Remarks

ON

THE ETIOLOGY OF CARCINOMA.

HAS IT A PHYSIOLOGICAL FUNCTION IN
THE BODY?*Read before the Edinburgh Medico-Chirurgical Society.*

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SOME recent utterances on the etiology of carcinoma have strongly endorsed the view that we have to deal with a microbic disease. This aspect of the question is not new to this Society, as it has already been placed before it on more than one occasion, and notably so by Dr. W. Russell in his able and instructive paper. The lately published researches to which I refer are those of Professor Doyen, of Paris, and those of Drs. Ford Robertson and Wade, of Edinburgh. In the former we have the "micrococcus neoformans" regarded as the exciting cause of the disease, and in the latter the "plasmodiophora brassicae," the organism found in the "finger and toe" disease of the root of turnips, has been histologically identified in every phase of its life-cycle with similar appearances in mammary and intestinal carcinoma. One cannot allude to the above contributions without bestowing on them a warm encomium of praise for the careful, elaborate, and painstaking work that they represent. The scientific spirit of inquiry that pervades them has the warm sympathy of all of us, no matter what our views be on the nature of carcinoma; for it is only by such thorough and independent work, and by hearing both sides of the question, that we can arrive at a right conclusion, and solve the mystery surrounding this disease. I do not propose in this paper to discuss the conclusions arrived at by Professor Doyen and by Drs. Ford Robertson and Wade. All I would say of them is that so far apparently they do not fulfil the postulates of Koch, and that there is yet wanting in connexion with them that crucial test of the reproduction of carcinoma in animals by means of the respective micro-organisms that is almost an essential for the establishment of the position taken up. At the same time special importance attaches to the work of Professor Doyen, seeing that he has put his theory to the test clinically, and asserts that he has found a serum which has a curative effect in carcinoma. If this be so, it is most convincing evidence in favour of his theory, and this serum merits that most careful and unbiassed trial that I am sure it will obtain. Time, of course, is needed to test the value of any results, and it does not do to be too sanguine in the early days of any new remedy. What has struck me most in the communications I have read on the effects produced by Doyen's serum is the absence of any evidence of changes in the cancer cells themselves. The great point on which stress is laid is the mobility it induces in the growth. This, I think, is just what one would expect when we consider the source of the serum and the conditions that exist in the large majority of cancerous tumours. One of the most constant of these latter is the presence of a variable but generally extensive area of small cell infiltration. This is regarded as a disturbance of the nutritive processes of the part, or, as it is commonly expressed, is inflammatory in its nature, and it is the factor that probably serves in many instances to fix and anchor down a growth to the surrounding tissues. It may be described as its rootlets, and its presence is not regarded by surgeons as a favourable condition for operative work, for it seems associated with a tendency to recurrence. It is not at all unreasonable to hold that a serum made from microbic tissue, as Doyen frankly admits his is, should have an effect on this inflammatory area, as is seen in other instances of serum-therapy, and thus allow of an operation being done that otherwise would have been contraindicated. If this be so, such a serum should prove of great value, and possibly its future rôle may be as an adjunct to operative treatment, a preliminary course of it being gone through to localize the tumour, and by its effect on the surrounding tissue lessen the tendency to the dissemination of the cell growth, just as Watson Cheyne advocates the preliminary injection of antistreptococcus serum in operations on the tongue so as to diminish the risk of sepsis. Any such agent would be of the utmost value in all operative work for cancerous disease.

