AN ADDRESS

ON CERTAIN

CONSIDERATIONS IN REGARD TO THE
INFECTIVE NATURE OF CANCER.*Read before the Medico-Chirurgical Society of Glasgow on
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I.—INTRODUCTION.

CONSIDERABLE interest has of late been shown in regard to the question, Does cancer depend on the action of a parasite? I do not here propose to offer any decided opinion on the various microscopic appearances which have been described. My main object is to consider the subject of cancer from the point of view of general pathology, and to endeavour to obtain some light on the question, Do the facts with which we are acquainted in regard to the structure and mode of growth of cancerous tumours fit in with the view that it depends on the action of a parasite?

In putting this question in the front, I am following the line which was followed in the case of a disease which within the last ten years has come to be fully regarded as due to the action of a specific microbe, namely, tuberculosis. The infective nature of tuberculosis was recognised by pathologists long before Koch discovered the tubercle bacillus. For my own part I find that in the course of a discussion on the pathology of phthisis pulmonalis in the year 1881, I used these words:—

In a typical case of local tuberculosis we have an "infective" disease... An infective process is one in which lesions are to be traced to the direct action of a virulent agent.... Acute miliary tuberculosis is an infective disease because each miliary tubercle owes its origin to the action of an infective particle. And so local tuberculosis is infective, because we have evidence of some infective material acting directly on structures, and producing the particular form of lesion called a tubercle.

It was because the general pathology of tuberculosis pointed to the existence of a particulate infective material as the cause, that Koch's discovery obtained such early and universal acceptance. We have to inquire whether the case is similar as regards cancer. Are we in the position to say that the discovery of a cancer parasite will complete and round off the pathology of cancer, as a similar discovery did in the case of tuberculosis?

II.—THE GENERAL PATHOLOGY OF TUMOURS.

In order to answer this question it is necessary to have clear ideas as to the pathology of tumours in general and of cancer in particular. The modern use of the term tumour, at least in the pathological sense, is considerably narrowed from the literal and original use of the word. In speaking of a tumour we nowadays think of a piece of tissue which lives and grows for itself, irrespective of the needs of the organism, or of the conditions around it. Such a piece of tissue living and growing must have in itself some stimulus, which is not the ordinary physiological stimulus under which the various tissues of the body are formed and grow.

On the other hand, in most cases the stimulus must be of a kind nearly allied to the normal physiological one, because the structures produced closely resemble the normal tissues. The structure of a fatty tumour or of a bony, cartilaginous, or other simple tumour scarcely differs from that of fat, bone, cartilage, or other simple tissue. The tissue grows by the multiplication of its elements, that is, by the division of its cells in precisely the same way as the corresponding tissues. The essential difference is that in its growth the piece of tissue is not under the command of the general physiological laws of the body as a whole. These general physiological laws determine the growth of the tissues in relation to the needs of the body as a whole, but here is a piece of tissue growing for which there is no need. It is as if the piece of tissue were in rebellion against the constitution of the body, and refused to be subject to its laws.

¹ *Glasgow Medical Journal*, xv, 257.

The stimulus which induces this excessive growth ought therefore to be something allied to, but yet apart from, the ordinary physiological stimulus. It was a happy idea of Cohnheim's to suggest that the tumour might originally be a piece of tissue which in the process of development or growth has, as it were, been left over, and not included along with the proper tissue of its kind. A piece of fat, or of the tissue which is to form fat, has in the embryo been separated from the rest, and has not been worked up with the tissue around it. The piece of tissue will usually lie amongst tissue of its own kind, but it may get included in some other structure. A piece of tissue originating in this way, lying over as it were from the embryo, will retain presumably certain powers possessed by the embryonic tissues. By virtue of these powers it may take to growing, and in its growth will not be subject to the needs of the body. As an example of what is meant, we may take the case of a wen in the scalp. It is difficult to think of any explanation of the origin of this form of tumour other than that in embryonic life a bit of primordial skin has got included or nipped in beneath the regular skin. This bit of embryonic tissue will lie separate, but with its embryonic powers retained, and if it takes to growing there is no control by the ordinary physiological forces. We know how wens will sometimes grow on till they form considerable tumours.

