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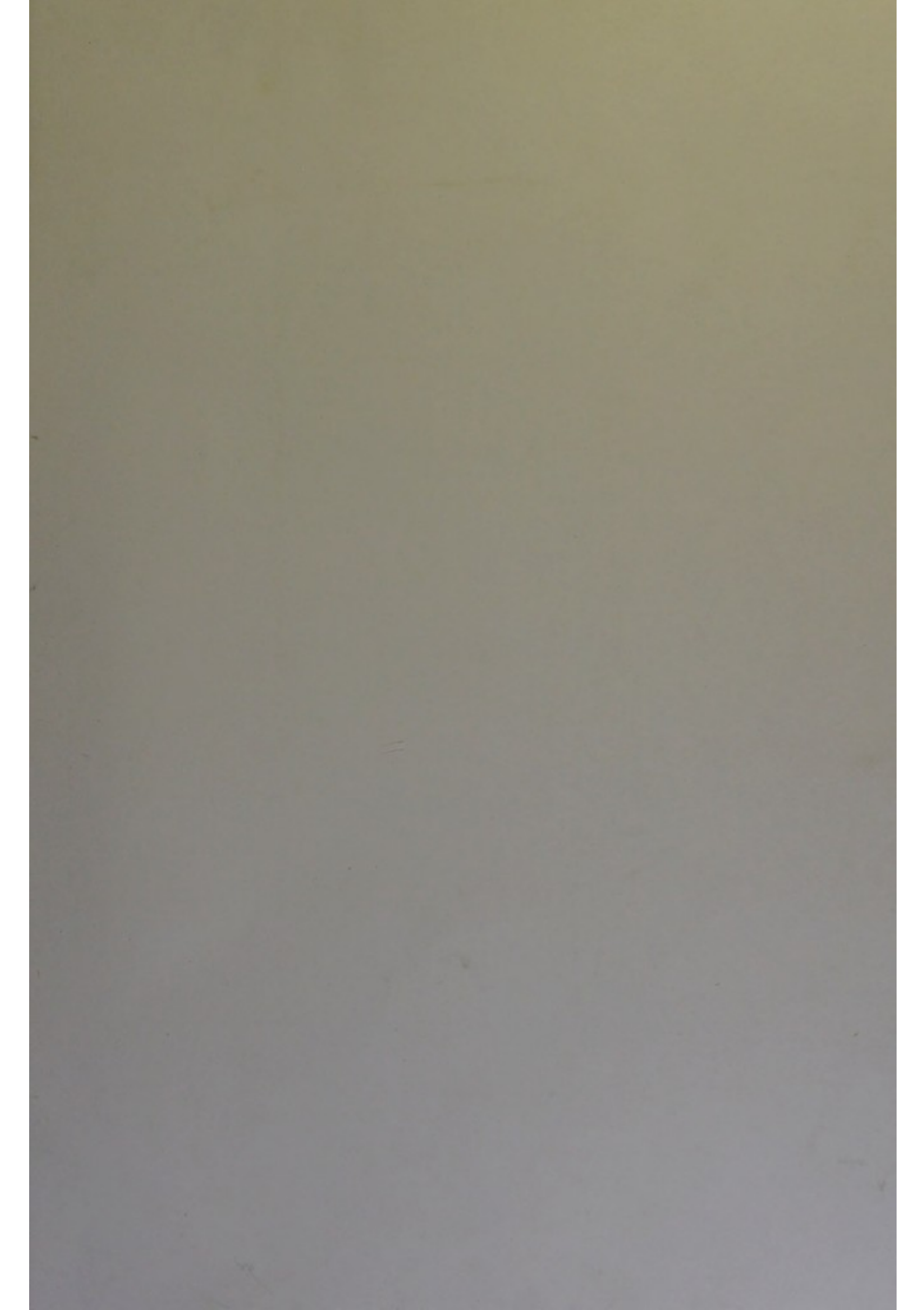
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CANCER:

ITS ORIGIN, NATURE, AND GENERAL
PRINCIPLES OF TREATMENT.

