Two Lectures
ON
UNICELLULA CANCRI:
THE PARASITE OF CANCER.

DELIVERED BEFORE THE ROYAL COLLEGE OF SURGEONS OF ENGLAND.

BY

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(With Special Plate.)

II.—THE PARASITE OF CANCER.

IT will now be convenient to consider how far this theory will account for the phenomena of malignant disease, as we know them in man and animals. Dr. Charles Powell White, in his *Lectures on the Pathology of Cancer*,[1] says:

> We can say, then, that cancer is not due to a specific parasite or parasites, but, on the other hand, we can say that cancer cells themselves act as parasites. This view will explain all the phenomena of cancer.

And Dr. James Ewing, in his *Cancer Problems*,[2] says:

> The whole basis, objective and theoretical, of the cancer parasite has been traversed again and again, with the uniform conclusion of those who finish the journey that the cancer parasite is the cancer cell.

Dr. White's statement is general and sweeping, but I believe it to be in the main correct, although I am not aware of any detailed analysis on which it rests. So far as time will permit, I propose to supply the deficiency.

There are two great phenomena of malignant disease (cancer) which overshadow all the others, and to which most of the other phenomena are subordinate, and on which they are more or less dependent:

1. The tumour.
2. The metastases.

The tumour may exist without metastases, and there are reasons for believing that metastases may exist without the presence of a tumour.

1. THE TUMOUR.

The tumour is the primary disease, so far as we know it. Until a very few years ago the presence of a mass was regarded as an essential to the diagnosis of malignant disease. Now we know that the primary—the initial—lesion of cancer (I use the word as synonymous with malignant disease) may exhibit nothing more than a really trivial thickening of a small area of the skin or mucous membrane. From this trivial beginning arise all the various phenomena which go to make up the history of a case of cancer, and from it originate all the misfortunes and sufferings of the individual—the host. For, if this tiny area be examined with the microscope, it will be found to be composed of cancer cells, which are either massed together, as if without law or order, or which may, on the other hand, be arranged with singular and wondrous skill, so that the appearance of the disease may closely simulate that of a natural tissue or organ of the body. (Fig. 6.) There is also provision for the maintenance of the cells, in the form of vessels, and often of scaffolding or framework, in which the cells are arranged. And there are usually numbers of other cells—leucocytes, lymphocytes, granulation cells for the most part—in the outskirts of the tumour. So that the mass is made up of several elements, of which the essential element is the cancer cell. All the conditions connected with the tumour depend, directly or indirectly, on the behaviour of the cancer cells.

The cells may fail to maintain themselves, in which case the tumour comes to an untimely end. They degenerate, shrink, waste, die, and are devoured by phagocytes. How often this happens no one can conjecture, but probably much more frequently than is supposed.*

On the other hand, the cells may thrive, may grow and multiply, in which case the tumour extends its area. When it occurs in the substance of an organ, such as the breast, it may become quite a large lump, or if it occur in a limb around the bone, it may attain an enormous size. Examine the structure of such a mass, and you will find that the cancer cells and framework have taken the place of the tissues which ought to be there. Fat, fibrous tissue, muscle, have disappeared, or are broken up and separated by groups and masses of cancer cells with their framework. Examine the tissues beyond the apparent limit of the tumour, and you will often find isolated cells or groups of cells between the muscular fibres or in the minute or larger lymphatics.[3] (Fig. 8.) And you may find little masses of cancer cells projecting into the lumen of a blood vessel the wall of which may be destroyed or still unbroken.[4] (Fig. 9.)

These conditions are not discovered in all cases of malignant disease, even in all cases of the same variety of cancer of the same part of the body. In some cases not a single isolated cell or group of cancer cells will be discovered in the tissues beyond the apparent limit of the tumour. I do not say they are not there, but they are not recognized, so that they cannot be either large or characteristic. Where they are found, however, they may directly produce new phenomena, for a single cell or group of cells may grow to form a mass in the midst of the muscle or tissue where it lies.

The advance of the tumour is characterized by one great phenomenon—destruction. Every tissue which it attacks is destroyed, and replaced by the cancer cells and their suite. Hard tissues, soft tissues, vascular tissues, and tissues without vessels, are all destroyed—not all at the same pace or all precisely in the same manner. For, such tissues as cartilage and elastic tissue resist the attack much longer than soft tissues, and even than bone. There is also indirect destruction of tissues whose nutrition is interfered with by the growth of the tumour. If the tumour makes its way towards the surface, the epidermis is raised and stripped off, and the mass of cancer cells is exposed. With the exposure of the cells a new series of events may be expected. Micro-organisms, bacteria and bacilli, gain access to the cancer cells. Sepsis, suppuration, ulceration, and sloughing take place, and the condition of the host is seriously prejudiced by these occurrences, which may even compass his death.

Sometimes the tumour may shrink, and, even when it is adherent to the skin, may not break through. It undergoes atrophy from the wasting and death of the cells in its central parts. But it is not cured; for, while the centre dies or withers, the margin often flourishes and widens.

In all these circumstances which attend the growth and development of the tumour there is nothing which does not equally occur in the attacks of certain parasitic protozoa on their hosts—for instance, *Myxobolus cyprini* invades, destroys, and takes the place of the kidney epithelium of the carp; *Myxobolus pfeifferi* destroys and takes the place of the muscles of the barbel. It is the same story, common to both the cancer cells and to the protozoa which are not toxic—destruction of the natural tissues, and their replacement by the cancer cells or parasite. And just as the masses formed by cancer cells are attacked by bacteria, and break down and ulcerate when they are exposed, so do the masses formed by *Myxobolus pfeifferi* break down from similar causes when they reach the surface of the body and are exposed. (Fig. 2.)

All these phenomena of the tumour are perfectly intelligible if the cancer cell is accepted as an independent organism, pursuing the two great objects which are pursued by the parasitic protozoa—maintenance of itself and continuation of its species.

