The Bradshaw lecture on the pathology of cancer, delivered at the Royal College of Surgeons of England, 1884 / by W.S. Savory. Savory.

THE BRADSHAW LECTURE

ON

THE PATHOLOGY OF CANCER

DELIVERED AT THE ROYAL COLLEGE OF SURGEONS OF ENGLAND

1884

BY

W. S. SAVORY, F.R.S.

SURGEON TO ST. BARTHOLOMEW'S HOSPITAL

London

J. & A. CHURCHILL,

11, NEW BURLINGTON STREET

THE BRADSHAW LECTURE

ON

THE PATHOLOGY OF CANCER

DELIVERED AT THE ROYAL COLLEGE OF SURGEONS
OF ENGLAND

1884

BY

W. S. SAVORY, F.R.S.

SURGEON TO ST. BARTHOLOMEW'S HOSPITAL

London
J. & A. CHURCHILL
11, NEW BURLINGTON STREET

THIS LECTURE IS PUBLISHED

AT THE REQUEST OF

THE COUNCIL OF THE COLLEGE,

TO WHOM THESE PAGES

ARE DEDICATED.

ON

THE PATHOLOGY OF CANCER.

"WHAT'S in a name?" Not very much, perhaps, in the sense in which Shakespeare puts the question into the mouth of Juliet. No great danger, probably, or source of error, when the matter under consideration is as simple and clear as the odour of a rose; but it is surely otherwise when ideas involving far larger and more complex issues come to be expressed by a single term.

It is often said, and indeed with truth, that for one's self it is no matter what you call a thing, so long as you understand the subject or nature of it; but this always signifies very much to others who may not so clearly comprehend it.

It would be easy enough to illustrate the tyranny of phrases in the study of pathology and in the practice of surgery; for here the power of words for mischief is oftentimes seen in a two-fold aspect; not only in the perpetuation of error, but in the maintenance of con-

fusion too. Certain terms and titles have not only given the stamp of currency to false doctrines, but by the changes they are prone to undergo, and have undergone, in their meaning, they signify different things at different times, and at the same time different things to different persons.

I say it would not be very difficult to find abundant illustrations of these remarks, but I will take now only the one that is to be found in the terms local and constitutional. In a general sense, perhaps, these are sufficiently intelligible, as when we speak of constitutional disturbance from local disease. When neither the patient nor the surgeon can detect any evidence of mischief, except in a limited portion of the body, such affection may very well be termed local. When the patient is conscious, or the surgeon can discover, that the functions in general are disturbed, the condition is very fairly expressed by the term constitutional. But when these same terms, local and constitutional, are employed more definitely, and in relation not to phenomena merely, but to the nature and origin of disease, difficulties soon appear which lead to error and confusion.

The oldest, the largest, the plainest, and most popular division of tumours, is into innocent and malignant growths; and, although it has always been easy to show that these two great classes often approach very closely, and even pass into each other, still, in the main, the several broad and well-defined lines of demarcation have been sufficiently obvious. Not only surgeons, but the public, have come to understand the great point of distinction. The crucial question is continually asked, If the tumour be removed, will it come again?

But then, of course, to those who think on these

things, the further question inevitably arises, Why are tumours in their nature and history thus different? Whence the cause of such a contrast? What does it mean? And these deeper questions have been replied to, over and over again, by the phrases—local and constitutional. The innocent tumour is a purely local one. There is no extension, save by the growth of the sensible mass. Its substance and whole influence lie within a small space of the body, which can be clearly defined. To this place it is strictly limited; and, if it be removed from this, it is gone for ever. But, of the malignant tumours, none of these conditions can be affirmed. Whatever may be true, at any given time, of the sensible mass, the existence of the disease is not so limited; and thus, in contrast to innocent ones, malignant tumours have been called constitutional. But then, when the inquiry is carried further, and some explanation of constitutional, in this sense, is demanded —when it is asked in what way the word constitutional advances our knowledge beyond the term malignant— it must be confessed that the answer is not altogether a satisfactory one.