BY

GEORGE THOS. BEATSON, B.A.CANTAB., M.D. EDIN.,

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GLASGOW CANCER HOSPITAL,

A Contribution

*TO A DEBATE HELD UNDER THE AUSPICES OF THE CHELSEA CLINICAL
SOCIETY, AT THE JENNER INSTITUTE OF PREVENTIVE MEDICINE,
11th, 18th, and 25th MARCH, 1902.*

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CANCER: ITS ORIGIN, NATURE, AND GENERAL PRINCIPLES OF TREATMENT.¹

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MR. PRESIDENT, LADIES, AND GENTLEMEN,—My first duty is to thank your Council and the members of this Society for what I regard as a great honour in being asked to be present and to take part in the debate. When I received the invitation, the interpretation I put upon it was not that anything I had contributed was of special value, but that you simply recognised that in me you had an interested worker in connection with a subject of the very greatest importance and the very greatest interest. I accepted the invitation because I felt I would like to hear what others had to say, and I have not been disappointed in the opening address by Dr. Galloway. The facts he has brought forward are all of them of the greatest importance, as bearing upon the subject. Again, I felt that a Society such as this, in having a debate of this character, did a good thing. In a problem of this kind, presenting such great difficulties, it is only by a united effort that we can in any way solve the problem.

The first thing, in carrying on a discussion of this kind, is for us to clearly understand what it is that we are talking about. In the present day, it is a proper thing to know that we are all worshipping in the same tabernacle, and that we have not each got a little kirk of our own. With regard to the terms cancer and carcinoma, in speaking of them I refer to a morbid process which begins in a situation where epithelium is present in the body, and results in a structure made up of epithelioid cells. The characteristic of that structure is that the cells continue to multiply and increase, that they invade the surrounding tissue, that they travel, as Dr. Galloway has told us, along the lymphatic vessels, and pass to the lymphatic nodes, and in a large number of cases that cells hive off from the primary growth and form secondary deposits in distant organs or parts of the body. That is the meaning which I attach to the terms cancer and carcinoma.

At the same time, in a discussion such as this I think it is of great importance that, although speaking of one particular process, we do not lose sight of the whole subject of tumour formation. If we have a theory which explains only one form

¹ Reprinted from the *Clinical Journal* for 21st May, 1902.

of tumour, it is, in my opinion, defective and unsatisfactory. In connection with that point, there are one or two statements which I think may be introduced here. First of all, we have to remember that there is undoubtedly a connecting link between malignant and benign growths. This arises from the fact that both are composed of tissues of the body, and that these tissues have all had a common parentage; they have all sprung from *two epithelial cells*, for the male and female cells by which this body of ours is created are, to all intents and purposes, epithelial cells. As a consequence of that, no matter what the ultimate history of a cell may be, it has, at one time in its life history, had an epithelial form. In the next place, differentiation does occur, so that we have the character of the cell altered and its epithelial form lost. This differentiation varies in amount. In some cases it is only very slight, purely functional, while in other cases it is very marked, and it results in the formation of tissues of a higher type. These specially differentiated tissues, as long as they retain their specialised form, breed true, that is to say, epithelial cell produces epithelial cell, and connective-tissue cell produces connective-tissue cell. Further, another important point is that differentiation lessens the proliferating power of cells. A daily proof of this is seen in connection with the amount of regenerative power shown by different tissues in the cases of wounds and injuries. While proliferation takes place actively and freely in the lower tissues, like epithelium and connective tissue, those of the higher type, such as muscle, are scarcely reproduced. Differentiation, therefore, lessens the proliferating power of cells. Again, certain facts seem to me to show that this differentiation only masks that epithelial type to which I have referred, and, what is very important, that the less highly specialised cells may lose that specialisation and revert to their primitive epithelial form. In no other way can we explain a fact which is familiar to all surgeons of experience, viz., that we have benign tumours suddenly becoming malignant. If, then, a benign tumour may become malignant, if it has, in other words, the power of reverting to a lower type; we must not deny to the tissue it represents the same power.