Assuming, then, as I think one has a right to do, that the parasitic theory of carcinoma has not yet been definitely established, I am entitled to bring forward any view that I may have formed of the disease either as the result of experimental or clinical observations, for in my opinion these latter have to be considered, and any theory that does not harmonize with them should be viewed with distrust. I confess that the more I work with carcinoma clinically the more I am inclined to regard it as a tissue vice, and the more I lean to the view I put before this Society nearly nine years ago, and which I may designate the germinal (reproductive tissue) theory of cancer. I then stated that I believed cancer consisted in the epithelium of the part affected taking on the active proliferation which is the marked characteristic of the germinal epithelium, and that the special cells seen in sections of cancer and known as cancer-bodies will eventually be shown to be special ova or germinal cells. Let me briefly allude to the grounds on which I came to this conclusion. In my paper I pointed out the very remarkable effects produced by the removal of the tubes and ovaries on carcinomatous mammary tissue, for under the operation there took place an actual disappearance of it. Apart from its therapeutic interest, such a fact had some bearing on the etiology of cancer, and thus I was led to theorize and enunciate the above hypothesis. At the time I wrote my paper I had only done a few cases, and my object in publishing them was to put the procedure in the hands of the profession, so that they might test its value. They have done so, and I consider with very great fairness. Speaking generally, it may be said that an analysis of the cases in which the operation has been done is favourable to the procedure. This is borne out by Mr. Alexis Thomson's figures published in the *BRITISH MEDICAL JOURNAL* of November 8th, 1902, and by some very recent ones given by Mr. Hugh Lett at a meeting of the Royal Medical and Chirurgical Society of London on January 24th, 1905, where he dealt with 99 cases, and showed that 36.4 per cent. of all cases operated on were materially benefited by the operation.

It may be taken, then, as a proved fact that under oöphorectomy mammary carcinomatous tissue is very much influenced, and may even disappear. The nature of the change consists in a great increase in the stroma of the growth, and a marked disappearance and fatty degeneration of the epithelial cells. In other words, there is a more cicatricial condition of the part affected, such as we see in the cases of atrophic or withering scirrhus mammae. This is well shown in the slides illustrating sections before (Fig. 1) and after oöphorectomy (Fig. 2) for mammary cancer.

It was on these grounds, and these only, that I based my germinal theory of cancer, but I fully recognized that to establish it on a scientific and reliable basis a good deal more was required, and that if I was correct we ought to find (1) nuclear protrusions (polar bodies) and (2) fewer chromosomes in the so-called germinal cells. Search was made for the former by Dr. Ernest Fortune in films that he prepared from carcinomatous tissue, it being recognized that any such protrusions, being nuclear, should be coloured green by the Biondi stain. In some of the films there were noted appearances in certain of the cells containing the so-called parasite that indicated a body, which stained green, either leaving or just entering the cells. In some cases it was surrounded by a distinct vacuole, but whether this body was an extrusion or an intrusion of a possible leucocyte was not absolutely clear, and it was decided that no definite nuclear protrusions (polar bodies) had been established. As regards the diminished number of chromosomes, no prolonged investigation was made, especially as a very able cytologist whom I spoke to held that it would be a very difficult if not impossible task to count the chromosomes in the cells of human carcinoma. Dr. Ernest Fortune, to whom I am under great obligations for all the microscopic sections in connexion with my cancer work, and also otherwise for much valuable and suggestive help, and who has also prepared the photomicrographs I shall show this evening, only confirmed the observation that cancer cells which were dividing and undergoing mitosis showed a clearer appearance than the other, as if the process of division had some clarifying effect on the whole protoplasm of the cell. He also observed that while in the films made from cancer tissue cells could be found in all stages of karyokinesis, those cells containing the alleged parasite had never been seen dividing themselves, although the cancer cells in their vicinity were doing so. No assistance either in the matter was gained from a series of experi-

ments I made in inoculating ovarian and testicular tissue into rabbits.

Although, however, I was unable to furnish the proof I was in search of, confirmation of it came from another and an independent source, for on December 10th, 1903, a paper was read at the Royal Society of London by Professor Farmer, Mr. Moore, and Mr. Walker, entitled "Resemblances Exhibited Between the Cells of Malignant Growths in Man and those of Normal Reproductive Tissue." As the result of a large number of careful observations on the intranuclear changes occurring in the cells of malignant growths undergoing multiplication, these gentlemen were able to establish the fact that the division of the nucleus of malignant cells very closely resembles that found in developing reproductive tissue. In other words, the mitotic division was of the heterotype order, and there were only half the number of chromosomes in several of the malignant cells. On my drawing attention to the view of carcinoma that I had put forward to this Society in 1896, the authors were generous enough to reply "that it would have been difficult at the time he wrote for Dr. Beatson to have come nearer to the facts since demonstrated by us." With this further development another very important fact bearing on the etiology of carcinoma was established.

