A Third Lecture ON UNICELLULA CANCRI: THE PARASITE OF CANCER.

BY

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III.—THE WORKING THEORY OF CANCER FOUNDED ON THE TWO PREVIOUS LECTURES.

WHEN I was a young man there were a good many surgeons attached to the hospitals in London who spoke of themselves as "practical surgeons." They not only exhibited no interest in pathology and in the scientific problems connected with their trade of surgeon, but they held such things in scorn and laughed at those who did pursue them. To them surgery consisted in the diagnosis of disease and in the treatment of it, particularly by operation. They prided themselves—often quite justly—on their neatness, skill, and boldness. They sometimes heard it stated that pathology is the foundation of surgery. But the statement had no meaning in their ears, and they seldom gave themselves the trouble to discuss it or even to consider it.

Practical surgeons may still exist, but they are not now in evidence as they used to be. They no longer make a boast of their ignorance of pathology and the scientific side of surgery, and now it is rather the fashion to admit that pathology is the foundation of medicine and surgery. It is a good sound principle; rather an abstract proposition than a practical suggestion. It is only the weak and unpractical men who allow themselves to be influenced in their diagnosis and treatment of a disease or accident by the views of its pathology which happen to prevail at the moment.

As a matter of fact, I am sure that physicians and surgeons, scientific or practical, are always to some extent influenced in their diagnosis and treatment of accident and disease by the idea which they have in their minds of the nature—in other words, the pathology—of the disease. But few persons are conscious of the extent to which they may be, and often are, influenced by the pathology of the day in relation to a particular disease. To illustrate this statement, I shall take the single example of cancer and of the influence of the pathology of the day on the treatment of cancer as I have actually myself known it.

THE HUMORAL AND THE LOCAL THEORIES OF CANCER.

In the course of the last sixty years two great theories of cancer have held the field: the *humoral* theory and the *local* theory. (I am not, of course, speaking of minor theories, of the parasitic origin of cancer, etc., which have sprung up later; but solely of the two great theories of cancer which were discussed by pathologists and scientific surgeons in all countries.) Was cancer in its early stages a local disease, which became constitutional as it advanced? Or was it from the beginning due to an unsound state of the blood?

I do not know how long the humoral theory had received the support of the scientific surgical world, nor do I know who was responsible for it in the first instance. It was maintained by Mr. Paget, in his lectures on Tumour at the Royal College of Surgeons, just over sixty years ago. My copy of his Lectures (1853) is, I believe, the first edition. Two or three extracts from it will suffice to state his views.

For the present I will say only that I think malignant tumours are local manifestations of some specific morbid states of the blood; . . . The general history of cancers and their analogy with other diseases that are, in the same senses, specific and constitutional, imply that, before the formation of a cancerous growth, two things at least must co-exist—namely, a certain morbid material in the blood, and some part appropriate to be the seat of a growth incorporating that material, some place in which the morbid material may assume, or enter into, organic structure.²

This was the pathology of cancer which was taught at St. Bartholomew's Hospital when I became a student in the middle Sixties. Such were the reputation and

eloquence of our great master that, if his views had differed from those of all other pathologists, he would have carried with him a large body of disciples. But they were the generally accepted views, and he happened to be one of the greatest exponents of them.

Now, see the pernicious influence of them on the treatment of cancer. I again quote from the lectures. Mr. Paget did not deal with the general question of operations for cancer; but he discussed the question of operation against cancer of the breast. For the study of the results of operations, he took two series of cases of scirrhus cancer. The first was a series of 66 cases in which no operation was performed. Of this series, he says: "The average duration of life, from the patient's first observation of the disease, is a little more than four years."³ The second was a series of "47 cases, in which the cancer was once or more removed by operation, the average duration of life, after the first observation of the disease, was again something more than forty-nine months."⁴ And, to leave no doubt regarding his opinion of the value of operation, he says, a few pages further on:

In deciding for or against the removal of a cancerous breast, in any single case, we may, I think, dismiss all hope that the operation will be a final remedy for the disease. I will not say that such a thing is impossible; but it is so highly improbable, that a hope of its occurring in any single case cannot be reasonably entertained.⁵

Under this pessimistic pathology the most that was ever expected from an operation was that the patient might die a little less miserably. The disease was often advanced before it was removed; the operation was quite inadequate; the objects of the surgeon were to obtain an immediate good result of his operation and to prevent recurrence *in situ*. But his operation was seldom wide enough to secure the second object. There was no hope, either for the present or the future. To the very end of their surgical lives, many surgeons of the surgical generation before my own, such men as Sir Thomas Smith, were under the influence of these views, and I have heard the expression many times: "Once cancer, always cancer."