The conclusions I would draw from these facts are these: (1) That, if the influence or influences—because there may be more than one—that cause tumour growth come into play, the effects will vary with the tissue involved; (2) if it is a highly specialised tissue at the time it is attacked, then we will have a limited growth, in other words, a benign tumour. If it is a very little differentiated tissue, as, for instance, epithelium or connective tissue, we have a great proliferation, an indefinite growth, in other words, a malignant tumour; (3) that malignancy or simplicity of tumours depends on the proliferating power of the cells attacked by the exciting cause of tumour growth, and that this proliferating power is to be measured by the amount of specialisation to which the cells attacked have attained, or that they possess at that particular time, for they

may have lost some of it and come down lower in the scale ; (4) that the mere division into malignant and simple growths is short-sighted, and, as Virchow, I think, long ago pointed out, merely to take that as a basis of classification would be as unscientific as in botany to divide plants into poisonous and non-poisonous, edible and non-edible.

We have, therefore, always present in the body one very important factor of tumour formation, namely, a proliferating power in its cells. It is also clear that this power varies with the natural differentiation of the tissues, and that this differentiation may be lost in amount, so that a tissue may be brought to a lower standard and thus acquire increased proliferating power. With this one factor in tumour growth present in the body a very important element in that process exists, and the only other factor required to explain tumour growth is the *necessary stimulus*. Of this I shall speak later.

I should like at this point briefly to draw attention to the similarity which exists between cancerous and early embryonic tissue. As I have said, the body springs from two epithelial cells. For a time those tissues which are formed from them are of the same structure as cancerous growth, and it is only in connection with such embryonic tissue and its power of development that we have anything approaching the proliferating power of malignant tumours. Again, I should like to note, also in connection with embryonic development, the relation of malformations to neoplasms. If we are right in the theory that we hold about uniovular twins, it is peculiarly a pathological process, as are also joined twins, instances like those which have been of such interest to our Gallic neighbours and some members of the profession over there, the Siamese twins as they are called. Then, again, we have children with extra limbs, or with simply incomplete bodies attached to them. The two-headed nightingale of my younger days is an instance of that. So, also, we have children with sacral tumours and teratoma, and, lastly, we have children with dermoids. We have thus, in connection with what is practically embryonic life, a complete series of gradations bearing on the question of tumour formation.

Now, you will expect me to give you, in speaking of such a subject as the nature of cancer, my views as to whether it is a local disease or whether it is a local expression of a general disease. I am not going into that question. All I will say is that I have made up my mind that it is purely local in its initial stage. It commences in alterations in a cell or cells of the parts affected. What exactly that alteration is I shall afterwards have a word to say upon.

We next come to what really is the crucial point in connection with this tumour question, a consideration of the factor or factors which start the local cell proliferation, in other words, the causes of tumour formation. The natural division of such a subject is causes from without and causes from within. Of those from without, the parasitic theory of which Dr. Galloway has spoken to-night and given us very useful illustrations, is the only one which requires

notice, and I shall only briefly allude to it. As regards its nature, the general feeling is that while bacteria may be the cause, they are not so likely to be so as those protozoa or yeast fungi which Dr. Galloway referred to. This view has been chiefly supported, I think, by the discovery of those so-called cancer bodies of which we have just had such excellent illustrations projected on to the screen. Now, it would be impossible, in a discussion such as this, to take up all the points connected with these bodies, and I cannot go into the explanation of their meaning, but I am of Dr. Galloway's opinion that they are simply cell degenerations. The chief points that weigh with me against the parasitic theory of malignant growths are as follows:—First of all, there is that one fatal objection, the question of congenital tumours. Secondly, there is what we observe in secondary growths. In the secondary growths, if they are due to a parasite, the parasite should travel there too. That is not the case, as has been demonstrated. Thirdly, there is the absence of toxins in the body, and that to me is a very important point. Anyone who has had experience of cancers, and especially of the early stages of them, is satisfied that the system generally is not poisoned by anything of the nature of a toxin, such as one would expect to result from a parasitic growth. Therefore, I am quite strongly of the opinion that in that view we have not got the solution of the exciting cause of tumour formation.