2. METASTASIS.

And now for the second great phenomenon—metastasis—the occurrence of masses in various parts of the body resembling in their elements, and nearly always in their arrangement, the tumour.†

Collections of cancer cells are found, sometimes in one part of the body, sometimes in another, composed, not of

* Dr. Clowes spoke to me of this on the journey up from the meeting of the British Medical Association at Exeter in 1908, and suggested to me that recovery from an attack of cancer is probably not so very infrequent.

† Almost all the knowledge we possess of metastasis—in any case, the useful knowledge—is the result of clinical pathology, not of experimental observation or of laboratory investigation. This is, in itself, so good an excuse for the continued pursuit of clinical pathology, and so admirable an illustration of its use, that it alone would suffice to encourage clinical pathologists, and to furnish proof that the day of clinical pathology is far from set.

cancer cells of different varieties, but of cells of the same variety as those which compose the tumour. (Figs. 10, 11, 12, 13.) Wherever they occur they are associated with the same conditions as are observed in the tumour—the formation of vessels and a framework, and a satellite collection of other cells (leucocytes, lymphocytes, and the like). The grouping of the cancer cells is the same, the substances which they secrete, the degenerations which they undergo, the mode of reproduction—all are those of the cells of the tumour. Every metastasis is, as the Director of our Cancer Research has truly said, a reproduction of the tumour, and corresponds with the results of implantation. It is due to the presence of cells from the tumour in those parts of the body in which the metastases occur. On this matter there is practically no difference of opinion, nor is there any serious difference of opinion on the coarse mechanism of metastasis. The cells may be deposited on a surface which is constantly or frequently in contact with the tumour, may become fixed there, and may grow and multiply (autoinoculation). They may be conveyed in the air or in the food, from the larynx to the lung, or from the stomach to the intestine, and may form metastases in either place. But these are exceptions to the general rule, and are of rare occurrence. The metastases which we see daily are due to the penetration of the cancer cells into the interstices of the tissues or into the lymphatic vessels, along which they spread, and to conveyance by the lymph and blood. They can often be easily demonstrated in the tissues, between the fibres of voluntary muscle for example, and in the lymphatics. But it is wellnigh impossible to detect them in the moving blood and lymph, probably because it is the young and least characteristic cells which are conveyed, and there is so little to distinguish them by, especially when they are on the move. In spite of the absence of direct evidence, the circumstantial evidence in favour of conveyance in the blood and lymph is so strong that it is not questioned, and I need not occupy time by repeating it.*

Seeing the variety of the mechanism of metastasis, it is only reasonable to expect that there should be some variation in the number and seat of metastases. And so, indeed, there is. Sometimes the metastasis is limited to a single tiny nodule in a distant organ, sometimes to a few tiny nodules within a limited area; sometimes it is greater in bulk than the tumour, and sometimes it seems as if it had been scattered broadcast, without order or method. Nor is there greater uniformity with regard to time than in regard to seat and size. Metastasis may be present at the moment the tumour is discovered, or it may be deferred for years, or it may never occur in cases in which it ought to. (Fig. 14.) No wonder such variations have been a puzzle to those who study cancer, particularly to the experimental investigators. It seems so inconsequent, so void of method, that it has led one of the most able investigators of the present day to aver that the study of cancer in man and animals is rendered peculiarly difficult by the extraordinary variety in the histology and clinical behaviour of the malignant new growths which attack them.[5]

I do not agree with this statement. It rests on a misapprehension, on a false conception of cancer, on imperfect observation, and on the manner in which the life-history of cancer has been studied. If all varieties of cancer in all kinds of animals are studied higgledy-piggledy—squamous carcinomas, spindle sarcomas, spheroidal carcinomas, myeloid sarcomas—in man and mice and dogs and rats, it is perfectly correct. It would be equally true of the parasitic protozoa if they were studied in similar fashion. If Sarcosporidiidae, Myxosporidiidae, Coccidiidae were all jumbled together, and an attempt were made to describe the histology and clinical behaviour of the jumbled mass, the result would be confusion and profound perplexity. But no naturalist thinks of studying them in such a fashion. Each family is studied separately—not only each family, but each variety—and the characters and life-history of each is gradually deduced with clearness. Precisely the same method must be directed to the study of the organisms of cancer. Each must be studied separately.

For more than thirty years I have insisted on the necessity of the separate study of each variety of cancer in the part in which it occurs.[6] And Mr. Stephen Paget more than twenty years ago, in an excellent paper in the *Lancet*,[7] showed the necessity for this same separate study, particularly in relation to metastasis. To some extent this has been done by the clinical pathologists, and here are some of the results:

Take, first, a round-celled sarcoma. Let it be of the femur and subperiosteal. It grows very rapidly, and is one of the most surely fatal of diseases. Amputate the limb above it—far above it—and take the bone out at the socket. It is, nevertheless, likely to return in the muscles of the stump. And even if it does not do so, the patient will almost inevitably die of metastasis, even if the tumour was removed as soon as it was discovered.

Of all places the lungs are most likely to be the seat of the metastases. The femoral and inguinal glands are not usually affected. But metastases may occur in distant lymphatic glands, in the skin and subcutaneous tissue, in the liver—indeed, almost everywhere. Most of the patients are dead within a year or fifteen months. And the instances in which a patient can be claimed to have been cured of this most terrible variety of cancer are so few that they can be counted in units.†

Now, take a spindle-celled sarcoma of the testis—also a very deadly disease, but not to be compared in this respect to subperiosteal sarcoma of the femur. It forms a tumour, often large, in the cavity of the scrotum. It is easy to remove it, and there are many instances in which there is no recurrence in the stump, and the patient is cured by the operation. But there are many more cases in which, at the end of an indefinite period—perhaps a year, two years, or more—a mass is discovered in the abdomen, which grows until it kills the patient. It is formed by metastasis in the glands, in the liver, and other viscera of the abdomen.