I do not remember when or where or how the theory of the *local* origin of cancer came before the pathologists and surgeons, or whether it was a British or a Continental inspiration. It was a very happy inspiration, and humanity has occasion to be very thankful for it. I have no recollection of discussing it and suddenly being struck with the belief that it was true. Probably, conversion came slowly, from the more careful study of individual cases of cancer and from the slow discovery that operations were more successful than they had been believed to be. I can well remember occasionally drawing the attention of members of the permanent staff (when I was Surgical Registrar to the Hospital, and working at the Pathological Society) to such successful cases. The reply was always: "Well, you may be sure it was not a case of cancer!" And, if the microscopical examination was adduced in proof of cancer, incredulity was expressed, which was by no means flattering to a young pathologist. The principle on which the results of operations for reputed cancer were regarded by the humoral pathologists was simple and ready of application; if removal of a cancer were followed by recurrence and death, there was no doubt of the correctness of the diagnosis; if there was no recurrence, and the patient lived and remained sound, it was because the disease was not cancer, whatever the microscopist might say.

I suppose the steady accumulation of observations, supported by more experienced microscopists, and the more careful recording of cases of cancer were the chief circumstances which shook the humoral theory of cancer. There were, too, certain weak points in the armour of its advocates. Thus, Mr. Paget had been obliged to admit in his lectures on Epithelial Cancer, "that in some cases permanent recovery and in some a long period of health follows their removal."[†]

Gradually belief in the curability of cancer was established. Hope was infused into the minds of surgeons and their patients. Operations for cancer were better planned; they were far better performed than they

² About forty-nine months.

[†] Loc. cit., p. 474. It is very important that a few pages further on—p. 478—he collects "from the facts of this lecture the grounds which seem to justify the inclusion of this disease under the name of 'cancer.'"

had been; they were performed at a much earlier period of the disease; and, thanks to the discovery of antiseptic surgery, they were performed with much less distress and danger to the patient; until, in these later years, operations for cancer have been extended far beyond the limits they were formerly intended to observe, and, I am afraid, sometimes beyond the limits which prudence and a better knowledge of pathology would justify.

It must not be imagined that all this was accomplished without a great deal of opposition, or that it was carried through in the course of a few years. Even when it was evident that the humoral theory, even in the strict sense of the humoral pathologists sixty years ago, could no longer be maintained it was by no means abandoned. The old humoral pathologists and those who would not admit the local origin of cancer, spoke of the constitutional origin of cancer; and discussions took place and battle was waged, with varying success, by the adherents of the two theories, and would probably still be waging had not the question been definitely settled by experimental investigation by our own and other cancer research associations in the course of the last ten years.

Since then the local origin of cancer holds the field. The object of the surgeon is to remove it early, while it still remains a local disease. He may remove the tumour alone, with a more or less wide area of the tissues outside, into which the cancer cells may have escaped; and he may extend his operation to the associated lymphatic glands, whether they are obviously cancerous or not, provided experience has taught him that they are liable to become cancerous. His working theory is plain and simple: it is to remove the whole of the existing disease—in fact, to get all the cancer cells out of the body of his patient. If he can do this, the patient will be cured.