III.—COHNHEIM'S THEORY OF TUMOUR-FORMATION DOES NOT
APPLY TO CANCER.

I am prepared to accept Cohnheim's theory for many tumours. It is at least a possible explanation in all cases where there is a single piece of tissue which goes on growing as an independent mass. I do not think, however, that it is applicable to the case of cancers, because their mode of growth is something quite different from this.

In considering this subject, it is necessary to distinguish between cancer in its primary seat, and the secondary growths or offshoots which are of such frequent occurrence, and form such a serious element in the disease. The case of secondary tumours will be afterwards considered, but in the meantime we shall confine our attention to the primary growth. Looking to the mode of growth of cancers in whatever situation, I think one of the most important facts which meets us is that here we have not a single piece of tissue growing separate from, and independently of, the surrounding tissue, such as Cohnheim's theory would imply, but rather we have the normal tissue itself taking on, in an ever widening area, a peculiar and independent mode of growth. A cancerous tumour has, as its most essential constituents, cells of epithelial type and origin. If the growing edge of a cancer be examined where the tumour has not passed beyond the organ in which it originated, then it will mostly be found that the normal epithelium of the part is actively growing, and is furnishing the constituent elements of the tumour. It is as if some stimulus were acting on the epithelium of the part, and this stimulus had its source in the parts already affected. In this sense cancer is an infective disease; it spreads, in its primary seat, by the normal tissue at the borders of the lesion being brought under the influence of the morbid cause. This, of course, does not exclude the increase of the tumour by new formation in its own substance. There is a great deal of this new formation; the tissue, having started to grow, continues its growth just as does the tissue of other tumours, but usually much more rapidly and with differences of other sorts.

It might appear that, having come to the position that cancer is an infective disease, at least in its primary seat, we are quite ready for the parasitic view of its origin. But there are many difficulties to be overcome before this position can be established.

IV.—INFECTIVE MICROBES PRODUCE IRRITATIVE LESIONS IN
TISSUES, AS IN TUBERCULOSIS.

In an address which I delivered in the year 1885, in introducing a discussion on cancer in the Pathological and Clinical Society of Glasgow, I got quite as far as the position which I have just indicated, but I distinctly stopped short of accepting the parasitic theory. The reasons which I then adduced concerned themselves mainly with a comparison between cancer in its pathology, and other infective diseases which were known to be due to a parasitic origin. It may be well to

refer again to these reasons, and inquire whether they remain cogent or not.

Taking tuberculosis and syphilis as infective diseases which are known to depend on the action of specific morbid poisons, and comparing them with cancer, we find certain points of resemblance, but we also find such important points of difference as to suggest a different mode of origin. The difference between the two may perhaps be best expressed by saying that in the one case we have a definite tissue growth, and in the other the mere results of irritation. In other words, we have in the one case a tumour formation, and in the other nothing more than a specific inflammation.

The application of an irritant to the living tissues of the body induces certain phenomena which by common consent are included under the designation "inflammation." These phenomena include under certain circumstances a new formation of tissue; but it is tissue of a comparatively rudimentary kind, and it is mostly the connective-tissue structures of the body which are concerned in it. In order to this new formation the irritant has to apply itself to the structures, and the phenomena are the result of a local reaction of the tissues to the irritation. In tuberculosis the process does not differ essentially from that in ordinary inflammations. The tuberculous virus applies itself to a part, and the result is the production of a rudimentary tissue, which as a general rule is subsequently killed by the continued action of the virus, the existing normal tissues being included in the necrosis which the virus has induced. This is the process both in the primary seat of the tuberculosis and in any secondary development which may subsequently occur. The process is always the result of the direct action of the virus, and if it takes place at a distance it is because the morbid agent has been conveyed to a distance. The process in the secondary seat is a mere repetition of that in the primary one, the tissue in the new situation reacting to the irritant precisely as that in the original situation.

V.—IS CANCER A TRUE TISSUE GROWTH?

In contrasting this with cancer we can see significant differences in the process both in the primary and secondary seats, but perhaps especially in the secondary ones.