I have a strong belief in an intrinsic cause which may explain the commencement of local cell proliferation, and I may say to you at once that it is based upon the results which have been obtained in oöphorectomy for mammary cancer. That procedure has been discussed from a therapeutic point of view, that is to say, the question of its value as a remedial agent. That, no doubt, is a very important point. To me it is not so much so as the explanation of the fact that under that procedure masses of cancerous tissue have disappeared. Now, I make that statement not simply upon my own work. Others have tried it, and have obtained the same results as I have. Therefore, it is a clinical observation which cannot be altogether ignored, and I believe it is of very great importance in connection with the subject of tumour formation. Various explanations have been put forward of the fact that, if you perform oöphorectomy in a case of mammary cancer, the cancerous tissue does disappear. One reason that has been given is that it is owing to a diminution of the vascularity of the part. Inasmuch as the ovary influences the part where the mamma lies, its removal lessens its vascularity, and accordingly the tumour disappears. Another view is that the oöphorectomy furnishes an increased power of resistance to the other body cells. And, lastly, some have asserted that it is the mere laparotomy itself which brings about the change. Well, gentlemen, I believe these explanations are quite inadequate. I am satisfied that we require to find something of a factor much more potent, and one which will explain it much more satisfactorily.

In my original paper, I suggested that the explanation was to be found in facts connected with the testes and the ovaries, and I put forward two channels by which the ovaries might be the exciting cause of mammary carcinoma. First of all, they might be so through the agency of migrated ovarian cells, or, secondly, by an altered secretion. Now, a word as to the migrated ovarian cells. When we think that there is possibly a daily discharge of ova, only a few of which enter the Fallopian tubes, the rest being probably lost in the peritoneal cavity, the possibility of this migration of cells is not a very far-drawn fact. Then, with regard to the occurrence of these cancer bodies which have been illustrated to us to-night, they raised the question in my mind—Are they germinal cells? Because we must remember—and it is a very interesting fact—that one of the first animal cells to be discovered under the microscope were the spermatozoa, and for a matter of two hundred years they were thought to be parasitic animalculæ, in the same way as these cancer bodies are considered by many pathologists to be of a similar nature. It was only well on into the last century, I believe, that the real nature of spermatozoa, as seen under the microscope, were demonstrated by Kolliker. With the view of testing this question, it was approached from two points: first of all by microscopical examination. Films were made, and in all these cases careful observations were made as to whether anything in the nature of extruded polar bodies could be detected. In one or two cases, structures that stained green were noted, apparently leaving the cells, but they might have been, and probably were, leucocytes. So, as regards the microscope, nothing confirmatory could be obtained. Next, a series of experiments were made, consisting of the inoculations of tissues, ovarian and testicular, into rabbits. Six experiments were done, the results of which I published in the *British Medical Journal*. In connection with those, nothing confirmatory was found. I felt then that I had no proof in support of my theory of migrated ovarian cells, and that it was one that I must at present abandon. Then came the question of altered secretion. With the view of testing that, the ovaries I had removed in oöphorectomy for cancer of the mamma were chemically examined, and no confirmatory evidence was found there. Consequently, with regard to the two original views which I put forward, I was bound to say I was wrong, or, at all events, that I had no confirmatory evidence. Was any other explanation available? It occurred to me that there was, and that it lies in what happens in connection with the function of the testes and ovaries. Briefly, both these organs have to prepare cells that will perpetuate the species. The testes do this by forming spermatozoa out of epithelial cells by a process of cell division, and the ovaries by carrying out those maturation phenomena which fit certain of their epithelial cells for fecundation. Both processes exhibit great cellular activity. By what agent are these changes accomplished? What is the stimulus that sets up the cellular division, and, in the