Take a spheroidal-celled carcinoma of the breast. The metastases will occur first and chiefly in the glands of the axilla, then in the liver and lungs, but particularly in the liver.[8] They may attack the bones—the sternum, the humerus, the femur, and the vertebrae—particularly the vertebrae of the lumbar region. And if the disease recurs *in situ*, it frequently forms numerous little flat nodules or plaques in the skin and subcutaneous tissue.‡

DESCRIPTION OF SPECIAL PLATE.

Fig. 1.—Barbel suffering from *Barbenseuche;* tumours formed by *Myxobolus pfeifferi* (after Doflein). *Protozoenkunde.* II Aufl., Jena, 1909, Fig. 730.

Fig. 2.—Section of a barbel, showing symmetrical tumours, that on the right side ulcerated (Doflein, Fig. 731).

Fig. 3.—Squamous carcinoma of tongue, the cells of which are elongated like spindle-cells.

Fig. 4.—Axillary glands removed twenty years after successful removal of the breast.*

Fig. 5.—Degenerated cancer cells in an organized thrombus in a blood vessel (after Martin B. Schmidt). *Die Verbreitungswege der Karzinome*, Jena, 1903, Plate, Fig. 3.

Fig. 6.—Columnar-celled cancer of the rectum (after Cripps). *Diseases of the Rectum and Anus*, 1884, Pl. VI.

Fig. 7.—Large round-celled sarcoma of testis.

* The history of this case is very interesting. In 1895 Sir James Paget sent me a lady whose left breast he had amputated for carcinoma about 1875. The glands had not been removed. About 1885 Mr. Stephen Paget destroyed with the cautery "some carcinomatous tubercles in the right breast." When I saw her in 1895 there was no recurrence in either breast, but a mass of glands in the left axilla, which were easily removed. She came to see me in 1898. There was no recurrence either in the breast or in the axilla on the left side, but there was recurrence in the right breast, for which I amputated the breast (XI, 201).

* There is really only one point on which there is grave doubt—whether the cancer cells are mere passive bodies in their migration or whether they are active agents (Bland-Sutton, *Clinical Journal*, 1910). As this does not affect the argument, it is not necessary to discuss it now.

† Dr. Coley claims to have cured some cases of subperiosteal sarcoma of the femur by his injections. We have not been very successful in this country, and I only hear of a very occasional success from the use of Coley's fluid. But it is probable Dr. Coley and his pupils are more skilled in the management of the fluid than the English and Continental surgeons.

‡ The mechanism of these metastases has been very well described by Mr. Sampson Handley in his book on *Cancer of the Breast*.

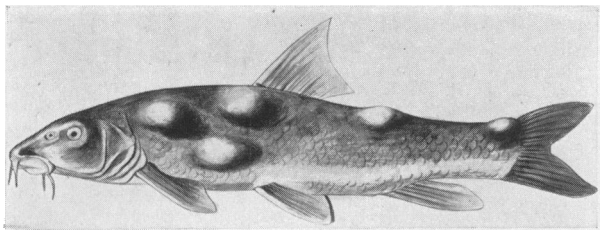
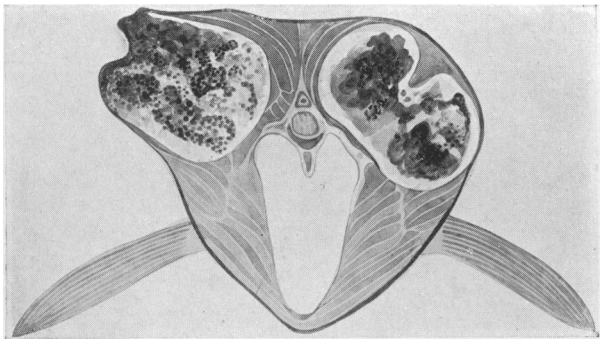


FIG. 1.



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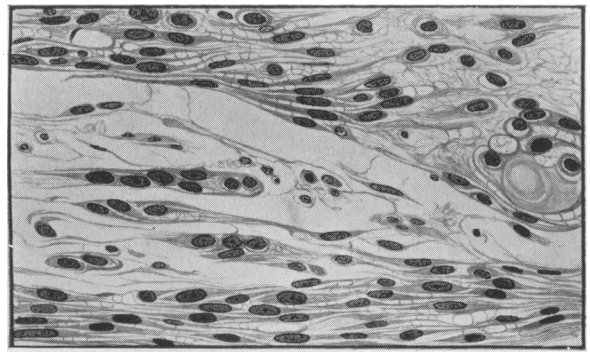

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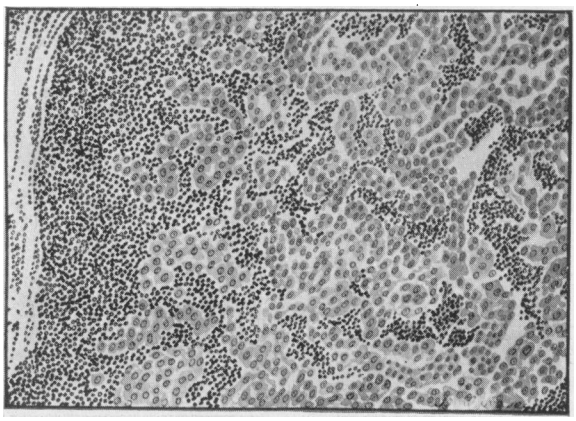