In its primary seat a cancerous growth is not a mere rudimentary tissue prone to decay, but it is really a finely-adjusted tissue growth. From the way in which it is sometimes described one would suppose that cancer was a mere overgrowth of epithelium; but it is much more than this. No doubt a new formation of epithelium leads the way; but we have also a formation of connective tissue, of blood vessels, and even of lymphatic vessels, such as to induce us to speak of a cancerous tissue. It is in many respects an abnormal tissue, but there are many cancers which in the details of their structure are as finely adjusted as any of the normal tissues. In its mode of growth also the primary tumour has the characters of a true tissue growth, like that of a growing or developing organ and not of a mere irritation.

All this comes out even more prominently in the secondary cancerous tumours. In these we have not merely, as in tuberculosis, a parasitic microbe conveyed to a distance and producing lesions in the new position by irritating the permanent tissue there. It is rather that actual grafts or outgrowths from the primary tumour are planted out, and the secondary tumour is, like the primary one, a tissue growth, frequently of an elaborate and finely-adjusted character. There is every reason to believe that in the secondary extension of cancers we have living cells of the original tissue conveyed to the new situation, and there left to multiply and grow. It is in this sense that a cancerous growth and its secondary extensions are really one, the offspring being directly derived from the parent tissue.

Even when the graft is planted in an epithelial organ, as so frequently happens in the liver—and we should on the analogy of tuberculosis expect that the cells of the organ would be stimulated to new formation by the supposed parasite—we see nothing of the kind. The new-formed and quickly-growing tissue merely crushes aside the normal hepatic cells and causes them to atrophy.

It is true that in all secondary cancers there are certain important structures supplied by the tissue in which they

grow, namely, the supporting stroma composed of connective tissue, and the blood vessels and lymphatics. But this simply follows the analogy of all developing and growing tissues. These supporting and nourishing tissues follow the growing structures, and arrange themselves according to the necessities of the latter. In the development of any epithelial gland, for instance, the primary process is a multiplication of the epithelium, and there follows on this a growth of connective tissue and vessels which become the supporting and nourishing structures, and arrange themselves according to the plan of the tissue concerned. In a precisely similar fashion do these structures conduct themselves in relation to the growing epithelium of a cancer. They follow its growth, giving it support and nourishment, apparently drawn on by the requirements of the more special tissue. And just as in each form of epithelial gland the supporting stroma and vessels have their special form and arrangement, so in each form of cancer these supporting and nourishing structures show special characters, as if the imported epithelial graft had the power of determining not only its own growth but that of the connective tissue and vessels which are destined to serve it in the invaded organ.

The differences in structure which cancers present among themselves constitute another divergence from what we meet with in tuberculosis, and this applies both to the primary and secondary tumours. In tuberculosis we have a specific microbe, and wherever it attacks the results are similar, any differences which occur being explicable by varieties in the sensitiveness or otherwise of the tissues. In the case of cancer, on the contrary, we have not only differences according to the organ attacked, but even in identical organs the most extraordinary varieties in structure in different cases. The different varieties of cancer are, to some extent at least, traceable to differences in their origin, and where we have an organ containing various kinds of epithelial structures, there we may have great differences in the forms of cancer occurring in that organ. Such an organ is the stomach, and many are the varieties found in it. There are cancers apparently originating in the deep epithelium, which in its multiplication tends to burrow beneath the surface so as to form a widely-extending infiltration of the wall of the organ without producing any protruding tumour at the surface. There are others which show a vigorous growth of the surface epithelium, and produce bulky, prominent masses, readily undergoing ulceration. There are, again, tumours which, presumably from some peculiarity of their origin, show from the first a peculiar tendency in their epithelium to undergo the so-called colloid metamorphosis. These three categories by no means exhaust the varieties of cancers of the stomach. There are differences in the structure and abundance of the stroma and vessels, and differences in the rapidity of growth, as well as in the malignancy of the mode of growth, of an almost endless variety. All this looks very unlike a microbe attacking a tissue such as we find in tuberculosis.

This difference appears all the more striking when we consider that each variety of cancer in its secondary extension breeds true. I have said that the secondary tumours are grafts from the primary one. The proof of this lies mainly in the fact that they repeat the tissue of the primary one with almost exact detail. The size and form of the cell in a primary cancer of the stomach, the character of the stroma, the amount and character of the vessels, the degenerative tendencies will all be repeated in the secondary tumours in the liver. How else can this be than that a germ of tissue has been carried off from the primary seat and deposited in the secondary one. How different, again, is this from what occurs in tuberculosis.