Many of us can remember the celebrated discussion on Cancer at the Pathological Society; and the fact that seems to stand out in it most clearly is, that then as usual, the term constitutional was employed by different speakers in widely different senses. And, moreover, I think it might be shown that the different ideas which different speakers associated with the term constitutional were mainly due to the relative importance which each speaker respectively attached to certain features of malignant tumours.

Of cancer, it was at the outset affirmed that the all-

but certainty of its recurrence, remove it as we will, its hereditability, its frequent association with other forms of irregular growth, its often rapid diffusion, its power of infecting the system—all, in fact, that we see in the life of cancer—naturally lead to a belief that the disease must, from the first, be more than a mere local tissue-change.

But then, again, in view of the hereditariness of cancer, of the constancy and of the method of its recurrence, and of the insusceptibility of bodies generally to the inoculation of cancer, the word constitutional was held to be equivalent to the total constitution of the body—that the constitution is, in short, the man ; all that gives to him his individuality.

But, again, the assumed facts that in cancer there is no distinct or specific anatomical or structural element ; that neither plurality of tumours, nor the property of recurrence *per se*, is distinctive ; that cancer is all-pervading, and appears as a disease, the one essential character of which is dynamical : such facts suggest strongly to some that cancer is a disease of the blood, or even that hereafter it may be found to be in close alliance with the so-called zymotic affections. In favour of this view, has been added the observation of the mode in which secondary cancerous tumours grow ; not as mere grafts undergoing increase, but as a definite sphere of the secondarily affected organ undergoing changes in its own elements, and growing, by way of such elementary changes, into the likeness of the primary tumour.

Furthermore, this view appears to be strengthened by a comparison of cancer with syphilis. Taking, on the one hand, a chancre inoculation, say of the lip, with

affection of the lymph-glands, followed after a certain number of years by gummata throughout the body; and taking, on the other hand, an epithelial cancer of the lip, with its secondary affection of lymph-glands, and subsequent identical affection of, say, the lung or liver; it is asked, can we affirm that these two cases differ more than we might reasonably expect two species of morbid poison to differ? This is even suggestive of a contagium from without. And yet further, in the manner in which it is inherited, a resemblance has been found to syphilis, gout, and tubercle.

Once more. In face of the fact that the hereditary transmission of cancer must mean that it is conveyed from parent to offspring, through the ovum or spermatic fluid, it must exist in the individual before the formation of the blood. And it has been maintained that the term constitutional, or all-pervading, may be true enough in regard to the ovum, but that it ceases to be true of the adult, because then we can realize the "condition of localization" in the various tissues of the body.

Thus, with such different interpretations from such high authorities of the term constitutional, it cannot be allowed that it has any precise or definite signification for us; and furthermore, I fear, it must be admitted, that when the several grounds on which these various forms of belief are based are critically examined—as, indeed, some of them were in the discussion alluded to—they will hardly be found adequate to the purpose in view.

For example: that a disease is hereditary is no proof that it is constitutional in any of the senses in which the term has been employed. Otherwise the term constitutional must be given to every form of tumour which has been shown to be occasionally hereditary; and thus

the significance of the expression, at least in its relation to cancer, would be lost. Neither does it appear to me that the view is supported by the manner in which cancer often proves to be hereditary.

Although the fact of the occasional hereditary transmission of tumours is common to all of them, it has been pointed out that there is a difference in the manner of transmission of tumours which are called local, and of cancers; that, when a local or innocent tumour is transmitted, it reappears in the same tissue, if not in the same place, in the offspring; whereas no such limitation is observed in cancer. But the difference in this respect seems to me to be more apparent than real, and such as it is, I think may be explained by the nature of the cancer-substance, of which I shall speak presently. When innocent tumours are transmitted, they often appear in the offspring in widely different parts, although, for obvious reasons, somewhere in the same tissue; and cancers, when transmitted, have a strong tendency to reappear in the same part; perhaps, in half the instances, in the breast. The difference, after all, appears to be one only of degree, and, if the current view of the relation of cancer to epithelium, and of sarcoma to connective tissue, be correct, of a degree perhaps not very significant. For it may be said that no kind of tumour which is hereditary is limited to a particular place, and every kind of tumour which is hereditary is limited to a particular tissue.