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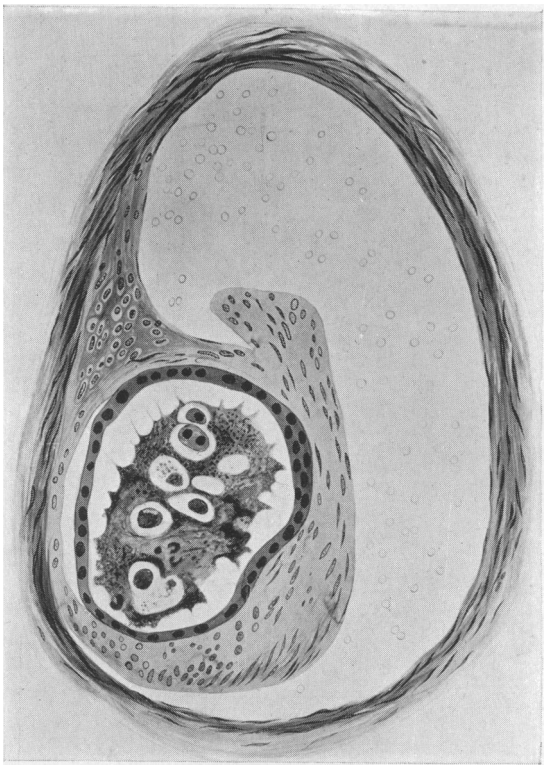

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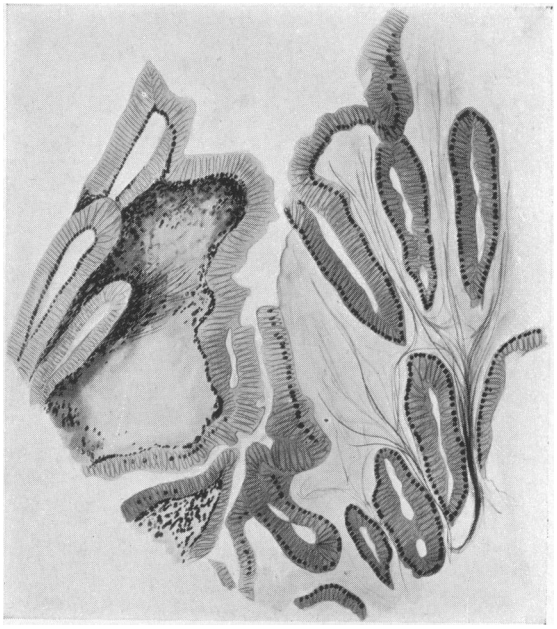

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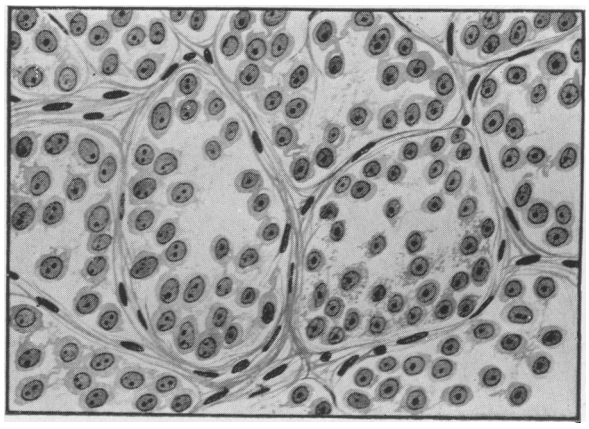

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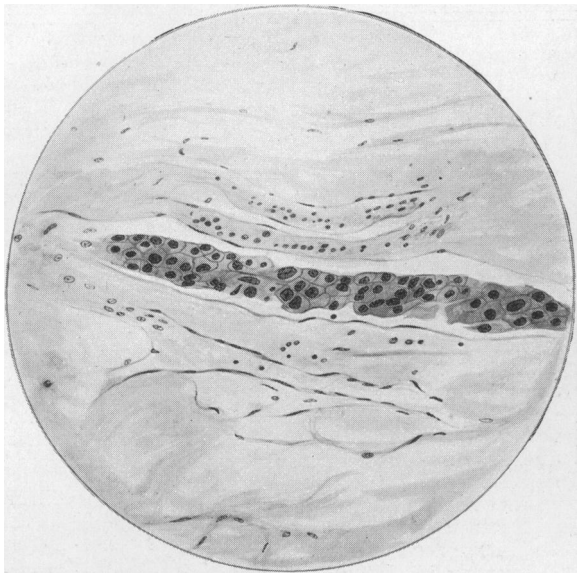

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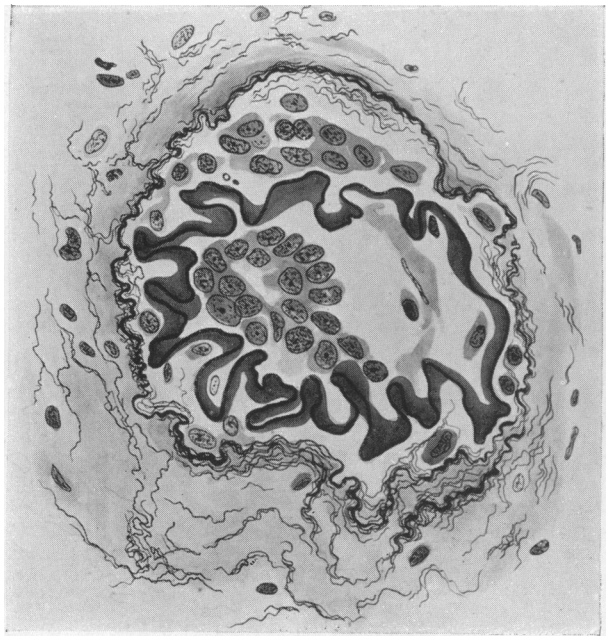
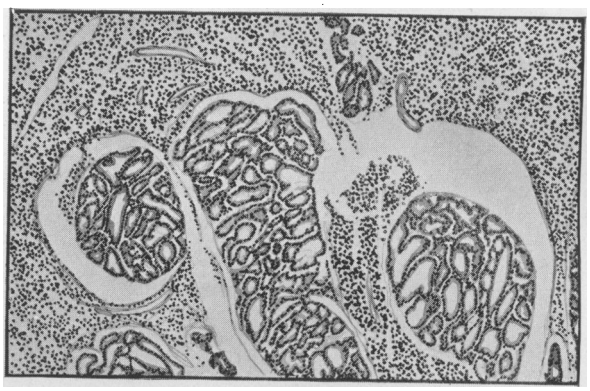


FIG. 9.