There is still another fact in regard to cancers which is of some consequence in this connection. We have seen how striking is the limitation in the individual case of the advancing infection to the kind of epithelium in which the disease began. There is a no less striking limitation frequently seen to the organ in which the cancer has originated. How common, for instance, is it to see a cancer of the stomach advancing right up to the pylorus and stopping strictly short there, refusing to involve the duodenum. This applies to superficial as well as to deep tumours, although one might suppose that the superficial epithelium of the duodenum was strictly comparable to that of the stomach, and would be equally susceptible to a parasitic influence.

Allied to this is the fact that cancer does not extend along surfaces in its primary seats except by continuity. In the case of tuberculosis the particulate infection, carried from its primary seat, frequently deposits on neighbouring surfaces and there produces its effects. Tuberculosis of the testicle frequently extends along the vas deferens to the vesiculae seminales, prostate, bladder, and kidney, and tuberculosis of the lung to bronchi, trachea, larynx, and intestine. We have nothing analogous to this in the case of cancer. A cancer of the stomach never plants itself down the alimentary canal. A cancer of the cæcum never has isolated offshoots in the rest of the large intestine. A cancer of the lip does not extend to the rest of the mouth except by continuity.

It is this which to some extent accounts for the important practical fact that in the individual person a cancer is always one lesion. In its primary seat it does not scatter, it extends, and the entire primary tumour is one continuous whole. The secondary tumours are parts of this whole, being grafts from it. The question we have to face is whether a fact such as this is consistent with the parasitic origin of cancer.

The accumulated effect of all these considerations seems to be that the mode of growth of cancer is such as to make it differ from any lesion known to result from any of the bacteria. Cancer is a tissue growth, whereas the ordinary microbes produce merely irritation with inflammatory reaction in the tissues; secondary cancers are grafts of the primary one, and not due simply to extension of the causative agent. Cancers are so varied in their structure, even in the same locality, that it seems difficult to believe in the existence of one infective agent for all, and to suppose that a different agent is provided for each suggests too great a stretch of probabilities; and lastly, the limitation of primary cancers to organs, so that they do not extend to neighbouring surfaces, even though their nature is very similar, suggests something different from ordinary infection by a morbid poison.

It must be confessed that these considerations—and there are still others which might be adduced—make us hesitate very greatly before admitting even the possibility of cancer being due to a parasitic organism. Similar considerations have induced most pathologists who have looked closely into the subject to come to an opinion adverse to the view referred to. It may at least be safely inferred that if a parasitic organism has to do with the causation of cancer, it must be something very different in its mode of action from the bacteria with which we are acquainted.

I have put in a tolerably strong light the considerations which are adverse to the view of the parasitic origin of cancer. I have now to say that there are certain considerations on the opposite side which make me hold the position of antagonism to the parasitic view with less tenacity than I did a few years ago.

VI.—CAN A TISSUE GROWTH BE PRODUCED BY PARASITIC AGENCY?

It ought perhaps to be said here that whilst cancer is obviously an infective disease, that is to say, is a spreading one inside the body, there is as yet no evidence either that it is communicable from person to person as infectious diseases are, or that it is derivable from some morbid poison outside the body, as in the case of malarial diseases and others due to the action of a miasma. We have now to inquire whether any morbid condition consisting of a tissue growth comparable with that of cancer is capable of originating in consequence of the action of a parasitic agent acting on the tissues. Is there anything either in observed cases of cancer or otherwise which lends any degree of probability to the view that an actual tumour with definite tissue growth may be referable to parasitic agents?

In reference to this question, I will first refer to two observations of my own which had considerable influence on my mind. The first of these was a case of what may be called malignant goitre. In it there were tumours consisting of such a distinct tissue growth, that I have been in the habit of adducing the case as an example of the difference between a tumour proper and the mere result of irritation, as in tuberculosis and syphilis. And yet this case itself seems to me to lend some support to the newer view of the parasitic origin of cancer.