In spite of errors of judgement, of ignorance of the special pathology of cancer of different parts of the body, of faulty application of operations, and of all the pitfalls which attend the steps of even the most prudent and accomplished surgeons in the exploration of new fields of operative surgery, the advantages which have been gained for cancerous persons by the institution of a good working theory of cancer for a bad one are greater than the mind of man could have conceived. So far as the surgery of cancer is concerned, I was reared by pessimists, and lived in their society and held their views, and was myself for some time a fatalist on the subject of cancer. For some years past I have been living in the society of optimists, to the formation of which I did contribute, though but a small part. Their enthusiasm seems to know no bounds; and the optimism of some of them is so great that I verily believe they regard every variety of cancer as curable by operation, provided the operation be sufficient and the disease is in an early stage. However, it is a much better atmosphere than the other, good both for the surgeon and the patient, and I do not complain of it.

Working Theory.

My theory is neither *Local* nor *Humoral*: it is probably first *Local* and secondly *Constitutional*.

1. It is *Local* in so far that our belief is now well founded that spontaneous cancer is, at its commencement, a local condition. If we turn our backs upon the question of its origin, and regard it just as we find it in the body, it is to all intents in exactly the same relation to the host as most micro-organisms which have entered the body from without, and which are fitted to live in it. Cut it freely out, just as a primary syphilitic sore is sometimes cut off the prepuce, or a little tuberculous sore is cut out of the tongue or tip of a finger, and, if the micro-organism which each of the three primary lesions contains is limited to the lesion, the attack will be cured by the operation. The host may suffer from subsequent attacks of the same nature, but that particular attack is cured. The operation is frequently successful in tubercle, frequently in cancer, less frequently probably in syphilis.

2. *Constitutional*.—But if the micro-organism has already begun to travel (migrate), the disease can no longer be considered to be *Local*. In each case the micro-organism has broken bounds, and may reach some part of the body in which it can live and multiply. It may reach some place where it may still be cut out with success. This is particularly the case with the glandular affections of tubercle and cancer; so little the case with syphilis that it is rarely tried.

In most cases of all three diseases the surgeon abandons the attempt to cure by removal, and the only hope lies in the resistance of the patient, assisted by medicine and other remedies. For syphilis the results are, in percentage, exceedingly good; many patients are cured and the spirochaete dies or is destroyed. For tubercle they are not bad. Fresh air, fit food, cleanliness, tonics, cod-liver oil, and tuberculin cure many patients. The tubercle bacillus dies or is destroyed. For cancer the case is very different. We have no specific medicine for cancer, no general measures (such as we use in tubercle) in which we place the least confidence. The cancer cell is not habitually influenced (or likely to be killed) by drugs, or inoculations, or diet, or air, or by any known treatment. When once, therefore, the cancer cell has broken bounds, the fate of the patient might be regarded as sealed and all hope lost.

Practically, this view prevailed until recently, but it is largely modified by our better knowledge of cancer, particularly that which depends on experimental investigation.

Why Cancer Cells which have Broken Bounds do not always Kill.

But cancer cells which have broken bounds do not always kill. Some, such as those of rodent ulcer and recurring fibrous sarcomata, are quite incapable of living and multiplying in other organs and tissues than those in which or in the vicinity of which the disease first appeared. Others may be so feeble that they are not able to live and multiply, even in those tissues and organs which are generally suitable to the needs of this particular variety of cancer cell. Or the resistance of the host may be so strong that the migrating cancer cells are not able to overcome it.

These are not mere matters of conjecture. Experimental investigation has established them beyond dispute. We have learnt that cancer cells of the same variety are not all possessed of equal vigour, and that the resistance of different hosts varies within very wide limits.

Further, clinical observation has taught us that an attack of cancer may be severe or mild, like the attacks of so many other diseases. I do not mean that one variety of cancer is more fatal than another—spindle-celled sarcoma, for instance, than rodent ulcer; or that the same variety of cancer is much more fatal in one part of the body than another—squamous carcinoma of the tongue, for example, than squamous carcinoma of the lower lip or scrotum; but that two cases of the same variety of cancer in the same part of the body may vary enormously in their severity. Take, for example, two cases of spheroidal carcinoma of the breast in women of the same age. In the one case the tumour will grow four times as fast as in the other case, the glands will be early affected, and the case will run its course in a year or eighteen months. In the other case the tumour grows so slowly that it is still quite small at the end of four years, the glands are not affected, there is no distant metastasis, and the patient is not aware that she is suffering from a serious disease.