Then its recurrence after removal and its dissemination —the features which place it in such striking contrast to the tumours called innocent—in a word, the signs that are generally held to indicate an affection of the system—cannot be shown, I think, to be the usual attribute of cancer in the earlier stages of its history. If,

in its course, cancer becomes thus all-pervading, this does not involve the admission that it was constitutional at the outset; for a disease may be local at one time, and constitutional at another; and this is a point which, I venture to think, requires to be carefully distinguished. The character which a disease presents at an advanced stage of its progress is one thing; its mode of origin is quite another; and, in the case of cancer, I shall try to show that this distinction is a necessary one, and of fundamental importance. Nay, even a disease which, in an early period of its history, is emphatically recognized as constitutional, may, I suppose, in the earliest stage of all, be considered local. For, in whatever relation the induration of a chancre may stand to the infection of the system in syphilis, it will, I take it, be generally allowed that, after inoculation and certain local changes consequent thereon, a sensible period, though it may be a very short one, elapses before the poison becomes all-pervading. If the arguments in favour of the view that cancer is a constitutional disease be examined, it will appear, I think, that many of them are valid only in regard to the more advanced stages of cancer. The evidence in favour of the view that, when cancer first appears in a body, it is as a constitutional disease, seems to me far less clear and cogent.

Now let us discard for a moment these terms local and constitutional, and let us approach the study of cancer from another point of view.

Amongst the many attempts at an adequate classification of tumours, there is one which is founded on their structure, on the character of the elements of which they are built up. The fact is sufficiently clear that various tumours are composed of structures or tissues,

which, in sensible characters, are completely identical with some one or other of the normal tissues or structures of the body. Fatty and fibrous tumours are familiar examples of these. I suppose portions of fatty or fibrous tumours may be placed under the microscope side by side with portions of natural adipose or fibrous tissue, and no histologist, who understood his work, would venture to say that he could distinguish between them. But, again, it is clear that certain tumours present structures which are not identical with any of the adult structures of the body, but which may be distinguished from any of these by competent observation. Hence the famous classification of tumours into homologous and heterologous growths. But further explanation is necessary here. In this view, the term heterologous has been commonly employed in its full meaning; to signify that tumours so called do not, in their structure, resemble any of the natural tissues of the body. It should, I think, be, as I have already said, any of the adult or fully formed tissues of the body; for in truth—and this is of the first importance—these heterologous tumours, in their sensible structure, do resemble some natural tissues when in an embryonic or immature state. Just as portions of homologous tumours may be mounted side by side with portions of certain adult tissues, and no distinction between them can be discovered, so portions of heterologous tumours may be mounted side by side with portions of certain embryonic tissues, or tissues in course of development, and no distinction can be drawn between them. Let me be understood in this. I am not referring to the arrangement of the elements in a tumour, but to the sensible characters alone of the ultimate elements. A carefully prepared

section of cancer or sarcoma in a typical state has characters, of course, by which it may be distinctly recognized. These characters of arrangement have been described over and over again, and are familiar to all. But to these I do not now refer. My remarks here are confined to the primary forms themselves; to the physical characters of the ultimate elements of structure, not to the mode in which they are arranged; in short, to the so-called cells, either in their typical form or in some of the earlier changes they undergo.

So, then, of cancer and its allies—of the various forms of sarcoma—it may be affirmed that they consist of structural elements which, in their sensible characters, correspond to certain natural structural elements in a rudimentary state.

Now if we pass, for an instant, from the study of tumours to a comparative view of the phenomena of life, either in the vegetable or the animal world, we must remark in various individuals, of either kingdom, a wide diversity of structure; not only a wide diversity in separation of organs, or in complexity of combination, but a diversity yet wider, even more general, in truth universal, in the ultimate anatomical elements of which they are constructed. From a simple cell, or cluster of cells, we pass through various tissues which have been reached by further stages of development, until we arrive at the most elaborate, or highly specialized structures; for instance, at the spiral vessels of plants, and at striated muscle of animals.

