact that, though it grows fairly well under free access of air, it grows very much better without it. This is well exemplified by the striking difference in behaviour of epithelioma of the Lip and of the Tongue. Although these parts are very near neighbours, the growth in the one instance is extremely slow, while in the other it is exceedingly rapid. The epithelioma of the Lip is exposed to light, to the air, to low temperature, and there is an absence of moisture. The epithelioma of the Tongue, on the other hand, is situated in an ideal culture chamber, in the dark, where there are moisture, a fairly constant favourable temperature, and exclusion of air.

Since a specific disease can originate only from a specific cause, all other alleged causes can only bear the relationship to Cancer of, at most, the condition precedent.

The proof rests in the hands of the experimental pathologist, supplied with material by the practical clinician.

The time is more than ripe for combined and determined effort to investigate this subject, an effort which must be tirelessly persisted in until the problem is finally solved.

There are few who have not suffered in person or friends from this grim and terrible disease, and it is certain that every one will wish well to the search for the cause of Cancer, and no one more than our genial and royal Colleague, our august Sovereign, King Edward, who has already referred to the subject in most emphatic terms.

One great obstacle to investigation is absence of the sinews of war; we must have money and plenty of it if we are to hope for a successful issue.

It is hardly fair to look for help to the liberality of private individuals alone, as was recommended by the Prime Minister the other day, although some multimillionaire might easily less worthily dispose of a half or quarter million than hand such a sum over to the conjoined Colleges of Physicians and Surgeons for this purpose. It is the bounden duty of the State, and it ought to be considered a privilege, to grant, through the Government, a generous subsidy for a cause having as its object the benefit of the Commonwealth.

This country has had an example set by Germany and the United States, who have both set apart large sums of money for the investigation of the cause and nature of this disease which it would be well for England to follow.

Another obstacle, and it is a still greater one, is the supineness, the indifference, the utter apathy displayed by the members of the Medical Profession in general, who appear to be fettered by a paralysing fatalism. Let us rouse ourselves from this state of lethargy and by a determined, unanimous and sustained effort remove from the science of Medicine this most discreditable reproach.

Germany can claim the honour of having discovered the cause of Tuberculosis; let it be to Great Britain that the honour of the elucidation of Cancer shall belong, an elucidation which shall earn the undying gratitude of all mankind, and establish for Britannia a glorious fame which shall be imperishable.

In replying to the customary vote of thanks to the President for his address Dr. Brand said:—

"I feel very strongly on this subject, being convinced in my own mind that Cancer is, unquestionably, an infectious disease, and if I have convinced any one of this, or even if I have satisfied you that the Infection Hypothesis will indeed bear criticism, I shall feel that I have not addressed you in vain nor altogether wasted your time".