Fig. 1.

Before I pass to the consideration of the etiology of cancer, I wish briefly to allude here to a few points that I think have a special bearing on it. The first one is the cellular character of the so-called cancerous growth or tissue. In its structure carcinoma is always regarded as made up of two distinct elements, namely, (1) epithelial cells, and (2) a connective stroma, but its characteristic feature is the disorderly distribution of its large, irregular, and polymorphic cells. Any stroma that they possess is derived from the connective tissue spaces into which they are forced, and they have no blood vessels, no nerves, and no lymphatics of their own. We do not see amongst these cells any capillary formation such as occurs in the granulation tissue of a repairing wound. Cancer cells in fact show no tendency to organize. They simply lie in an intercellular fluid unpermeated by any new-formed blood vessels. In other words, a cancerous tumour is composed of cells only, its stroma being a pre-existing element into which the cells have been forced by pressure. There is in such a tumour only a massing together or heaping up of cells that have no tendency to develop into permanent tissue, and are entirely devoid of organization. Cells so situated must be of low vitality and be liable to decay, a characteristic that specially marks carcinomatous swellings. We all know how readily they break down, especially the central or oldest cells, so that we have formed these large crateriform ulcers that are clinically recognizable as malignant. Then cell proliferation itself is an indication of weakness, for, as Virchow says: "All

cellular formations which lose their nucleus have a mere transitory existence, they perish, they disappear, they die away, or break up." The striking feature, then, of a carcinomatous tumour is that it is entirely made up of cells, which proliferate, but do so apparently only to perish, and have no building up or constructive power.

Another special characteristic of the carcinomatous cell is its unirritating character. When it is cast off by the primary tumour and finds a lodgement elsewhere, its arrival in a distant part of the tissues or in an organ is not heralded by any special local disturbance or by constitutional irritation. Every physician and surgeon knows the great difficulty in deciding in cases of carcinoma as to the existence or non-existence of secondary deposits that might be a bar to operation. For example, small local foci of dissemination in the lungs or liver will often not reveal their presence by any physical signs, and *post-mortem* examinations often show metastatic deposits in organs where, owing to an entire absence of symptoms, their presence was never suspected. I need not give illustrations of what is a common experience, but this fact has always seemed to me a strong point in favour of the view that we were dealing in the case of the carcinoma cell with one that is the offspring of the body tissues and is in no way a stranger to them. Were this not so, we ought to

Fig. 2.

have present in the primary tumour as well as in all secondary deposits that disturbance of nutrition known as inflammation, such as is generally observed in the case of microbic or protozoal infection. As a general rule, all such signs of irritation are absent in the early stage of carcinomatous growths.

This fact has a bearing on another matter on which stress is often laid, and that is the importance of the medical man seeing cases of carcinoma early, and patients are sometimes blamed for not having sought advice sooner. The truth is it is not always their fault. It is not uncommon for cases to come under our notice where carcinoma has made extensive progress in both the mamma and the uterus without giving rise to any symptoms of sufficient importance to attract the attention of the patients. It is only when the cancer cells have begun to act by their bulk like a foreign body that they set up irritation locally. Constitutionally they give no sign; many of those who are the subjects of this serious and fatal disease showing outwardly all the appearance of perfect health. Delay in seeking medical advice is consequently often unavoidable, and I am not in favour of the view that is being put forward of late by some of our profession that with the object of getting hold of cases in an early stage the general public should be instructed in the early manifestations and symptoms of carcinoma. Against this I would most emphatically protest. To begin with, there is very little to teach them, and if people are to be on the watch every day of their lives for the possible occurrence of this

disease, there will be induced that unhappy and apprehensive frame of mind that I regard as a powerful predisposing cause of the very condition we want to avoid. The greatest blessing we have is that we do not know what lies before us, and to be constantly on the look-out for the occurrence of cancer would make life unbearable. By all means let it be generally known by the public that the moment a swelling or lump is detected medical advice should be taken about it, just as should be done, too, when any symptoms of illness show any persistency or are of an unusual character. In the same way it cannot be too strongly impressed on the profession that the possibility of carcinoma being the exciting element in troublesome cases of indigestion must never be overlooked, and that swellings of every kind should be thoroughly investigated on their detection and carefully watched.