Again, by such a survey, the fact is revealed that there is the widest difference in the power of multiplication, or propagation, among the various forms of animal and vegetable life; and, furthermore, that a relation may

be observed between the simplicity of original structure or degree of development and this power of reproduction—that the creatures whose structures and mode of formation are simplest, which are most akin to the primary elemental form, can increase and multiply with most rapidity and ease; on the contrary, in those creatures called highest, which consist of structures and organs most elaborately formed and highly specialized, the power of growth and reproduction is most limited.

And yet, further; in such a study a deep difference is observed in the relation which such different creatures hold to the conditions under which they live. There is, of course, a constant action and reaction between them and what are called the external agents of vital action, both material and dynamical. All are dependent on, and influenced by, food, air, and the operation of the physical forces; but this in widely varying degrees. While the higher or more complex creatures are less influenced in their character by these than are the lower or simpler, the lower or simpler are less dependent on these than are the higher or more complex. The simpler forms can exist, can maintain life, under far more variable conditions than the more elaborate ones. Their power of endurance is manifestly far greater.

Who needs to be reminded of illustrations of this, in either the vegetable or the animal kingdom? Compare the power of endurance of exposure, deprivation, and extreme change of the simplest plants, with the tenderness and susceptibility of the more elaborately developed ones. In the animal kingdom, even among invertebrata, compare the simpler with the more elaborate forms of life, in their power of sustaining deprivation of food, and air, and heat; and, above all, witness the striking

contrast in this respect between fishes and reptiles on the one hand, and birds and mammalia on the other.

Now, this great law of nature—for such it seems to be—governs not only the various individuals of the living kingdom, but it is in force also in the several tissues and structures of the same individual. Note now how widely they vary, not only in design and pattern, but in their degree of elaboration or complexity. Compare, for a single instance, fibrous tissue and striated muscle; and now note, too, the wide difference between these various tissues in their power of reproduction. The simplest of them may be said to be capable of perfect reproduction. Witness, on this side, the result of the division of a tendon; witness, on the other, the result of the division of muscle. It is doubtful, perhaps, whether, in such circumstances, muscle can ever be perfectly restored. It is certain that, as a rule, it is not; but that, in repair, its place is supplied—and observe the significance of this fact—by the lower or simpler form of tissue, the fibrous. Then, further, observe the relation in which this power of repair or restoration stands to the mode of original development, whether in the creature as a whole, or in the several tissues of which it may be composed. There is surely a relation, but an inverse one, between the extent of change through which any individual or structure passes in the course of its development and, when fully formed, in its power of reproduction after mutilation.

In the vegetable kingdom compare, in their power of recovery after mutilation, the simpler cellular plants with the higher exogens and endogens; and in the animal kingdom the like power in polyps, worms, and amphibia, with that of birds and mammalia. And let

me remind you here of the significant fact that this power varies, not with type of organization, but with grade of development; not with the relation to each other of parts and organs, but with the nature and extent of change through which the several creatures in the course of their development pass. And what is true of creatures as a whole, is also true of the several tissues of which they are constructed. Compare the power of recovery of the cellular tissue and woody fibre of plants, or of the fibrous tissue or even nerve and muscle of animals, with their mode of development. It would seem, indeed, that, in proportion to the amount of force engaged in original formation, so is the power of subsequent repetition reduced; or otherwise, that there is an inverse proportion between the power of attaining a high grade of development and the power of reproduction.

So that, while on the one hand, from a knowledge of the mode of development, one might foretell the capacity for repair after mutilation of an individual or tissue: on the other, from a study of this capacity of repair, whether in the individual or tissue, one might be able to judge of the degree of change through which it passed in the course of its original development.

And it may be affirmed of individuals, and their tissues, that the lower the grade of development, the greater is the power, not only of reproduction, but of endurance of life; that in proportion to the extent of change which any individual or tissue passes through in the course of its development, so not only is its subsequent power of reproduction limited, but so also is its maintenance of life dependent on the special conditions under which it exists.