I have already published the case in the *Transactions* of the Pathological Society of London, and I have here, for your inspection, museum preparations and microscopic specimens in illustration of the points to which I propose to refer. The case was that of a woman affected in the first place with an ordinary goitre which had lasted for sixteen years. The enlargement of the thyroid, which is so visible in the specimen as you see it, shows in its structure that it had been of considerable duration. There is in some parts great fibrous induration and calcareous impregnation of the stroma of the enlarged gland, these being evidences of a high degree of chronicity. Whilst the original goitre was thus of old standing, there appeared about a year and a half before death a soft tumour in the occipital bone. This tumour grew till, at the time of death, it had destroyed the bone in a circular area nearly two inches in diameter, the gap being filled with tumour tissue, which, during life, projected both outwards under the scalp and inwards towards the brain, and formed externally a prominent pulsatile swelling at the back of the head. Besides this there were several other tumours occupying the bones of the skull, and causing destruction of the bone, but this was the largest. It was a fact astonishing to me to find that this tumour in the skull presented the structure of the thyroid gland. There were the usual sacculi lined with epithelium, and these presented in many instances the colloid contents so characteristic of ordinary goitre. The specimens under the microscope show this.

The significance of this case for the subject in hand connects itself with the etiology of goitre. It is well known that this disease is endemic in certain localities, in this respect resembling malarial disease. The most likely explanation of this endemic character is the existence in these localities of a morbid poison which has its residence in the soil, and finds its way into the bodies of men, just as the malarial poison does. Some unknown miasma is the cause ascribed by many pathologists, among whom Cohnheim may be mentioned. It is supposed that the presence of an excess of lime in the water is the cause of goitre, but it is difficult to understand how such a cause should produce the effect. It seems more likely, if there is any connection between the lime and the disease, that the former fosters the propagation of the morbid poison concerned.

Consider what effect this morbid poison produces in an ordinary case of goitre. Endemic goitre consists in an enlargement of the thyroid gland dependent on new formation of the tissue of the gland. New formation of gland tissue is the essential process, sometimes in the form of a simple increase in the existing gland tissue, but frequently in the form of more independent glandular masses, so as to form separate tumours. If the view which I have stated as to the etiology of goitre be correct, then we have here an instance of a tissue growth, a formation of fully developed tissue of a complex kind, brought about by a morbid poison introduced from without.

But the case to which I have made reference carries us a step further. We have here an example strictly comparable with the secondary tumours in cancer. There is a transplantation from the original seat, and there is a growth of the graft in its new situation. The secondary tumour imitates in the minutest detail of structure the primary growth, presenting the glandular sacculi and colloid secretion just like the primary one. If the primary growth is due to a miasmatic poison, then this agent is not only capable of inducing tissue formation in the normal site of that tissue, but also of continuing its action when transplanted along with germs of the tissue. I confess, then, that this case, although it forms one of a very rare series, had considerable influence on my mind in the direction of admitting that true tissue growth, such as we have in cancer, may be produced by the action of an infective agent, and that this tissue growth may assume the characters of a malignant tumour.

The other observation which influenced my mind was one perhaps of less importance, but it concerns cancerous growths themselves. I have already made reference to the fact that cancer, in its primary seat, confines itself to the organ in which it originates; but this statement is not absolutely without exception. I have on two occasions seen what, to me, was an interesting and suggestive appearance at the lower end of the œsophagus in cases of cancer of the stomach,

Some years ago I met with a case of cancer of the stomach which did not quite reach the cardiac orifice, but on opening up the œsophagus I found, at its lower part, a considerable number of flat elevations of rounded shape, separated by normal mucous membrane. These flat elevations were not truly cancerous in structure, consisting rather in an increase of the surface epithelium of the œsophagus. They had more the character of soft warts, with no appearance of the infiltrating tendency which is the characteristic mark of cancers. It is some years since this case occurred, but I remember that even then it suggested a certain infective character in the sense of a causative agent which might be transported from its primary seat. It seemed to me that the agent which produced the cancer in the stomach had regurgitated into the œsophagus. It had not found there the same conditions as in the stomach, and had not therefore produced a cancer, but it had induced a marked new formation of epithelium. The second case was not so striking. In it there was also a cancer in the cardiac region of the stomach. In the lower part of the œsophagus the tube showed several prominent ridges, which were found to consist of new-formed epithelium. The prominences of the folds of the œsophagus during its state of collapse had undergone an increase of the surface epithelium. This case also suggested a regurgitation of the agent which caused the cancer of the stomach into the œsophagus.