The general good health that is often present in those who are the subject of carcinomatous disease has its analogy in the *post-mortem* room, for I have often been struck in our examination of the bodies of those who have died at the Glasgow Cancer Hospital with their well-nourished condition, even when they have suffered from the disease for a lengthy time.

Another point, too, that has attracted my attention has been the very pigmented condition of the fat in some of these cases. It presents a reddish-yellow, yolk-of-egg appearance, and has a colouring matter present that is not seen in ordinary fat. I was especially struck with this in a case last year, and tried to get a chemical analysis of the fat, but it seems that the chemistry of human fat is not very well known, and has not been very extensively studied. It is possible that the appearance to which I refer may be entirely a *post-mortem* one, or be present in other chronic diseases, and thus have no particular association with carcinoma, but it may have, and it may also be associated with the so-called lemon-tinged cachexia that is often remarked in cancerous patients. As bearing on this point, I have sometimes noticed when operating on cancer cases, especially in mammary ones, an oily and fluid state of the fat. And it is, I think, a very general experience that in these cases carcinoma disseminates itself more rapidly than in patients of spare build.

I come now to the last point I wish to draw attention to, and that is, the source of the procreative fluid of the human body. In view of the germinal theory of carcinoma that I am putting forward, some reference must be made to this subject, for I consider that it has a close relationship with it. As is well known, the ovaries and testes prepare certain modified epithelial cells, termed respectively ova and spermatozoa, by the union of which the human embryo is produced. Before, however, this can be accomplished the ova have to undergo a maturation process and the spermatozoa a series of cell divisions, by which in each case there is a reduction of half the number of their chromosomes. In both these organs this process is accompanied by great cellular activity; and the question may very fairly be asked, what is the stimulus that sets it in motion so that we have the extrusion of the polar bodies in ova and the reducing division that leads to the formation of spermatozoa? It must be a secretion of some kind, and it may be elaborated by the testes and ovaries themselves, or by all the tissues of the body, in accordance with the old Hippocratic idea. In the latter case the testes and ovaries are merely instruments for elaborating the work done by the rest of the body, which is in reality the source of the fructifying fluid which confers on the ova and spermatozoa their procreative power. I confess that this latter view commends itself more to my mind, and it is, I consider, not altogether unsupported by facts. Thus, experiments show that the fluid portion of the semen largely furnished by the accessory sexual glands, such as the seminal vesicles, the prostate gland, and Cowper's glands, is not only essential to the motility of the spermatozoa, but also to their fertilizing power. Again, the removal of the tubes and ovaries leads to the deposit of an increased amount of fat in the body, as if some secretion of the tissues was being stored up and was no longer being removed from the tissues, in the same way as mucin accumulates in the body in myxoedema, when the thyroid gland is excised. If this be as I suggest, we have in the body tissues a secretion which has to be reckoned with, a secretion that not only probably bestows vigour on the tissues themselves and might even under certain circumstances confer on them a proliferating power, but seems to have a special affinity for one particular tissue, namely, the fat of the body. In this latter it may be retained and kept as it were in reserve, as, for instance, when failing functional activity on the part of the testes and ovaries does not utilize it to the extent that it is created or does so slowly and intermittently. Further

on I shall refer again to this matter, so will say nothing more upon it now, but I regard it as having an important bearing on the etiology of carcinoma.