Now of tumours, it may be remarked, in the first place, that, various as they are in structure, they almost invariably consist of one or more of the simpler tissues —of tissues of comparatively simple structure, and whose mode of formation does not involve any very elaborate series of changes. Among the tumours called homologous, or those which consist of adult or fully formed tissue, fibrous tissue, in its various forms, and adipose tissue, are very common; muscular tissue is very rare. When muscular fibre appears in the substance of a tumour, the plain, or unstriped, or simpler form of fibre, is far more common than the more elaborately developed striated fibre; and perhaps, in most of the instances when either of them is found, its presence is due rather to the inclusion of normal tissue in the tumour during growth than to an independent formation or distinct outgrowth of muscle. Again, in glandular tumours, which are by no means uncommon, it is the acinous portion of the gland — that which, in original development, is first of all formed — which is chiefly represented in the substance of these tumours; ducts, which are more complex, are not very often completely produced. Still, the tissues which compose these innocent tumours, comparatively simple as they are, nevertheless are wont to obtain their mature or adult condition; so that although, being of a comparatively low grade of development, they are readily produced, and can therefore grow almost without limit, yet withal, being fully specialized structures, their life more immediately depends on certain external conditions.

But the structure of cancer and its allies is characterized by the presence of the lowest and simplest of living forms. The so-called cancer-cells — the structural elements of

cancer—are the very type of the rudimentary or embryonic form of tissue; and beyond this early stage the typical cancer-cell seems never to pass. Both in positive and in negative characters, it corresponds to the simple animal or vegetable cell. In its indifferent endowments, in the total absence of any special function, in its tenacity of life and endurance of change of external circumstances, it very closely resembles it. If one were asked to enumerate the characteristic properties of the lowest and simplest forms of life—of the cell—I think reference would be made to rapidity of growth, to power of reproduction, to wide extension and dissemination. And do not these characters form the prominent features of cancer, in its worst or most malignant form? The absence of any attempt at what is termed differentiation or specialization is in accordance with its surpassing power of multiplication and tenacity of life. And, as we pass from cancer through the more malignant to the less malignant forms of sarcoma, we find a departure from the typical form of cell to be associated with more limited power of mischief. As the elements of a tumour become fusiform or spindle-shaped, as the first steps in development towards the formation of some special kind of tissue are taken, so is the property of dissemination, or the power of living under various conditions, restricted; until, as we pass farther on to the production of distinct fibres, as the power of individual development advances, the attribute of indifference to surrounding conditions, or to its environments, disappears, and the elements of the tumour become limited to a particular place. It is, from first to last, local, or what we call innocent.

But one word further on the so-called cell of cancer. The history of this word cell, in its relation to physi-

ology and pathology, is not without interest and importance.

When the famous cell-theory was first set forth, a cell was very clearly and accurately described. Schwann, and many of his successors, in their definition of a cell, took care to leave no doubt on what they regarded as its essential structure. At length, however, certain facts were established, which were fatal to the cell-theory as it was then understood and accepted by all. It was shown, for instance, that in the development of muscular fibre, cells had no share; and it then appeared how deeply rooted in the minds of physiologists this great doctrine had become. To me, at least, it seems that mischief has arisen from the proceeding by which an attempt has been made to evade the fatal objection opposed to it by facts. The scarcely ingenuous scheme has been devised of modifying or enlarging the definition of a cell, so as to make it include structures which really can have no claim whatever to the title of cell, in any fair signification of the word. Cells have more recently been described as mere masses of protoplasm, each around a nucleus; and the existence of a wall or limitary membrane, as an integral part of a cell, has been quietly ignored. To me, it seems, in all candour, that no better reasons for applying to such a structure as this the term cell can be given, than that such compromise is essential to the maintenance, in some shape or other, of a so-called cell-theory. It is affirmed, indeed, that "the existence of animal-cells destitute of envelope, although more insisted on of late years, has been all along recognized in the study of cell-development, and was expressly pointed out by Schwann himself." But, although it is true that Schwann admits, in more than one place, that the presence of a