case of the testes, produces cellular activities which lead to extrusion of the spermatozoa? What is it that excites those polar bodies and the preparation for fecundation? It must be a *secretion* of some sort, and, that being so, where is it elaborated? Is it elaborated by the testes and ovaries themselves? Or is it elaborated by all the tissues of the body under the stimulus of these organs in accordance with the old Hippocratic idea? Are the testes and ovaries merely the instruments for carrying out the work done by the rest of the body? In other words, is the fructifying power which gives the spermatozoa or the female ova their procreative power a product of the whole body, or merely a local manufacture? I am inclined to the view that it is furnished by the whole of the body, and such an explanation is not altogether unsupported by facts. Let us take what has been observed in connection with the thyroid gland, one of the so-called ductless glands. It was for a long time considered that it did nothing in the way of secretion or excretion; but we know now, by clinical observation and by other experiments, that the thyroid has a very important duty to perform, and that its function is connected not with elaborating any special secretion itself, but by dealing with the secretion which is poured out by the whole of the tissues. So much is this the case that, if atrophy of that gland takes place, we have a general affection of the tissues, as in myxœdema; while, if the gland is completely extirpated, we have effects disastrous to the whole fabric of the body. The subtle influences that the testes and ovaries exert on the general nutrition of the body, and the profound impression made upon it by their removal, are well known, and proof of it is seen in eunuchs, and also after oöphorectomy for many ovarian diseases. What, then, is the actual relationship between the rest of the body and testes and ovaries, supposing these conditions to be such as I suggest? When these organs dwindle with age, or become functionless, what happens to this body secretion? Does it diminish also under the lessening influence of these organs, and does it cease entirely with their complete atrophy? Or does this body secretion continue after they are functionless, or are rendered functionless by disease, and is again taken up by the tissues themselves? Lastly, when do these organs lose entirely their influence over the functional activity of the body? You can understand it is impossible to answer these questions in our present state of knowledge, and, consequently, reliable conclusions are difficult. Facts, however, seem to me to point to the tissues ceasing to give up (secrete) this fluid on the removal of testes and ovaries.

We can now judge, I think, of the bearing these views have on the causation of the cancerous process. I need hardly point out that the existence of such a stimulating or fructifying fluid in the body tissues furnishes an explanation of many observed effects, and opens up also other possibilities. Of the greatest importance is it in cell proliferation and tumour formation. It furnishes the factor

that is alone wanting to explain the growth of tumours, for, as we have seen, the tissues already possess, in varying degree, the power of cell division and proliferation, and they simply want something to call it into existence. What cells is it likely to influence? Those, naturally, whose proliferating power is greatest. Now, special proliferating power may exist under two conditions. First, it may be *natural*; secondly, it may be *acquired*, as I pointed out at the beginning when speaking of certain facts about differentiation. I then showed that loss of differentiation in cells—in other words, loss of functional activity, so that they are no longer of any service in the economy—causes such cells to revert practically to their embryonic state with its unlimited power of proliferation. When dealing with conditions about which we can only theorise, any explanation put forward can be judged in one or two ways. It can be disproved by facts, or it can be strengthened if it is found to be supported by facts on which there is agreement. Let us take a few well-accepted facts and apply the theory.