Various as have been the theories put forward to explain the formation of tumours, in all the definitions of them there has generally been evident an undercurrent of feeling that they perform no physiological function in the human body. Some have even openly expressed this view. Thus, Lücke describes a neoplasm as "an increase of volume by the production of a new tissue without a corresponding physiological function," and Coats, too, takes up the same position, stating that tumours are "pieces of tissue which have a life and growth of their own irrespective of the needs of the organism and that without any apparent object." Of none of the tumours has this view been more strongly held than of the carcinomata, the cells of which are regarded as inimical and hostile to the rest of the body cells and have been likened to an invading host advancing to the conquest and eventual destruction of every tissue in the body. Like others I have shared this view, but the more I have thought over the subject the more have I felt that the so-called autonomous proliferation of cells was a mere assumption, and that possibly the carcinomata were doing work for the organism by eliminating or dealing with some body product. If so, this would bring them into line with the action of the other body cells, and present them not as rebels running amuck in the body commonwealth of cells, but as taking up some new work, or as performing the duties of other cells no longer functionally active. Could any ground for such a view be shown to exist, it seemed to me to put the whole question on a more scientific basis, and carried with it some ray of hope in the direction of therapeutic measures.

As bearing on such an aspect of the matter, I could not but be interested in some recent investigations on the tumour formation that occurs in the form of rounded bulbs or nodules on the roots of healthy bean or clover plants. To them I should like to refer, as they bear indirectly, I think, on the work recently published by Drs. Ford Robertson and Wade, and my remarks will be a summary of an article that appeared in the last October number of the *Century Magazine*.

It had often been observed that the roots of bean or clover plants have on them tumours or swellings varying in size from small pinhead nodules up to good-sized potatoes; and it was further noted that though such plants appeared diseased, they were in reality the most healthy. This seemed even more remarkable when examination of the tumours showed that they were packed with bacteria. Matters were, however, presented in a different aspect when investigation of these bacteria revealed the fact that they were constantly absorbing free nitrogen from the air, and were supplying the plants affected with the very food they needed. In other words, every nodule or tumour was acting as a feeder to the plant, whose vigour might be measured by the number of growths upon its roots, for in every one of these tumours the never-tiring bacteria were separating the nitrogen from the air and changing it into plant food. This furnished an explanation of a fact that had previously been noted—namely, that after a crop of beans or any leguminous plant, the soil gave a much better crop of wheat, this being due to these leguminous plants not only obtaining their necessary nitrogen from the air instead of the soil, but actually putting nitrogen back into the latter. I need hardly say that botanists and agriculturists were not slow to grasp the practical aspect of this matter, and by breeding and colonizing the bacteria they tried to inoculate the soil, and thus make it favourable not only for the growth of leguminous plants, but subsequently for wheat. The first attempts in this direction by Professor Nobbe of Tharandt with his so-called "nitrogen" failed, but Dr. George Moore of Washington showed that the failure was due to a wrong cultivation of the bacteria. They had been fed with too much nitrogenous food, and this dulled their appetite for nitrogen. They were surfeited with it and would not work, any more than will the son whose rich father has given him everything he asks for without making the boy do anything for himself.

Dr. Moore reared his bacteria on such food that they still retained a desire for nitrogen, and worked vigorously to obtain it, and they have now become invaluable. They are sent about in packets to vaccinate or inoculate the ground, with the result that crops on soil so treated have increased a hundredfold, and tumours that gave plants the appearance of being diseased have proved to be powerful workers in the economies of plant life, furnishing man with the means of

tapping the sea of nitrogen around us in the atmosphere and conveying it to the impoverished soil, thus making the barren places to rejoice and the desert to blossom like the rose. Paget long since drew attention to the nodosities and nest-like growths seen on trees, and they have always been of interest in connexion with the subject of tumour growth, but they become doubly so if increasing knowledge reveals that possibly they are doing work, and that of a beneficent kind, in the world of Nature.