These differences have been well known for many years, and have been attributed to various causes. Now we should certainly ascribe them to difference in vigour of the cancer cell in the two cases, and to difference in the resisting power of the tissues of the two hosts. How much is to be ascribed to each of these two great factors we are not in a position to state.

There is reason to believe that in some of the cases the vigour of the cancer cell and the resisting power of the tissues of the host may undergo considerable change. A severe case may become much less severe, and a mild case may become active and even severe. In the first set of cases we assume that the vigour of the cancer cells has diminished, and that the "strain" is changed in quality, or that something has occurred to strengthen the resisting power of the tissues of the host. In the other set of cases we assume that a more vigorous "strain" of cells has taken the place of those which formerly grew out of the tumour or that the resisting power of the tissues of the host has been lowered.

The lowering of the resisting power of the tissues of the host sometimes appears to result from what may be termed an accident. Most surgeons have listened to the

* Imperial Cancer Research.

story of the patient of how the glandular enlargement he is examining came suddenly after very free use or straining of the arm. The breast had been removed a long time ago but the glands had been left. I suppose that most of us are disposed to treat this story with small belief, feeling that it is due rather to the wish of the patient that it were true than to conviction that it is true. But I suspect it is far more frequently true than we are disposed to believe, and I will give two cases in point:

Some years ago a gentleman consulted me on a hard glandular mass in the upper carotid (parotid) region. Three or four days previously, at an evening entertainment, he had sat in a seat where, for two or three hours, a cold draught of air had played upon the side of his neck. The following day his neck was stiff and swollen. And so it remained, for it was due to a cancerous affection of the glands secondary to an epithelioma of the tongue, which had been removed by Sir Jonathan Hutchinson a few months previously.

In December, 1895, I removed the left border of the tongue for a small epithelioma which had developed on a patch of leucoplakia. The glands of the neck were not removed, for I had not yet begun to remove them as a routine operation. The patient remained quite well until the beginning of 1898, when he contracted mumps from his sons. The attack of parotitis on the right side subsided within the usual time, but the attack on the left side did not subside, but a hard fixed mass remained in the neck. It was not a proper case for operation, because the tumour was so fixed, and he died of it in the course of a few months after I last saw him.

Ten years ago these cases would have been explained by suggesting that the "chill" and the mumps had drawn a quantity of blood into the neighbourhood of the lymphatic glands, and that the glands had in consequence been able to furnish better sustenance to the cancer cells. The terms in which we speak of these occurrences are of small importance. There was no recurrence in the tongue in either case. It must therefore be assumed that the cancer cells had already migrated to the glands before the operation on the tongue, and that they had remained lethargic there until the conditions had been disturbed by what may be spoken of as an accident.

There has been, as long as I can remember, an impression among surgeons that cancer, when it attacks young people, is likely to run a rapid course—much more rapid than that of the same variety of cancer of the same part of the body in an aged person. I do not attack the impression, for I really do not know whether it is correct. But the obverse must not be relied on—that cancer runs a very slow course in aged people. I have many times seen persons 70 and 80 years of age suffering cruelly from cancer which might have been removed two or three years previously; but the operation had not been performed, because the opinion had been expressed that the disease would run a slow course in so old a patient and would never be likely to cause serious pain or trouble.

In cases, then, in which the cancer cells have broken bounds and are wandering or migrating, the hope of the patient lies in these factors: (1) In the inability of the cancer cells to exist and flourish at a distance from the tumour; (2) in the possibility that the cancer cells in the individual case may be wanting in vigour; and (3) in the possibility that the resisting power of the host may be high.