Besides the considerations arising from observations such as those I have mentioned, there are others which have important bearings on the subject before us. The first of these which I shall refer to is connected with the form of skin disease, usually named "molluscum contagiosum." This name is applied to little growths of the skin, which occur chiefly on the face, showing a preference for the eyelids, but sometimes extending so as to be almost universal over the body. Each molluscum is in the form of a flat elevation of the skin, of rounded outline and with a central depression. In their appearance the tumours have been compared to pearl buttons. Each of these growths, as may be seen from sections which I have placed under the microscope, is little less than an epithelial tumour, consisting of lobulated masses of epithelium grouped in relation to the central depression. It is a moot point whether these little tumours are altered sebaceous glands. They suggest this in their general appearance, but the weight of opinion seems to me to be against that view. They arise by a great new formation of epithelium, and are properly epithelial growths. So much is this the case that, from the pathological point of view, the name epithelioma molluscum is often applied. Here then we have an epithelial growth which, as its ordinary name implies, is contagious—that is to say, depends on some morbid agent acting on the epidermis. It is probable that the morbid poison finds entrance by the hair follicles, and the central depression probably represents the original place of entrance. In this case it looks as if a proper new formation of tissue such as occurs in cancers did result from a contagium, and under modern views a contagium certainly suggests a parasitic organism as its vehicle or essential form.

VII.—OCCURRENCE OF COCCIDIA IN MOLLUSCUM, ETC.

The disease under consideration introduces us now to an aspect of the question under discussion which in quite recent times has entered on a phase of great importance. It is believed by many that the parasitic agent in molluscum is not only present, but is obtrusively visible in all tumours of this kind. The parasite does not, in this view, consist of such minute vegetable organisms as we are in the habit of calling bacteria or microbes, but belong rather to the animal kingdom. As the microbes are lowly vegetable organisms, each consisting of a single cell, so at the lowest place in the animal kingdom there are also unicellular organisms. The terms *amoebæ*, *coccidia*, *psorosperms*, and others have been applied to some of these forms. They are much less known in their structure and habits than the bacteria, but some of them, at least, exist as parasites in the bodies of higher animals.

In the case of molluscum contagiosum, you can see in the sections before you the bodies which are asserted to be parasites of the kind referred to. In the central and therefore older parts of the little growth a large number of peculiar glancing bodies are visible. These are about the size of epi-

thelial cells, and seem to take the place of these, arising either by a transformation of these cells or by a replacement of them by an intruded body. There is no doubt that these bodies arise within the epithelial cells. One can see in such sections as those before you how there first appears in the cell a granular structure which enlarges and fills the cell, and then undergoes the peculiar change which gives the bright glancing appearance which you can see. So characteristic are these appearances, that the structures have received the name of mollusc bodies, and I am not aware that anything similar is met with in any other form of disease.

There is much difference of opinion as to the nature of these mollusc bodies. Neisser, Pfeiffer, and others consider them to be unequivocally parasitic. On the other hand, Török and Tomasoli² have subjected the mollusc bodies to chemical tests, and have found them extraordinarily resistant to the most energetic chemical agents. They have, therefore, concluded that we have here to do with something very different from living creatures. Israel³ also, in his paper on Epithelioma Folliculare Cutis, does not see more than a superficial resemblance in the supposed parasite of molluscum contagiosum to coccidia and amoebæ. In a recent short note Virchow⁴ agrees with Israel, and reiterates his former opinion that he could not see anything in the mollusc bodies which could be regarded as demonstrating their parasitic nature.

In regard to this condition, then, we must wait for further evidence, with the assurance, however, that if these bodies are parasitic, they belong to the lowly order of animal organisms to which I have referred.