To assume that some kind of physiological work may underlie tumour growth in man is not, I consider, unreasonable, and the possibility of this should not be overlooked. Harm may be done by taking for granted that, because a process is inexplicable and apparently detrimental, it is therefore aimless and meaningless. A more sensible and more encouraging attitude to take up is that it may be a modification of some one of the many activities of the body functions. In the case of the carcinomata, I believe that there are indications that this is so; and the most confirmatory fact bearing on it is that established by Farmer, Moore, and Walker—namely, that there exist in malignant growths special cells characterized by a reduced number of chromosomes, and that have their prototype in the reproductive

FIG. 3.

cells of the body. From this it would almost seem as if, through some functional inactivity or disease in the testes or ovaries, the part affected by the carcinoma was doing vicariously their work or helping them in an excess of work thrown upon them. If, as I suggest, the body tissues elaborate the procreative fluid, the possibility of this interchange, and the necessity for assistance in their work, is not an unlikely or an unreasonable suggestion. Not only is there nothing in the carcinomata structurally irreconcilable with such a view, but there are rather some points that tell in favour of it. The absence of all organization in the crowds of cancer cells that fill the tissues and form the tumour would suggest that they are cast-off cells, which, were they not shut in by the tissues, would escape in the same way as do the cells thrown off in the tubuli seminiferi, and which find an outlet by the vasa deferentia. A disintegration and degeneration takes place in many of these latter, just as occurs in the cancer cells that fill the alveoli of a breast tumour. I am inclined to regard a carcinoma as made up of two separate portions, as it were, one part being composed of cells that have been thrown off as a secretion, and another part that is glandular in the sense that it is doing work as a secreting tissue. Some of the secreted cells will divide and subdivide, and will reach the stage of what may be termed germinal cells, but many of them will degenerate and perish. In short, there is being enacted in the tissues the same cell activity and proliferation that goes on daily in the ovaries and testes, where alone can be found a parallel to the profusion of cell life that marks the

carcinomata. Others have noted the glandular character of these neoplasms. Bland-Sutton speaks of them as "aborted and aberrant glandular tissues." No doubt they are imperfectly glandular, though they assume an acinous type, but the relation of their cells to the interstitial connective tissue with its blood vessels and lymphatics quite allows of any secreting action being carried on. Sometimes the arrangement of the cancer cells seen in sections is suggestive of gland formation (Fig. 3), and this is very well shown in one that I will put on the screen. At least it is a possible explanation of what is an unusual and rather striking appearance.

Another interesting point that I think has some bearing on this question of cancer as a secreting organ is the effects of operations for carcinoma. Of course, I leave out those cases where operation has removed ulcerated growths or some constriction in the digestive canal that has mechanically interfered with nutrition. Apart from such cases, it is a very general experience that in successful operations patients put on flesh and get stouter. Even those suffering from the so-called cachetic symptoms often lose them and regain a healthy appearance. It is not easy to explain this, unless the removal of the carcinoma has put a stop to something that was draining the tissues and markedly modifying them.

I have said that such patients get stouter. Does this in any way explain matters? Does it point to the fatty tissue of the body again taking on its storage property to deal with a secretion that was no longer being used up by the carcinoma—a secretion that, as I have already said, is probably manufactured by the tissues themselves, and in which they are bathed, deriving from it strength and vigour, and even in some cases, should they be degenerate, a fertilizing power? If this be so—and I incline to the view—then we have the fat of the body bearing some relation to carcinoma both before the occurrence of that disease and after its successful removal by operation. Under both conditions it has a salutary influence, and it may be that it is only when its storage power is weak, or has been strained to the utmost, that the more specially developed though degenerate cells of any body organ or tissue may draw upon the body secretion that the fat contains, and by dealing with it in a different way manufacture it into an epithelial secretion on the lines of the normal reproductive tissue of the body.

Apart from any influence that oöphorectomy in inoperable breast cancer may have on the blood supply of the mammary region it may exercise its beneficial effects by not only lessening the amount of my suggested body secretion but also by adding to the capacity for development of the fatty tissue and thus increase its storage power.

It is an interesting fact that lutein occurs in all fatty tissues as well as in blood serum, egg yolk, and milk. I am indebted for this information to Dr. Malcolm, of the University of Edinburgh Physiological Laboratory, to whom I had written on the subject of lutein in fat and the possibility of estimating the amount present in it, as I was anxious to know if an excess of it was the cause of the rich colour observed in the fat of cancer patients. As to the significance of lutein in fat everything is at present problematical, for it has not yet been isolated in the pure state and several varieties are supposed to exist. Staedeler and Holm have published a paper describing a crystallizable lutein found in the corpus luteum of the cow, and recently, in the December number of the *Practitioner*, Mr. Cuthbert Lockyer has drawn attention to the occurrence of lutein cysts in the ovary in cases of deciduoma malignum. In the last edition of Schäfer's *Histology* the opinion is expressed, on the authority of Fraenkel and Cohn, that the corpus luteum produces an internal secretion which causes the fixation of the embryo to the uterine wall and thus controls cell proliferation. In view of this latter property I have made trial of the extract of corpus luteum in mammary cancer, but with no appreciable effect on the growth.