The first of these factors requires no treatment; the second is quite beyond our control at present; and the third has been for some years constantly before us—so much so that the attempts to discover a specific against cancer have given way, in the minds of most scientific physicians and surgeons, to an attempt to discover some means of increasing the resisting power of the host. This is the object of experimental investigation in laboratories; and means have been discovered of raising the resisting power of the tissues of animals, but not against the spontaneous occurrence of cancer. These means have not been successfully applied, hitherto, in human beings. Those which have been tried are, for the most part, empirical. But some of them rest on observation and some on theory. Coley's treatment is an example of a method resting on observation; Beatson's (removal of the ovaries) of a method resting on theory. As to the empirical methods, they are legion. Special diets; the avoidance or taking of particular articles of food; drugs; animal extracts; external applications; preparations made from cancerous patients and cancerous tumours—these

are representative of the means employed to "kill the cancer," or to raise the resistance of the host.

THE MIGRATION OF THE CANCER CELL.

The application, then, of this theory as a working theory of cancer reduces itself to a consideration of the migration of the cancer cell on the one hand and the resistance of the host on the other. As regards the migration of the cancer cell, we have to ask ourselves whether the cells of every variety of cancer migrate; whether the cells of every case of the same variety of cancer migrate at the same time and to the same extent; and when do cancer cells migrate?

1. Do the Cells of Every Variety of Cancer Migrate?

I do not know of any data to settle this question. The proof of migration is the presence of metastasis. It may be maintained that the cells of those tumours (like rodent ulcer) which do not produce metastasis do not migrate. I am disposed to think that they do migrate, but that they cannot find subsistence in the organs and tissues which they reach.

2. Do the Cells of Every Case of the Same Variety of Cancer Migrate at the Same Time and to the Same Extent?

Here, again, we are obliged to depend rather on conjecture than on ascertained facts. But such evidence as there is strongly suggests that there is very considerable difference both in respect to time and to extent. Quite apart from the variations observed in the occurrence of metastases in a series of tumours of the same variety in the same part of the body—for instance, a series of tumours of the breast, where the variations might be attributed to differences in the resisting power of the tissues of the respective hosts—the variation in the rate of growth of the primary lesions (the tumours) and the great difference which microscopists find in sections of a series of primary lesions (tumours) point very strongly to this conclusion.

In some cases the tumour is very well defined both to the naked eye and to the microscope. The cancer cells are not numerous for that variety of tumour as compared with other tumours of the same variety. They are not observed in the tissues outside the apparent limit of the tumour, and the general aspect is a lack of activity. The reports of microscopists on such tumours are that they are "slow-growing." In forming this opinion they also take into account the arrangement of the cells and are disposed to consider those tumours less malignant in which the cells are arranged in a very orderly manner, so as to represent more or less normal tissues. They may be correct in the opinions which they express, but I often think they far exceed the limit of the scope of the microscopist. Many of them know little or nothing of the clinical pathology of cancer. And they do not understand that the prognosis of an individual case of cancer depends on all the conditions of the case, and should not be hazarded on one particular condition by persons who are not in possession of all the other conditions.

In other cases, even when the tumour is well defined to the naked eye, the cancer cells are very abundant, grossly formed, irregular in size and shape, and are very coarsely arranged. In such cases single cancer cells and groups of cells are observed in the tissues outside the apparent limit of the tumour. The reports of microscopists on these tumours are to the effect that they appear to be particularly malignant. I believe this opinion to be generally correct.

I will give one case in support of it, which I have already published elsewhere:⁶

I removed a portion of the right half of the tongue to an inch behind a flat plaque of epithelioma right on the border. Finding it a little thicker than had been expected, I cut out a lump of muscle in the floor of the mouth beneath the seat of the ulcer, but did not pretend to remove any muscles, or groups of muscles, to their insertions. The contents of the anterior triangle were removed two or three weeks later. The parts were examined by the Imperial Cancer Research. Dr. Murray reported that no cancer was found in the glands, but that the primary lesion exhibited a very high degree of malignancy. Columns of cancer cells infiltrated the muscles far beyond the apparent limit of the disease. I examined the sections myself, and fully agreed with Dr. Murray's report. I was, therefore, very unhappy about the future of the patient, and wrote to Dr. Joseph Bryan and to Dr. Collins Warren, of the United States, begging them to keep the patient under observation, as

I thought there would probably be recurrence in the muscles of the tongue. But there was not any.