Of considerable importance in connection with our subject is the undoubted occurrence of coccidia and psorosperms in the liver and elsewhere in the lower animals. This subject has been very fully worked out by Leuckart in his work on *Animal Parasites*, and by Professor Delépine, of Manchester.⁵ Delépine points out the extraordinary fact that the lesions produced by psorosperms were visible to the naked eye in 92 per cent. of the rabbits which he examined, numbering 50 in all. The lesions produced by these parasites are distinctly connected with an overgrowth of epithelium. The parasites inhabit the hepatic ducts, and they there cause the development of a cystic condition, the interior of the cyst being lined with sprouting papillæ covered with epithelium. The cysts contain large numbers of the mature coccidia, which are very obvious bodies closely resembling the ova of certain round worms, and also resembling the mollusc bodies of molluscum contagiosum. It is not difficult, however, as I can say from personal observation, to see that these bodies begin their development inside the epithelial cells which line the cysts. They first form granular masses in the epithelial cells, where they grow and distend the cells, pushing aside the nucleus. By and by the epithelial cell with its parasite becomes detached, and the coccidium assumes a hard capsule, which gives it the characteristic appearance, lying free in the cyst. The presence of these parasites, although they ultimately destroy the epithelium, has the effect of greatly stimulating the epithelium, the cystic nodules found in the liver being really the consequence of the excessive epithelial growth. In this disease we have something very closely approximating to, if not identical with, a cystic tumour due to a parasitic organism. Cases of a similar kind have been observed in the human subject, accounts of some of which will be found in Leuckart's book on *The Parasites of Man*.⁶ One of these is exceedingly striking, as the liver presented about twenty tumours of a cancerous appearance, some even as big as an egg.

Coccidia seem to be very common also in the intestine of many of the lower animals, amongst them the rabbit, and what is called in Hoyle's translation of Leuckart "the domestic mouse," and they have also been observed, but very rarely, in the intestine of man. In all cases they have been described as occurring in the epithelial cells.

VIII.—ALLEGED ANIMAL PARASITES IN CANCERS.

And now as to the existence of coccidia and psorosperms in

² *Monatschr. für prakt. Dermatologie*, x, 149.

³ Israel, *Festschrift Rudolf Virchow*, 1891.

⁴ *Virchow's Archiv*, vol. cxvii., p. 188.

⁵ *Path. Trans.*, xii, 346.

⁶ Hoyle's translation, p. 22.

cancerous tumours, I need hardly say that in the last few months there have been a number of separate papers containing descriptions of parasites of this nature within the epithelial cells which are the characteristic elements of cancerous tumours. These papers have generally been accompanied by illustrations from which the appearances may be readily gathered. I shall not here do more than enumerate the names of the authors whose papers I have seen and read bearing on this subject. There is Russell, of Edinburgh; Soudakewitch, whose researches are published in the *Annales de l'Institut Pasteur* (No. 3, 1892); Sawtshenko in the *Centralblatt f. Bakteriologie und Parasitenkunde*, July, 1892; Ruffer and Walker in the *BRITISH MEDICAL JOURNAL*, July, 1892; Steinhans in *Virchow's Archiv*, vols. 126 and 127, and there is the complete work by Pfeiffer, which takes up the whole subject of the action of these parasites in all the forms of disease in which they occur. This work, which seems to me to go rather beyond the bounds of certain knowledge, was originally published in 1891; already in 1892 there is a new edition much enlarged. Such is the eagerness with which this subject is being pursued at present.

There is not the slightest doubt that the epithelial cells of cancerous tumours do contain structures which are separate both from the nucleus and the protoplasm of the cell. They were observed long ago by Virchow, who seems to have observed and described almost everything, and by many others since then. These bodies may be visible as clear spaces, especially when fresh cells are examined without special methods of staining, but the spaces are generally filled with structures which are different in their appearance and in their reactions to staining agents from the rest of the cell. It is not difficult in fine sections of cancers to see such bodies, and I show you here two or three drawings of them as seen in cancers of the mamma. These drawings I made with the camera lucida, and you will recognise the resemblance to some of the forms figured by Ruffer and Walker. These bodies are of various sizes, and in their growth they often push aside the nucleus and monopolise the cell.

These structures have not, till quite lately, been looked upon as parasites. They were regarded as arising from changes in the cells, and many of them were taken to indicate a kind of endogenous cell formation. This latter explanation is probably incorrect. In growing cancers one can always plainly see evidences of multiplication of cells by the regular nuclear division or karyomitosis. These bodies in the cells have no connection with the nucleus, which they push aside. Yet in cells which are so rapidly formed as those of cancers are, and which are growing so quickly, there may be internal changes in their economy of which these appearances are the manifestations, without the assumption that the bodies are parasites. The existence of the bodies described, and the accuracy of the descriptions, cannot be denied, but the proof that they are parasites has by no means been furnished.