Gentlemen, from what has fallen from me to-night you will gather that I put forward as the most likely explanation of carcinoma what I may term the "germinal theory." In my humble opinion it harmonizes most with the facts and course of the disease as observed clinically, and it furnishes an explanation of many interesting points about it that are otherwise mysterious and obscure. It assumes, I admit, the existence of a general tissue secretion that cannot be absolutely proved, but in favour of which there is, I consider, a fair amount of reasonable and confirmatory evidence. With such a procreative fluid in the body, in the event of the testes or ovaries through functional decay or disease being unable to deal with it, and the fat of the body having no special

capacity for storing it, it is within the bounds of possibility that tissues or organs that have retrograded physiologically, and, by losing their differentiation, have reverted to a more primitive type, should under these conditions take upon themselves the function of secreting it when they would, of course, do so in the cellular form followed by the normal reproductive tissue. This, it may be said, is a return to the old "spermatic theory" of carcinoma, and it is so to some extent, but yet with an important difference, in that the older writers assumed a conversion of the normal tissue of the part into tumour tissue, whereas, in the view I put forward the masses of the tumour cells are not a tissue at all, but are cells thrown off by altered somatic cells in the elaboration of a special secretion. And, if I am correct in this conclusion, then in carcinoma we have a tissue secretion to deal with, in relation to which the fat of the body probably acts as a middleman just as lymph does in ordinary nutrition. This being so, I do not see that we should take too pessimistic a view of the therapeutic position in connexion with the disease or despair altogether of its successful treatment.

Gentlemen, nine years have elapsed since I last addressed this Society on the subject of carcinoma, and during that period it has occupied much of my thoughts. To-night I have again ventured to lay before you the trend of that thought and how the problem of this disease is presenting itself to me at present. As on the previous occasion I had to ask your indulgence for stating much that was theoretical and problematical, so again I feel I must do the same. I can only plead in excuse the conditions under which in this matter we have all to work. Carcinoma is a great mystery, and in its elucidation progress can only be made by observation and by forming a good working hypothesis. If facts in sufficient number and importance tally with that hypothesis, then one is justified in raising it to the dignity of a theory. I dare say I am premature in taking that step at present, but I conscientiously believe that all the indications point to a germinal (reproductive tissue) theory of cancer.

MALIGNANT DISEASE OF THE FUNDUS UTERI

TREATED BY X RAYS THROUGH THE ABDOMINAL WALL:
RECOVERY.

By ARTHUR J. CLEVELAND, M.D., M.R.C.P.,
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WITH A NOTE ON THE CASE

By DONALD D. DAY, M.B., F.R.C.S.,
Honorary Surgeon, Norfolk and Norwich Hospital.

It has been stated dogmatically, and the opinion is generally held, that the treatment of all but quite superficial malignant growths by *x* rays is useless; and without affirming that this view is disproved by the case I now record, or that the case is undoubtedly one of a deep-seated cancer cured by *x* rays, I think it is worthy of attention even if it should only have been a coincidence that recovery followed the treatment.

History.

The patient, a married woman of 40, who had always enjoyed good health, and had been born and had spent her youth in India, was seized with pain in the lower part of the abdomen and sickness in September, 1903. This attack was immediately preceded by a menstrual period accompanied by an excessive loss. Prior to this the menstrual functions had been normal. During the next few days she had a temperature of 99° to 101°, was very constipated, and had much pelvic pain and tenderness.