Six months after the operation a lump was unexpectedly found on the left side of the neck. An attempt was made by an expert surgeon to remove the contents of the left anterior triangle, but extensive and fixed disease was discovered, and the patient succumbed to the attempt. The sequel of the case proved the correctness of Dr. Murray's report. There was early and extensive reappearance of the disease, but not where we expected to find it.

I can only assume that the glands provided better maintenance for the squamous cells than did the muscles of the tongue. I cannot believe that I did not leave some of these vigorous cells in the muscles of the tongue which were not removed. And cancer cells must, before the operation, have been conveyed to the glands on the left side of the neck. The glands apparently suited them better than the muscles.

3. When do Cancer Cells begin to Migrate?

This question is the most important of the three. But, in endeavouring to answer it, we have to rely largely on conjecture and circumstantial evidence. Theoretically, there is no reason why the cells of any and every case of cancer should not begin to migrate from the first moment of their existence as independent creatures. But reasons have been given in the preceding paragraphs for believing that the cells of many cancers do not migrate so early. On the other hand, thousands of cases can easily be furnished to show that they migrate within a few months of the discovery of the tumour, cases in which the successful removal of the tumour has been followed by metastasis, either immediately or after a period which may be very considerable. And there are other cases which suggest that migration of the cells of some primary tumours commences at a very early period.

I will give two cases in point:

An old gentleman had a very tiny ulcer of the front part of the floor of the mouth and a number of large fixed glands under the floor of the mouth and in the neck. I cut out a fragment of the ulcer, had sections made of it, and found that it presented the characters of squamous carcinoma. The patient was very unobservant, but believed the little ulcer and the glands had appeared about the same time. The ulcer was so trivial that Dr. Mackenzie Davidson cured it with a single application of radium (the only case of buccal epithelioma which I have myself known to be cured by radium). We sent him to Paris to see whether radium could be successfully applied to his glands, but he died there in the course of a very short time.

The details of this case leave much to be desired. The second case is much more to the point:

In the spring of 1901 I removed by a trivial operation one of the smallest squamous carcinomas of the tongue that I have ever seen. It was just under the left border of the tongue in the middle of an old area of leucœma and glossitis, due to past

syphilis (Fig. 1).^{*} In October, 1934, three and a half years after the operation on the tongue, the patient consulted me on account of a large, hard, glandular mass in the parotid (upper carotid) region on the same side. It had only been noticed three months. I removed it and found it to be squamous carcinoma (Fig. 2).

There was no disease in his throat, or cheek, or mouth, or tongue, for I had cut out the whole of the little area of leucœma and glossitis. And the whole operation had been so small that the doctor who first saw the tumour in the neck and examined the mouth, and particularly the tongue, for a possible primary lesion, did not perceive that an operation had been performed on the left border of the tongue.

THE RESISTING POWER OF THE HOST.

It is quite evident that the resistance of the host plays a much more important part in relation to the prognosis and treatment of cancer than it has hitherto been supposed to do. Most of our knowledge regarding resistance is due to experimental investigation, and is quite newly acquired.[†] Amongst other things, we have learnt that resistance lies more in the individual tissues than in the blood or fluids of the host. So far as animals are concerned, we have learnt that resistance is much greater in some animals than in other animals of the same species; that it is not always the same in strength; that it may be increased or diminished by certain definite measures; together with many other matters on which I need not dwell now.

Hitherto we have been in the habit of believing that the success of our operations has been consequent on the complete removal of the tumour,

including every outlying cell and group of cells, and in the wide removal of glands which contain metastasis or in which metastasis may be expected. To this we have rightly added the removal of the tissues between the tumour and the glands for the cancers of certain parts of the body, such as the breast. In those cases in which the glands which are liable to metastasis have not been removed, and the result has, nevertheless, been successful, we have attributed success to the fortunate circumstance that the tumour was removed before the cancer cells had reached the glands. No doubt these assumptions are often correct. But I think there is equally no doubt that migration has already commenced in other cases

which are successful, and that success has been dependent on the resisting power of the tissues of the host. I do

Fig. 1.—Squamous carcinoma of tongue.