cell-membrane cannot always be demonstrated—as, for instance, in the following passage: "Many cells, however, do not exhibit any appearance of the formation of a cell-membrane, but they seem to be solid, and all that can be remarked is that the external portion of the layer is somewhat more compact"—yet, I think, an impartial study of what he has written will show that he never contemplated, by his theory, the inclusion of such facts in development as appear to be now established. If it were true, as Schwann and his more immediate successors believed, "that there is one universal principle of development for the elementary parts of organisms, however different, and that this principle is the formation of cells," then it would be all very well to admit the occasional existence of such structures, imperfectly formed, without doing much violence to the doctrine; but it is altogether different when, in the development of certain most important tissues, no cell in any form appears, to persist in applying the term to simple fragments of protoplasm—a term which has been long and properly associated with a definite and different structure. It may be suggested that the alternative of throwing over an exploded doctrine is preferable to the confusion which must inevitably result from such vague and inaccurate employment of words. Surely the cell-theory, as it has been long understood by all, is no longer tenable. Why attempt to avert its fate by what cannot be characterized otherwise than as a perversion of language?

And this question of the constitution of the so-called cells points to the further fact, which I believe to be at the root of the erroneous view of their nature—the changes in aspect and character which living substances undergo at death. The conclusion has, for the

most part, been too hastily and unconditionally accepted, that the characters presented by tissues after death, and even after treatment by powerful reagents, are those that naturally belong to them during life. The structural changes which ensue on the cessation of life have, indeed, been long recognized in certain nerve-fibres, but hardly, I think, anywhere else; yet I believe it to be, in some degree, common to all tissues. There can be no doubt, I think, of the fact of great change in striated muscular fibre; and some years ago I tried to show that the nucleus of the red blood-cell in those vertebrata in which it is supposed to be constant, has no existence during life and health. And I believe that the same fact is true of many forms of the nucleated cell—of the cancer-cell, for instance, here. During life these are but fragments of simple protoplasm, the substance of which, uniform during health and vigour, separates, at death, into cell-wall, nucleus, and contents, after the manner of the coagulation of the blood and the rigor mortis of muscle.

Surely this seems to apply with especial force to the pathology of cancer. Its elements are, in truth, not differentiated even into complete cells. When fresh and unaltered, there is no distinction of cell-wall and cell-contents. In the living particle, I doubt whether there is even the distinction of a nucleus. In short, they are I believe, but separate fragments of protoplasm equal to, but not higher in rank than, the amœba or white blood-cell, or the utricle of the plant. I say this view especially concerns us in its relation to the pathology of cancer. Cancer, strictly so named, we have been taught, is the outcome of the epithelial tissues. Now, fully formed or mature epithelium is, undoubtedly, composed of cells, of

individual structures showing distinctly enough cell-wall and nucleus. And yet, even here, development into a complete cell is through the shortest and simplest changes. Then see how even this contrasts with the so-called cell of cancer, for these fragments of cancer-protoplasm are but the embryonic or rudimentary form of a cell of epithelium. Their power of individual development does not reach even to this level. Judge, then, what their power of endurance and of multiplication must be.

Then, again, this concerns the relation which the cancer-cell bears to some cells of natural structures. If the cancer-cell were really a complete and fully formed cell in the proper acceptation of the term, it might be argued that in this view it should have no further power of malignancy than, say, a fat-cell. But herein consists the difference. A fat-cell, although a comparatively simple structure, is yet one thoroughly specialized. It is no longer indifferent substance, but its life is devoted to a particular function. It is fully formed, adult, mature. So, again, with the cells of secreting glands. They probably are not, and, I think, for the same reason, so far removed from cancer-cells as are fat-cells. But still gland-cells are not in a state of indifference. They are so far specialized, that they have a definite function, and clearly the whole purpose of their life is devoted to its fulfilment.

I will only add, with reference to this matter, that I believe the same view may be carried into the structure of sarcoma. The characters which the elements present after death, still more after the action of various reagents, are not those which belong to them during life. The so-called fusiform and spindle cells are, again, but

separate fragments of protoplasm, altering their shape in the first step towards the production of some definite tissue.