IX.—CONCLUSIONS.

In what has gone before I have indicated the considerations which have induced me to listen with more favour to the suggestion that cancer is due to an infective parasite introduced from without. It remains as obvious as ever that the minute vegetable parasites are not capable of producing such tissue growth as we observe in cancers, but it does seem possible that minute organisms belonging to the animal kingdom may, by entering into the substance of the cells, and there undergoing their stages of evolution, produce phenomena of a kind similar to those of cancer.

When all is said there is much in the causation of cancers which remains unexplained. We have, for instance, the great varieties of cancers. Are we to suppose a separate parasite for each? There is the limitation to organs—Does each organ have its own form? There is the curious limitation as to age, cancer being a disease of the decline of life, but not of old age. All these are questions which suggest themselves, and call for explanation on the parasitic hypothesis. It is clear that for the development of a cancer a certain preparedness of the tissues must pre-exist. This is usually brought about, apparently, by the changes in the tissues incident to declining years. It may be induced by an imperfection in the tissues, as where a cancer starts in an old scar. It may have its origin again in an abnormality of

the tissues, as in a case which I met with not many months ago, in which a congenital sacral tumour developed a cancerous condition, and, at the time of death, when the child was only 2 years of age, there were already secondary tumours in the liver.

It seems to me that on the whole question we should keep an open mind, ready to admit any light which observers, who are specially working at the subject, may be able to throw on it.

ON DEFECTS IN THE PRESENT MODE OF CERTIFYING AS TO THE CAUSE OF DEATH FOR THE PURPOSE OF REGISTRATION.

By SIR HENRY THOMPSON.

(A STATEMENT LAID BEFORE THE SECRETARY OF THE HOME DEPARTMENT).

No one, I presume, will deny that it is one of the first duties of the State to obtain satisfactory evidence as to the fact and as to the cause of death, whenever it occurs to any one of its citizens, without exception, whatever the class of society to which the individual belongs.

This being so, I have to show that the means employed in this country, although evidently framed to fulfil that duty, are defective, and fail in doing so to a serious extent. This I have at various times endeavoured to point out.

The method at present adopted is to obtain a written certificate from the medical man who has personally attended the deceased; for it is necessary to possess certain facts concerning the death such as can only be determined and testified to by a qualified medical man, together with the inference which he draws therefrom. This is the design and scope of the present medical certificate.

Now, the evidence regarding the working of this plan is accessible and complete. I believe it produces a satisfactory result in in the great majority of cases; at the same time, not a few exceptions must be admitted. Moreover, in many of those cases where no doctor has been present and evidence is most needed, no provision for any special medical examination and testimony is made, and registration is accepted without it unless some obviously suspicious circumstance becomes known to some one who will demand a coroner's inquiry.

I ask your attention, Sir, to the last Report of the Registrar-General of Births, Deaths, and Marriages in England and Wales (for the year 1890). Let me say that it is the most favourable in regard of this subject yet issued; these reports, showing during the last few years very gradual improvement in the care with which the mode of certifying is performed.

The measure of defect most apparent at first view, may be thus set forth:—

In 1890 there were registered	562,248 deaths;
And of these were buried without any certificate	15,947 or 2.8 per cent.
But besides these a much larger number is reported by the Registrar-General as so "inadequately certified" as not to be classifiable	25,683 or 4.6 per cent.
Making a total of	41,630 or 7.4 per cent.,
of which the cause cannot be stated.	
Besides these it should be added that the coroner certified after inquiry in no less than	31,581 or 5.6 per cent.

The remainder, about 87 per cent., were medical certificates of the average kind.¹

It is thus clear that about one death in every thirty-six is registered without any certificate, and that one in every twenty-four certificates is without value. I may add here that uncertified deaths are far more numerous in Scotland. In Glasgow they form 4 per cent. of the entire number; in Edin-

¹ Let me point out an illustration of the "slight improvement" referred to at the outset, that in 1885 the uncertified cases were 3.5 per cent., while in 1890 for the first time they are as low as 2.8 per cent.