FIG. 10



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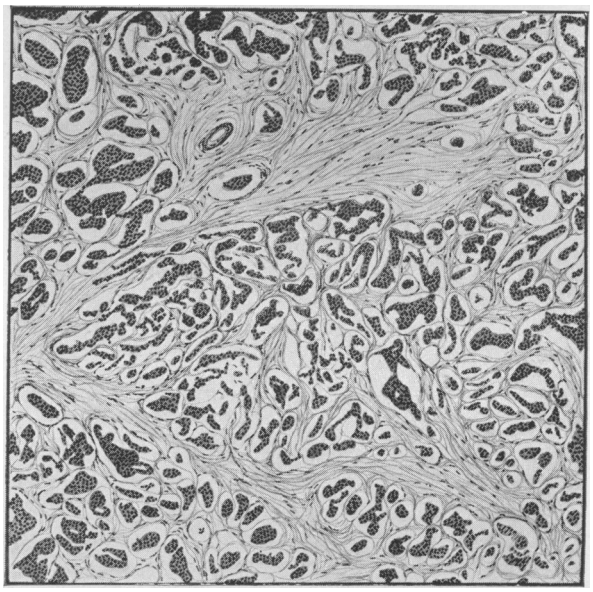

FIG. 12.

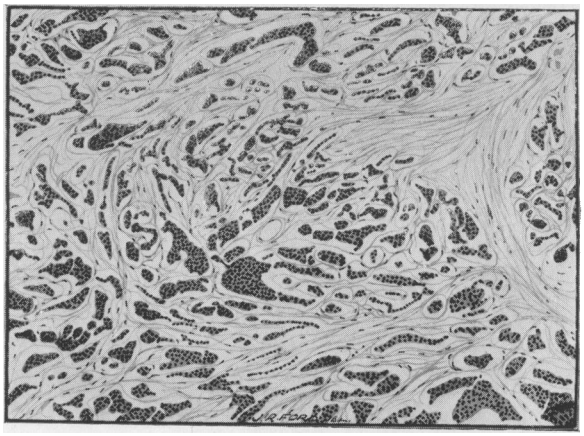

FIG. 13.

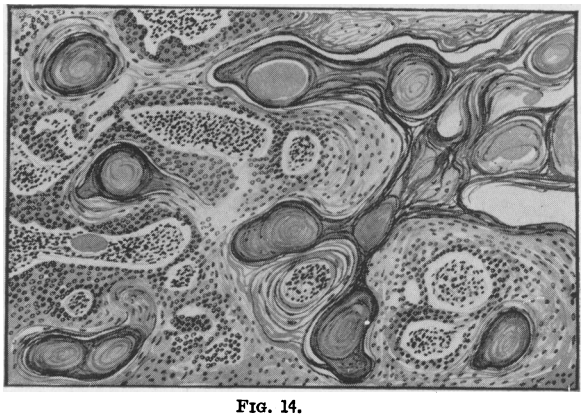

FIG. 14.

If the breast and glands are removed there may be no distant metastases. But the pathologist would be a bold or ignorant man who would assure the patient that the disease would certainly be cured by the operation.

Again, take a columnar-celled carcinoma of the rectum. The metastases will be in the abdominal lymphatic glands and in the liver, in preference to any other part.

Take squamous carcinoma of the tongue, where the limitation of metastasis becomes much more restricted. It takes place in the neighbouring lymphatic glands, and sometimes in the glands on the opposite side of the neck. If the primary disease and the glands are successfully removed, so that there is no recurrence in tongue or glands, there is so little likelihood of distant metastases that they are practically left out of the account. The possibility is admitted, but the event is so far infrequent that we do not fear it.

Finally, take rodent ulcer of the face. The extension of the disease beyond its apparent limit—the destruction effected by the cells—their tenacity of life and power of multiplication—have long assured for rodent ulcer a place among the malignant tumours. But the cells of which it is composed seem to be quite incapable of flourishing in any other parts than the immediate neighbourhood of the tumour, and there are no metastases. I do not say that metastasis never takes place, but it is so rare that its occurrence is not provided for in the pathology of the disease.

Every case of a particular variety of cancer of a particular part of the body does not run precisely the same course as every other case of the same variety of cancer of the same part. Nor does every case of parasitic protozoon of a particular animal run precisely the same course as every other case of the same protozoon in the same animal. But compare a hundred cases of squamous carcinoma of the tongue with another hundred cases of the same disease of the same part, and let the conditions be similar for each hundred cases as regards operation, etc., and I ven ture to say that the resemblance of the second hundred to the first hundred cases would be marvellous. I am sure that no greater differences would be discovered than would be discovered if one hundred cases of *Sarcocystis miescheriana* were compared with another hundred cases of the same parasite in the same animal, and not so much difference as would be found if one hundred cases of *Myxobolus pfeifferi* were compared with another hundred cases, but the barbel were taken from two quite different streams. In the same way, compare a hundred cases of carcinoma of the breast with another hundred cases of the same variety of carcinoma of the same part, and see how little difference there will be between them.

When studied in this fashion the results are so constant that we, the surgeons, presume upon them. We trade on them. We do not remove the lymphatic glands in cases of rodent ulcer because we are confident, however long the disease has existed, the glands will not become diseased. And we are equally confident that there will not be metastasis in any other part of the body.