Fig. 2.—Glands removed more than three years after successful removal of the tiny tumour of the tongue.

^{*} A section of it is figured in the Second Scientific Report of the Imperial Cancer Research Fund, 1905, page 45, Fig. 35—not because it was cut in their laboratory, but because, owing to its minute size, some microscopists at that time would not have accepted it as an undoubted squamous carcinoma, and on account of the subsequent history of the case.

[†] We are largely indebted to the Imperial Cancer Research for our information, and I would refer those who desire to make themselves acquainted with what has been done in relation to this matter to the Scientific Reports of the Fund.

not know how otherwise to account for some of the conditions which are not of uncommon occurrence.

Take, as an example, the history of the case of spheroidal-cell carcinoma represented in Figs. 12 and 13.⁷ The operation included the entire breast, the contents of the axilla, the tissues between the breast and the axilla, and a part, but not the whole, of the greater pectoral muscle. Five years later I removed a single recurrence, as large as a broad bean, from the muscular tissue below the scar, and perhaps $1\frac{1}{2}$ in. from it. It was undoubtedly due to cancer cells which had not been removed at the operation. For the structure of the tumour and of the recurrent growth is identical. The cells seemed to have remained inactive for more than four years, and then to have grown and multiplied to form a small mass. The resistance of the host held them lethargic for several years. I cannot believe that this was the only group of cancer cells left at the operation. It is far more probable that it was one of several or many groups, which had escaped removal; but that it was the only one of them which succeeded later in overcoming the resistance of the host. I know this patient was quite well five years after the second operation. From indirect information I have received I believe she is still quite well. I judge that her resisting power is still maintained. It may possibly have enabled her to destroy other groups of cells which might otherwise have developed into tumour masses.

Again, take the case of cancer of the tongue which has been described, in which recurrence was expected in the muscle, but actually occurred in the glands of the opposite side of the neck. I do not believe that I removed every piece of muscle which contained cancer cells. Yet no mass grew from those that were left, and this I attribute to the resisting power of the muscles which lay at some distance from the primary disease.

THE VALUE OF PROPERLY DESIGNED AND EXECUTED OPERATIONS.

It may be inferred from what has been said that I have much greater faith in the resistance of the host than I have in extensive operations, and that I attribute a great part of our success rather to good fortune than to skill. I hasten to correct this impression. If there be one thing which is more clearly proved than another in relation to malignant disease in the course of the last thirty years, it is the wonderful improvement in the results of operations for cancer. Wide and early operations, adapted to the pathology of the particular variety of malignant disease in each particular part of the body, have been attended with very great success. Nor is this to be wondered at. For the tumour is the manufactory and the storehouse of cancerous cells. And even in those cases in which the cells have begun to migrate, it is most desirable to get rid of the chief source of cancer cells. The resistance of the host has a much better chance of contending successfully with scattered cells, perhaps not yet firmly established where they lie, after the removal of the tumour. Indeed, I have thought for a long time past that if a "specific" against cancer were discovered it might even then be very desirable to remove the primary lesion—the tumour.

It will be noted that, in connexion with "wide and early operations," it is suggested that the operations must be "adapted to the pathology of the particular variety of malignant disease in each particular part of the body." For thirty years I have urged this. But it is not yet by any means generally accepted or acted on. Because a particular scheme of operation is successful for a particular variety of cancer of one part of the body, a scheme as nearly like it as possible is recommended for a different variety of cancer in another part of the body. This method of reasoning by analogy has led to very serious errors in the scheme of operations. The operative treatment of cancer of the breast has been taken by a large number of surgeons as indicating the ideal which should be aimed at in operations for malignant disease of all parts of the body. It includes two very important features—the removal of the entire breast, and the removal in a continuous mass of all the tissues between the breast and the axillary glands. The success which has attended operations for cancer of the breast has led many persons to believe that precisely the same principles should be applied in every operation for cancer in which it is possible to apply them. Not many years ago there were distinguished surgeons who insisted that the entire tongue should be excised in every case of cancer of the tongue. For quite a number of years there were surgeons and laryngologists in the United States and on the Continent who removed the entire larynx in every case of cancer of the larynx, whether intrinsic or extrinsic, whether large or small.