On October 6th, 1903, she was seen by Mr. Donald Day, who has very kindly written some notes for me on the case. He thus describes the condition of the patient and the operation performed:

"She was in a state of great debility and anaemia induced by frequent uterine haemorrhages. The uterus was somewhat enlarged, and the fundus could easily be felt bulging to the left and tender to pressure. Per vaginam the uterus felt fixed, especially on the left side; the cervix was patulous, and a probe passed 4 in. A diagnosis of carcinoma of the body of the uterus was made.

On November 9th laparotomy was performed in the Norfolk and Norwich Hospital, but, as was feared, it was found that removal was out of the question. The fundus was occupied

by an irregular mass like a small orange, which grew into the left broad ligament, was adherent to the pelvic wall, and implicated the sigmoid flexure, where it crossed the broad ligament.

Removal of the growth would have necessitated resection of some inches of the sigmoid, and considering the fixity of the mass and the impossibility of removing the entire disease, this was considered inadvisable. No doubt existed in the minds of those present that it was a malignant growth. Recovery from the operation was uneventful, but no improvement occurred in her symptoms until she came under Dr. Cleveland's treatment. I examined her again last summer (1904) and found the uterus of normal size and freely movable. No sign of disease existing in it or the broad ligament could be detected and she was apparently completely recovered. I consider that the entire credit for this must be ascribed to the *x*-ray treatment."

Treatment.

On December 12th, 1903, the patient came to me, and as a "forlorn hope" she agreed to try *x*-ray treatment. She had recovered well from the operation but was suffering considerable pain, had a bloody vaginal discharge, which had been foul, was constipated, and occasionally passed blood per rectum. The pain caused insomnia and necessitated opium both by mouth and rectum. She was occasionally sick and ate badly. Her weight was 8 st. 3 lb., about a stone below the normal. A hard mass could be felt in the left iliac fossa extending to the middle line and downwards into the pelvis. This was tender, and walking a short distance caused pain in it.

I treated her with a moderately high tube excited by a mica-plate static machine, applying the rays directly over the pelvis for fifteen minutes at a time, three times a week, the tube being about 6 in. distant from the skin of the abdominal wall. After thirteen exposures she developed some dermatitis and I discontinued treatment.

On January 9th her weight was the same, and her general condition unaltered. She had some haemorrhage and pain when the bowels were opened, often wanted opium at night, and used to have attacks of constipation with abdominal distension.

Towards the end of January she began to improve, and the pain and discharge became less. As she had had a fairly sharp reaction to the rays I did not recommence treatment till February 5th, and then gave her another twelve exposures, causing some more dermatitis. She was by this time getting much better, sleeping well, and could walk two or three miles without pain. Her weight on March 16th was 9 st. 7 lb., a gain of 13 lb.

From March 9th till April 9th she had no treatment, and during the latter part of this time the pain and haemorrhage returned. She got depressed and ate badly, but her weight was maintained. Under further treatment all these symptoms quickly disappeared, and in June she weighed 9 st. 8 lb., could walk four or five miles, and one day played two sets of tennis. Mr. Day examined her on June 4th, and said that he could find no tumour, and the uterus was freely movable.

Since June she has had treatment from time to time, and has been as well as ever she was in her life. Menstruation is quite normal, and there is no discharge from either rectum or vagina. She has maintained the gain of 1 st. in weight, and has just started for India. Beyond a little opium when necessary and an occasional purge she had no other treatment than that described.

Remarks.

There is no strict scientific proof that the very happy result which followed the application of *x* rays was entirely due to it, for it has often happened that tumours diagnosed as malignant at an operation and left as irremovable have remained quiescent for a long time, and the accuracy of the diagnosis consequently called into question. Whether in certain rare instances an exploratory operation can have the same effect on a cancer as it can on a tuberculous affection of the peritoneum need, I think, hardly be considered in this case, for it was not until ten weeks after the operation that any sign of improvement was manifest—and, indeed, during this time the disease was apparently progressing. Again, in March the cessation of treatment was accompanied by a return of the symptoms, and a resumption of it followed by a rapid amelioration. It is difficult to explain these results on the hypothesis that the operation was the beneficial factor in the case.

The other point for discussion is, Was the disease really of