We remove the primary tumour and the associated glands for squamous carcinoma of the tongue, with the full assurance that if the operation is successful in preventing occurrence or recurrence in those structures, we shall save the lives of many of our patients.

We amputate the breast, remove the muscle and the contents of the axilla, and dissect away wide areas of the fascia for spheroidal carcinoma. When the disease is not extensive or rapid in its course we expect to save the lives of more than half our patients. But we have not the same hope of the result of a successful operation as we have if the operation is successful in rodent ulcer or in squamous cancer of the lip. For the spheroidal cell may thrive and multiply in the liver, the lungs, and bones. And this may happen five or six or more years after the successful removal of the breast and the associated structures.*

So with regard to other varieties of cancer in various parts of the body. In all cases our treatment is adapted to what we know, or believe we know, of the course of that particular variety of cancer in that particular part of the body. And if it be charged against us that we are often wofully at fault in our estimate of the effect of an operation, or in our prognosis of an individual case, it must be remembered that the observations on which our present methods of treatment and prognosis are founded have all, practically, been collected during the last forty years, or little more.

The explanation of metastasis is migration of the cancer cells, and the explanation of the seat of metastatic tumours is precisely that which explains the occurrence and seat of the metastases of the parasitic protozoa—the penetration of the cells into those places which are suitable to their existence—those places in which they can live and thrive and multiply.

Time will not permit me to deal with all the phenomena of cancer as they have risen before my mind in the course of the last few months, during which these lectures have been in preparation. I shall have to reserve some of them for future publication, and I shall also have to reserve the consideration of this theory as a working theory of cancer. But there are two or three phenomena to which I should like to refer. The first has puzzled many pathologists for many years. I tried to explain it more than twenty years ago, with indifferent success.[9]

It is the occurrence of metastases without the evidence of primary disease. The best examples of it have been observed in the occurrence of squamous carcinoma of the groin glands in sweeps, in whom no primary growth or sore has been discovered by competent observers. I suggested that the primary disease had "aborted"—in other words, got well—but not before some of the cells containing the material of cancer had been conveyed to the lymphatic glands. My explanation was very near the truth. That cancer should "abort"—get well—was not much in the minds of pathologists twenty years ago. To-day, everybody knows that it does get well, both in animals and human beings,[10] and many of us are prepared to believe that it gets well much more commonly than we know of at present. But, in these cases, before it does so, some of the cancer cells have already migrated to the groin glands, and have made good their footing there.

The occurrence of ossification, calcification, and chondrification in many of the sarcomata is a phenomenon which has never puzzled me when the tumour is connected with a bone, or when the metastasis is of a tumour growing from a bone. It seems natural—only what might be expected—that the framework of such tumours should contain bone or cartilage. But I confess it has puzzled me when the tumour is of a part which has no connexion with bone or periosteum. For instance, such a tumour is sometimes—though very rarely—found in the female breast. Why should cells derived from the glandular or connective tissue of the breast command a framework or scaffolding in which bone or cartilage are prominent constituents? Bashford explains it on the grounds that

DESCRIPTION OF SPECIAL PLATE.

Fig. 8.—Lymph vessel filled with cancer cells (lymphatic permeation; from Sampson Handley). *Cancer of the Breast*, Pl. III, London, 1906.

Fig. 9.—Cancerous infiltration of vessel wall (E. E. Goldmann). *Studien zur Biologie der bösartigen Neubildungen.* Taf. IV, Tübingen, 1911.

Fig. 10.—Duct cancer of breast.

Fig. 11.—Glands removed from same case (10)—duct cancer—at same time.

Fig. 12.—Spheroidal carcinoma of breast, removed December, 1896.

Fig. 13.—Recurrent nodule removed from muscle of same case (12). Removed October, 1900; patient well in 1906.

Fig. 14.—Squamous-celled carcinoma of the groin glands of a chimney-sweep, in whom no primary disease was discovered.*

[The drawings reproduced to illustrate the lectures have been very carefully made by Mr. J. R. Ford.]

* This case is published in the BRITISH MEDICAL JOURNAL, 1892, ii, p. 578, by Dr. John Stacy, of Norwich. After the death of the patient Dr. Stacy sent me slides cut from the glands. I do not know whether any similar case has been drawn.

* In speaking of "successful operations" in the preceding paragraphs, I hope it will be understood that I am only referring to the success of the operation in preventing recurrence in the parts which were diseased.

such conditions occur in association with inflammatory processes. He shows how frequently it occurs in mammary tumours in the dog, and says:

> It seems to demonstrate that the connective tissue of the dog is very liable to such metaplastic changes, just as the connective tissue of the rat or of the mouse is liable to the changes characteristic for these animals.[11]

There is one phenomenon of cancer which no theory explains—the constancy with which spontaneous cancer begins at one point instead of many. It can scarcely be made to fit in with the theory of "removal of restraint," but it does not threaten the stability of this, or many other theories. At present I have no explanation to offer of it.

Reviewing, in a few sentences, the application of this theory to the phenomena of cancer, I will not undertake to affirm that all the known phenomena of cancer can at once be explained by it, but it *does* offer a ready explanation of the first great phenomenon of cancer—the tumour—and of all the changes which may occur in it. It offers an explanation of metastasis, the other great phenomenon of cancer; of the reasons why it occurs; why it occurs in one place rather than in another; of deferred metastasis; of metastasis without primary tumour. In fact, it explains so simply so many of the phenomena of cancer that it is necessary to make diligent search to discover the two or three phenomena which are not explained by it. And of these it may be said that there is not one of them which endangers the acceptance of the theory, and that they are equally inexplicable by any other theory which has yet been advanced.