Seeing that no satisfactory explanation of the clinical facts of cancer can be given by way of the constitution, or blood, or germ, some have sought to find it in the mobility and dispersion of the cells. To account for the infection of neighbouring and distant parts, and ultimately the contamination of the system, attention has been called to the fact that the cells are dispersed around a cancer-tumour, and that the direction and rapidity of dispersion will vary according to the density of the tissues, and the abundance of connective-tissue spaces, or of lymphatic or vascular networks, in which it lies. We have been reminded that cancer is, for the most part, a structure infiltrating itself amongst the tissues in which it grows, not surrounded by a capsule or limitary membrane of any sort, as are so many non-infecting tumours. Once set free, it has been argued, the cells may travel either along the lymphatics to the glands, or through the surrounding tissues in the direction of the least resistance; or they may pass through the blood-vessels into the general current of the circulation. At times, too, they may pass through cavities by gravitation. No doubt such physical conditions as those alluded to may have some influence on the rate and direction of the distribution of cancer, but all of them together will surely not suffice to explain the clinical facts. A comparison of the dissemination of cancer with the wandering of white blood-cells, which, indeed, has been brought forward to support the view, seems to me, when considered, to destroy it. The white cells wander freely, but they do not form new and distinct growths composed of masses of white

blood-cells over the body; but they soon change, are either developed into some form of existing tissue, or otherwise disappear. It is, on the contrary, in the very nature of the cancer-cell not to advance in development, but to multiply. Moreover, it has been pointed out that there are cancers and sarcomata which multiply themselves in distant and dissimilar parts, whose physical condition looks as unfit for travelling as any that could be named. It is quite true that, in the typical forms of cancer proper, the cells themselves are free and mobile in the spaces within which they are enclosed. But when we study malignant tumours as a class, and compare them with innocent ones, it cannot, I think, be affirmed that there is anything like a constant relation between the rate and extent of their distribution and the mobility of their cells.

Again, the attempt has been made, by Cohnheim, for example, to explain malignancy by assuming that the physiological resistances to invasion are somehow diminished. He argues that germs of cancer implanted into fresh tissue are sure to perish when the changes which go on in the tissue are normal. Their development implies that the tissue-changes in which they live and grow have ceased to be normal. But there is no evidence of this in relation to tumours; and, even if established, it would not afford any adequate explanation of the malignancy of cancer. Why should it not apply to other tumours which are innocent? It does not touch the question of distinction between these and cancer.

The phenomena of cancer, then, the facts of its clinical history, cannot be adequately explained by any reference to the constitution, in any of the senses in which the phrase constitutional has been employed. The arguments in favour of this view in any form fail from want of pre-

cision. In the sense that an original flaw or defect exists in the vital endowments of a part, it may be admitted to be true; but, in this sense, innocent tumours must be admitted to be constitutional, and so must every individual feature be which is hereditarily transmitted. Neither can the clinical facts of cancer be explained by regarding it as an affection of the blood. Inasmuch as this view has some advantage over the other in precision, so it fails more conspicuously to cover all the phenomena of the disease. Nor can the malignancy of cancer be explained by the mere mobility of its elements; for ceaseless change and constant transmission is the law of life everywhere. All fluids, all solids, the loosest and the firmest textures, are in continual motion. Look where we will, we know full well that the appearance of stability and endurance is illusory. Vital action is inevitably associated with molecular movement. Freely, then, to cancer we may grant great mobility of its elements; but to explain its clinical facts we require much more. And I, at least, believe that what is wanting here is to be found in the nature and vital attributes of its so-called cells, or of the formless plasm out of which they come; for this matter, or these fragments, possess an ability of living after the fashion of the lowest and simplest forms of life. When we call these structures embryonic, it must never be forgotten or overlooked that this term has reference only to their position in the scale of life, to their grade of development. They resemble, indeed, during the whole period of their individual existence, embryonic substance in the simplicity of their physical characters. But they differ in the widest possible way from embryonic structures in their vital attributes and life-history—in the almost, if not quite