I think the "entire organ" craze has by this time died out, except for such organs as the breast, ovary, testis, etc. But the removal of the tumour, the associated glands, and the intervening tissues in one continuous mass still possesses great attraction for certain surgeons. It is recommended as a routine operation in cases of cancer of the tongue, in spite of the fact that it seriously adds to the danger of the operation and impairs the powers of speech and mastication. It is quite unjustified by careful observation and comparison of the results of operations.⁸ I think I have recently seen it recommended for cancer of the lower lip, for I have seen some ghastly pictures of quite up-to-date operations on the lower lip. But I suppose they refer to very extensive primary disease of the lip. I cannot conceive that any surgeon in his senses would make a routine practice of such horrible operations.

Some of these operations are recommended on the microscopical findings of some of the cases in which continuous sections have been cut from the tumour to the glands. Cancer cells have been found in the intervening tissues, and the conclusion has therefore been drawn that the intervening tissues ought to be removed in every case, in spite of the much greater danger to life from the operation and the much greater permanent crippling of the patient. Fortunately, this routine, which has been particularly urged in the treatment of cancer of the tongue, has not been adopted by the majority of surgeons.

The tumour of the tongue and the associated glands have been separately removed, and the results have been such as to justify separate removal as against continuous removal. These cases and other similar cases in other parts of the body clearly show that every cancer cell or groups of cells which the microscope discovers do not develop into tumours, even when they seem to have made good their footing in the tissues at some distance from the tumour. I have been so impressed with the danger of trusting implicitly to microscopical findings and planning operations on them; that I have ventured to lay down the axiom—

*"That if an operation does not fulfil the requirements of pathology and is, nevertheless, exceedingly successful, the pathology which relates to it must be revised: either the observations are incorrect, or the deductions which are drawn from them are not justified."*⁹

REFERENCES.

¹ *Lectures on Surgical Pathology*, by James Paget, F.R.S., vol. ii, London, 1853, p. 18. ² *Loc. cit.*, p. 529. ³ *Loc. cit.*, p. 344. ⁴ *Loc. cit.*, p. 346. ⁵ *Loc. cit.*, p. 351. ⁶ *A System of Operative Surgery*, edited by Burghard, Oxford, 1909; vol. ii, p. 241. ⁷ *Lecture II, BRITISH MEDICAL JOURNAL*, vol. ii, 1911, p. 1459. ⁸ *Burghard's Operative Surgery*, Oxford, 1909; vol. ii, p. 247. ⁹ *Ibid.*, p. 241.

THE eighty-fourth meeting of the German Association of Scientists and Medical Practitioners will be held this year at Münster in September (15th to 21st). Among the addresses delivered at general meetings will be the following: Professor Czerny (Heidelberg), on the treatment of tumours without operation; and Professor Küttner (Breslau), on modern military surgery.

THE Anglo-American Medical Association, which was founded in Berlin some eight or nine years ago and reconstituted in 1910, has recently acquired well-situated quarters of its own at the Hotel Atlas, 105, Friedrichstrasse. They are open daily from 12 to 2 for luncheon; the assistant secretary is in attendance from 1.30 to 4.30 to give information; and from 9 p.m. to 12 p.m. the rooms are open for social purposes, writing, and perusal of the journals with which the association keeps itself supplied. In addition, there is a formal meeting each Saturday at 8 p.m., when dinner is taken and a paper read and discussed. One of the special objects of the association is to make the visits of British and American medical men to Berlin pleasant and informing by putting them promptly in touch with what is going on in medical and surgical circles, and by enabling them to meet on a social footing their colleagues in Berlin. The association is, therefore, likely to be found very useful to those who wish to study in Berlin. It also publishes a year-book, the current issue of which contains, in addition to other notes, information as to courses on various subjects more or less constantly in progress, and also as to vacation and other special courses. The honorary secretary and treasurer of the association is Mr. H. R. Carstens.