It fulfils also the conditions laid down by a writer in the BRITISH MEDICAL JOURNAL,[12] who pointed out that, to make my case good, my parasite must be tried by the laws laid down by Koch—to wit: "A specific micro-organism must be constantly associated with a given disease; it must be isolable and studiable apart from the disease, and when introduced into a healthy animal it must be able to reproduce the disease in that animal; and in the animal in which the disease has thus been experimentally reproduced the organism must be found under the original conditions."

It fulfils these conditions with a fidelity which is remarkable. The only one of them on which any dispute could arise would be whether the cell is "isolable and studiable apart from the disease" in the sense in which Professor Koch used the expression. If that is all that is lacking, we are not likely to have to wait long for it. Indeed, Carrel and Burrows maintain that they have already solved that problem in the Rockefeller Institute of Medical Research.*

I now come to the last part of my task: Where does the cancer cell come from?

Six years ago[13] I summed up the evidence in favour of the only two views which could reasonably be put forward: *Entrance from without* or *formation within* the body; and came reluctantly to the conclusion that the evidence of "*formation within*" was stronger than the evidence in favour of "*entrance from without*." I say "reluctantly," because it led to the logical conclusion that new species of living creatures are created from a source and in a manner which has never hitherto been imagined. Nevertheless, during the last six years the evidence in favour of "*formation within*" the body has grown steadily stronger, while nothing has been added to the evidence in favour of "*entrance from without*." I cannot stop to dwell on the points of each piece of evidence, but must content myself with enumerating them:

1. The resemblance of the cancer cells to those of the natural tissues in which the cancer appears to start.
2. The resemblance of the secretion of the cancer cells to the secretion of the natural cells.
3. The resemblance of the degenerations of the cells to those of the normal cells (fatty, caseous, calcareous, etc.).
4. The resemblance of the grouping of the cells to the grouping of the natural cells.
5. The resemblance of the phenomena of reproduction in the cancer cells to those of the natural cells which they resemble.

All these may be regarded as traits of atavism, and it is upon these that the explanation of some of the phenomena of cancer rests. Students of cancer, research workers, biologists who have studied cancer, are all practically agreed that the cancer cell is derived from the cells of the part in which it takes its origin, or appears to take its origin, and they are bent on finding an explanation of the reasons which lead the cancer cell to behave so differently from the cells from which it is derived. Escape from natural restraints—the acquirement of the habit of growth—the theory of embryonic rests—chemical stimulation—a self-contained and ordinarily invisible micro-organism living in symbiosis with the cell—these are some of the theories by which learned men have sought to explain the strange conduct of the cancer cell.

Empty phrases! They might account for variations in colour, size, shape, secretion, degeneration, physical activity—for a multitude of the variations from the normal cell exhibited by the cancer cell—but how can any of them account for the vital difference which I will express in two short sentences? Implant the normal cell, and you cannot make it live. Implant the cancer cell, and you cannot kill it.

There is one, and only one, explanation of the conduct of the cancer cell—that it has been endowed with that wondrous gift which no man has seen, and which no man can understand—the gift of life; and that, owing to that gift, it has become an independent creature, a new creation of living thing.

The host in which it dwells has fashioned it out of his own tissues, and in the likeness of his tissues, and, to borrow the figurative language of Scripture, the Creator has breathed into it the breath of life—and it becomes a veritable Frankenstein, bent on the destruction of its host. After ages of past and present civilization, during which searchers and philosophers have sought to explain the origin and nature of life, we have come no further than this, and he who discovers the true origin of cancer will have solved the enigma which has hitherto baffled the searchers and philosophers in all ages and of all countries.†

If the cancer cell be in truth a new creature, to what class of creature does it belong?

It is nearest to the protozoa—so near, indeed, that it is difficult to keep it out of the protozoa. Every new observation of the last six years—every new discovery—has brought it nearer to the protozoa. But the biologists will have none of it. I must therefore make a special place for it and provide it with a name.

It shall be *Unicellula cancri*. And, for the different varieties, the shape of the cell can be expressed in simple terms which will be familiar to us all. On the one hand, *Unicellula* (*cancri*) *squamosa*, *Unicellula spheroidalis*, etc.; on the other hand, *Unicellula* (*cancri*) *fusiformis*, *Unicellula rotunda*—and so on. These names will serve still, even if the cells eventually join the great phylum of the protozoa.

I am perfectly conscious of the far-reaching consequences of admitting that unicellular bodies, derived from such a source, are a new species of created beings, but there is no alternative. The facts are plain, and cannot, I believe, be otherwise interpreted. If the theory is false, I can only say it is very remarkable that it should explain, in so satisfactory a manner, the chief and nearly all the subordinate phenomena of cancer.‡

In conclusion, I should like to tell you a parable. A learned professor, walking in the desert, observed a curious little object on the ground. It had a rounded snout and flattened head, large eyes, a flattened body, short fore-legs and very long hind-legs. It sometimes walked and sometimes jumped. The professor asked whence it came, and it replied: "I am a child of the desert, born of the grains of sand." This astonished the learned man. He took it home with him, and called together many of his friends, and set the little beast in their midst.

* Alexis Carrel and Montrose Burrows, *Journal of the Amer. Med. Assoc.*, 1910, vol. lv, pp. 1379, 1554, 1732. Mr. Arbuthnot Lane told me he had seen the specimens of growing sarcoma cells in the Rockefeller Institute.

† "No power of genius has ever yet had the smallest success in explaining existence."—Emerson, *Representative Men*. London: Macmillan, 1893, p. 314.

‡ Mr. Darwin, in the last chapter of the *Origin of Species*, says: "It can hardly be supposed that a false theory would explain, in so satisfactory a manner as does the theory of natural selection, the several large classes of facts above specified. It has recently been objected that this is an unsafe method of arguing, but it is a method used in judging of the common events of life, and has often been used by the greatest philosophers."—*Origin of Species*, sixth edition. London, 1889, p. 421.