There is none more generally acknowledged than this—*that long-continued irritation is a predisposing cause of cancer*. What does that mean? It means loss of differentiation and lowering of the functional vitality of the cell, and thereby a greater proliferating power. Again, what fact is more recognised than *that organs where senile changes occur early, as, for instance, the breast and uterus, are especially the seats of cancer*. What is it that happens in these senile changes? There is a physiological atrophy and reversion to a lower type of tissue, so that these organs simply need such a stimulus as I have described to start the commencement of cell proliferation. Further, what fact is there that is more acknowledged than the one that has been brought out by Mr. Tatham in his communication to this debate, that when the natural powers of the body are declining, in other words, *when age comes on, cancer manifests itself most*? Recently Dr. Woodhead and others have shown what is the nature of these changes in old age. They are characterised by the loss of the sub-epithelial tissue and by the greater activity of the epithelial cells, these latter showing an increase, with a tendency to dip down and to proliferate. In the same way Cohnheim's inclusions, Ribbert's isolations, and Adami's groups of cells are all liable to be the seat of tumour growth, because their tissue standard is low, and under a stimulus they will begin to proliferate. I removed once a tumour from the parotid region of a young woman, which showed itself when she was about 24 years of age. It was a myxo-fibro-chondro-adenoma, and sections of it showed prickly cells scattered therein. No other explanation of such a tumour could be given than that there had been a congenital inclusion (Cohnheim) in connection with the region affected; but why had it not shown itself all the earlier years of her life? As puberty came on, in all probability that fluid of which I have spoken made itself felt, and this tumour which contained the elements of rapid proliferation only wanted a stimulus. It

received the required stimulus, and, accordingly, began to grow just previously to her marriage, and when I removed it she had to wean her first child.

There is another point, namely, that of heredity in tumour growths, to which I would like to refer. The view I put forward to you affects not only this, but the question of heredity generally. As you know, the theory regarding the latter that has probably received most acceptance is that of the continuous germ plasm (Weissman). I have never been much taken with that theory. I consider that the theory of a secretion from the whole of the tissues meets better the question of general heredity.

As regards heredity and tumour formation, my experience at the Glasgow Cancer Hospital is that heredity cannot be put down as a strong factor. I do find this, however, which others also have observed, that there is in the family history of a great many cases of carcinoma evidence of great *longevity*, implying an inheritance of a certain inherent vitality of the tissues, which I consider a factor in the question of the so-called hereditary tendency to tumour growth. Among my hospital patients there was a most interesting case bearing on this point. The patient was an elderly woman, *æt.* 72, who developed carcinoma of the breast. Her son, who had a severe burn in early life, developed, between 30 and 40 years of age, an epithelioma in the scar long before his mother was attacked by carcinoma. He showed the tendency to this disease when young, because in his case it was brought to the surface early by means of the lower differentiated tissue in the scar of the burn, while in the mother it showed itself later in life, only when her tissues had begun to deteriorate and she was advanced in years.

As regards cancer houses and cancer localities, it is a point to which my theory can also apply. If there is one thing which we are agreed upon it is that our surroundings affect our vitality and well-being. If you have an environment which lowers the vitality of the body cells in the sense of lessening their functional activity, you can have coming into play the force connected with the fructifying fluid. It is a curious fact that the statistics in Glasgow of cancer show that out of 1,000 certificated deaths there are about 20 from cancer. If you go, however to the East Coast, you have in Dundee 28 per 1,000, in Aberdeen 43, and in Edinburgh (only 40 miles from Glasgow) you have 49. Is that to be explained on a parasitic theory? I consider that impossible. It is explained on local conditions of environment which affect the dwellers in the towns, interfering with the vitality of the general tissues of the body.

Passing next to carcinoma during pregnancy, and to mammary recurrences after long intervals, I would point out that it is well known that when cancer occurs during pregnancy it grows with a rapidity quite out of proportion to what is seen in ordinary cases. It must be that during pregnancy the tissues of the body generally are stimulated to produce material for the service of the tissues.

If there is present the fluid such as I have described, it is likely that it will be more in evidence in the condition we are considering, and cancer would flourish more.