They all looked at it, and said it must be a frog, for it looked like a frog, and behaved like a frog, particularly in its ability to jump. But when they heard its origin they were all amazed, and each one gave his explanation of the occurrence. One said, "It is a changeling; it is not what it looks to be." Another said, "It was surely made to swim, for its feet are webbed, and, having no water to swim in, it has acquired the habit of jumping." A third said, "It has been gingered." A fourth said, "Some restraint must have been taken off it to enable it to jump." And the professor himself said, "No, it has a flea inside which lives within it as its familiar spirit, and that gives it the power of jumping."

Then the professor said to the little object: "We are very sorry for you. You are neither animal nor vegetable, for neither animal nor vegetable can be created from the sands of the desert. There is, therefore, no place for you among living creatures."

The little creature jumped and crawled away. But as it did so it looked back at the group of learned men, and said: "There is no place in the living world for me owing to the misfortune of my birth. Thank you, gentlemen, but I have already found a place for myself, and you will find it very difficult to oust me from it."

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SOME MANIFESTATIONS OF PITUITARY GROWTHS.*

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BEFORE proceeding to discuss the signs and symptoms of pituitary growths, it may be well to refer very briefly to some points in the anatomy and physiology of this ductless gland.

The pituitary body, or hypophysis cerebri, is a small rounded organ situated at the base of the brain in the depression of the sphenoid bone known as the sella turcica.

It is made up of two parts—a larger anterior lobe developed from an ectodermal upgrowth from the stomodeum (Rathke's pouch), and a smaller posterior lobe derived from a downgrowth from the floor of the third ventricle with which the gland is connected by a stalk called the infundibulum.

A third subdivision is also described under the name of the pars intermedia, which seems to be formed by the fusion of the anterior or ventral wall of the posterior lobe and the invaginated posterior or dorsal wall of the anterior lobe. Histologically the anterior lobe consists of vascular glandular epithelium; the pars intermedia is formed of less vascular epithelium secreting a colloid substance, and the posterior lobe or pars nervosa consists mainly of neuroglia with a few colloid-producing cells.

The physiological functions of these parts have not been definitely worked out. The anterior lobe appears to be related to calcium metabolism, and the growth of skeletal tissues—bone, cartilage, and connective tissues generally—to the deposit of fat and the development of the sexual organs. Physiologists have not been able to define these functions, and the chief evidence in support of these statements has been derived from observations made in pathological conditions of the organ.

The pars intermedia produces a colloid which affects blood pressure and urinary secretion. As a general rule, this colloid material raises blood pressure by causing contraction of the blood vessels, and increases secretion of urine, but it may, on the other hand, have precisely the opposite effect in each case. Extracts of the infundibulum also cause contraction of non-striped muscle, such as that of the uterus, intestine, and dilator pupillae. The pituitary body appears to be a vital organ, and its complete removal results in death.

These anatomical and physiological data enable us to classify and correlate many of the varied signs and symptoms of pituitary growths, but it must be admitted that the pathogenesis of the manifestations is as yet by no means established, and it has even been said that the most striking condition ascribed to pituitary growths—namely, acromegaly—may occur without any apparent disease of the hypophysis cerebri.

For the purposes of this paper I propose to classify the manifestations of pituitary neoplasms into:

1. Those which may be ascribed to excessive action of the glandular epithelium of the anterior lobe—*Hyperpituitarism.*
2. Those which may be ascribed to a diminished functional activity of the anterior lobe—*Hypopituitarism.*

In view of our incomplete knowledge of the physiology and pathology of the pituitary and other ductless glands, it is possible that these two classes of symptoms may be due to perverted action of the hypophysis—*Dyshypophysia*—or to perverted action and interaction of several ductless organs—*Polyglandular syndrome.*

3. The mechanical effects of an intracranial tumour showing definite localizing symptoms, which can be explained by the anatomical relationships of the enlarged organ. These symptoms are common to Class 1 and 2 as long as the pathological condition of the gland is associated with its enlargement. In cases of atrophy these symptoms will be absent.
4. Confirmatory evidence of enlargement or atrophy of the hypophysis is supplied by radiographs of the sella turcica, though naturally the size of the gland and its bony recess is no guide as to the functional activity of the gland. Hypopituitarism, at any rate, may apparently be the result of either enlargement or atrophy of the gland.

I. HYPERPITUITARISM.

Under this heading we place *Acromegaly* and *Gigantism.* The pathological processes seem to be the same in these two morbid conditions, and the difference in their clinical characters is dependent on the period of incidence of the disease. "Gigantism is the acromegaly of the growing period; acromegaly is the gigantism of the period of completed development; acromegalo-gigantism is the result of a process common to gigantism and to acromegaly, overlapping from the period of adolescence into that of maturity." [1]

The essential feature in each case is exaggerated growth of the skeletal tissues, hard and soft, especially of the extremities, associated with alteration in the physiognomy and in the contour of the skull. These symptoms have been so fully described by Marie and others that it is almost superfluous to repeat them. I would point out, however, that, according to Launois and Casbron, the changes in the skull demonstrable by radiography constitute the only positive signs of acromegaly. These changes consist in very irregular thickening of the cranial parietes, which gives rise to a polygonal appearance of the skull. The external and internal tables are separated by an abnormal and irregular space owing to an alternate separation and approximation of the tables. The frontal and maxillary sinuses are increased in height and depth. The post-lambdoidal prominence is exaggerated, and there is more or less marked increase in the antero-posterior dimensions of the pituitary fossa. The sexual organs also show hypertrophy, though this is often associated with impotence, and may later be followed by atrophy of the organs and loss of pubic hair.

The symptoms which may be ascribed to the mechanical effects of the intracranial tumour (3) may include headache, vomiting, vertigo, tinnitus, polyuria or glycosuria, convulsive or apoplectic attacks, certain psychoses,

* A paper read before the Midland Medical Society.