As regards mammary cancers that recur at long intervals, I had recently a patient who came to me with a small carcinomatous nodule just above the scar left after removal of the breast eleven years previously. Now, why should that have been quiescent during all those eleven years? I believe the explanation is that when I removed that breast there was left behind a portion of the gland tissue that had not deteriorated, and had not lost its differentiation sufficient to become the seat of cancer. As time went on the tissue came into that condition, and the same influences were brought into play as in the primary growth ten years before, with the result of the nodule in the scar.

My views, then, on the cancer process are as follows:—

1. That it can only develop in tissues that have special proliferating power, either natural, as in Cohnheim's "rests," or acquired in one of many ways.

2. That the actual exciting cause of the cell proliferation is a secretion from all the tissues of the body and possessed of fructifying powers.

3. That a mutual relationship exists between the character and amount of this secretion and the testes and the ovaries.

4. That another factor in connection with it is the inherent vitality of the tissues themselves.

In this way alone can one satisfactorily explain the disappearance of cancerous tissue under oöphorectomy. It is an important and instructive clinical fact apart altogether from its therapeutical value. Such a view of carcinoma is apparently a return to the old spermatoc theory. It differs from it, however, in a very important point: it does not imply a conversion of the normal tissue into another kind of tissue. Cancerous tissue is composed of ordinary body cells. The only feature is their intense proliferative power. All that this body secretion does is to furnish the stimulus for proliferation when the condition of the cells allows.

At this point I will read to you a quotation which shows how the lines of thought that come to one are, in reality, common property. The late Dr. Ritchie, whose work on "Ovarian Physiology and Pathology" is full of interest, makes on the concluding page of it the following suggestive remark:—"Perhaps, by the careful study of ovarian growths, our knowledge of the nature of malignancy may some day be signally increased." He also adds, "It is well to bear in mind what Dr. Bright enunciates so well, that the ovaries in their natural structure seem to present a prototype of that involved system of cellular enlargement observed in malignant growths."

In regard to general principles of treatment, from what I have said you will understand that preventive treatment cannot altogether be ignored, and simple tumours should be excised when they exist.

I am a firm believer in the local treatment of carcinoma by removal with the knife, and if that is impossible in certain parts of the face caustics may be used. The removal, of course, should be as wide as possible, so as to include any mischief in connection with the growth. In treating limited local recurrences excision by the knife should be practised. In one or two cases that I have under the treatment of the Röntgen rays, it would appear that this means may be found to be an important element in their removal. It should always be remembered that, however carefully the knife is used, new tissues are opened up, and that leads to an activity that may do harm. In rodent ulcers unsuitable for excision I think the x -rays are of value. In those cases where you have no visceral complications with inoperable mammary cancer, I have no hesitation in recommending oöphorectomy and thyroid treatment. It has undoubtedly proved of use in many cases.

In the first case that I operated on all the cancerous tissue disappeared. The patient was a young woman, æt. 33, suffering from a recurrent inoperable mammary cancer, and she lived for four years after the operation, dying from a secondary growth in the spinal cord, probably caused by a cell which, I think, had possibly hived off at an early period.

As regards thyroid extract, I have given as much as 250 grains of it in the day without any great physiological effect; but I have come to the conclusion that from 5, 10, to 15 grains per day is as much as is necessary, and produces all the metabolic changes that are useful in this disease. In other operable cases, such as cancer of the rectum, the practice of colostomy will prolong life, for, to put it briefly, the means by which the cancer kills the patient are to be provided against as far as possible.

In conclusion I would say that working at cancer is really very disappointing work. All that one can say is—

“The reward is in the doing,
And the rapture of pursuing
Is the prize,”

but by holding debates and meetings, such as the present, individual effort is encouraged and collective work is stimulated. In this way only will true success come, and it is by such means that we may hope to wipe away the present reproach that cancer is to our professional skill.