complete absence of change of structure or of endowment; and it is in this contrast that their power of evil becomes manifest. The great feature of embryonic tissues is in the advance from a simpler to a more complex state; to the formation of a higher structure, with more exalted or, at least, with more special functions. In short, their great vital endowment is the power of development. But the protoplasm and fragments of cancer are just what they are, because they have none of this. They cannot "rise to higher things," and, according to a law of nature, they obstinately retain life and, in unbroken force, the power of propagation. Their power of growth is inversely to their power of development: and growth here is but synonymous with multiplication; for, as in the lowest and simplest forms of animal life—in structures composed of simple cells or fragments of protoplasm—no distinction can be drawn between extension of the individual and multiplication of individuals. And withal, combined with these characters of life is, after the manner of their kind, their independence of special environments. Thus, upon their increase, follows their dissemination. They are not bound by the conditions of their existence to be local; but they can invade various parts and flourish still.

It would appear then that much danger lurks in the designation embryonic to cancer substance, and that it is of the first importance to beware of this. Malignant growths are heterologous in structure, unlike in this respect any adult tissue. But their substance resembles in physical characters embryonic tissue. It is only on a level with it too—and this is of prime significance—in grade of development. But it contrasts strikingly with it in this: that, while the destiny of tissue which is

truly embryonic is to a higher form of structure, this, which has no such power, retains in full measure its primitive capacity of reproduction, and its comparative indifference to the conditions under which it exists.

Although, as we all know, it is not correct to say that the higher animals, in the course of their development, pass through states identical with those of the adult condition of the lower, it is not incorrect to say that the higher animals, in the course of their development, pass through successive stages which, in grade, correspond to, or are on a level with, the ultimate stages of the lower. It is thus, and thus only, that we compare cancer substance to embryonic tissue.

This view seems to me to be strengthened by some facts which at first sight may appear to be in direct contradiction to it. Cartilaginous tumours, for example, are homologous structures, that is to say, they resemble generally certain of the normal tissues of the adult body; yet cartilaginous tumours, although usually innocent, occasionally behave, as every one knows, like malignant growths. They grow with rapidity, and they reappear in distant and various parts. They are indeed singular among tumours in this respect; that apparently the same structure will in different cases be endowed with such different attributes. But then it should be remembered that there are two kinds of normal cartilage, distinguished not so much by their structure as by their life-history—the one called temporary, the other permanent cartilage. The one form does not throughout its life pass beyond the condition of cartilage; the other passes, sooner or later, into bone. There must therefore be something fundamentally different in the nature of these two forms of cartilage. Now the enchondromata, which in their

nature resemble the former kind, are localized, are innocent. They may be, and often are, multiple, and sometimes grow freely, and this quite accords with the simplicity of their structure. But the enchondromata, which in their nature resemble the latter kind, are more or less malignant. They remain on a level only with structures which are fœtal; and with the absence of further development is associated the power of increase and of dissemination. It may be said that the cartilaginous tumours which are innocent show no advance of structure beyond those which tend to malignancy. None indeed that we can yet discover; but then neither do some forms of permanent cartilage differ in this respect from fœtal cartilage; yet we must regard the one as fully formed tissue, and the other as only in a more rudimentary state. In such microscopic structures, it is not always practicable to discern the grade of development in the permanent aspect. The grade of a fat-cell or of a gland-cell must be interpreted rather by the specialization of its function than by its obvious structure.

And let me observe that this attempt at explanation is not affected by the view we take of the nature of the transformation of cartilage into bone. Whether we regard it as an act of development or of degeneration whether we regard bone or cartilage as the higher structure, still, in the passage of cartilage into bone, there is metamorphosis, further change, a tissue still further removed from the embryonic grade. In truth, the relation of cartilage to bone is by no means a peculiar one. Before we can determine to call any change either development or degeneration, we must become clear on the meaning of these terms; but it seems to me that any just view which will lead us to

call ossification of cartilage an act of degeneration will lead us also to consider the several stages of the formation of other tissues as acts of degeneration. In this view, the germ is the highest of all structures; for, of all structures, it possesses the greatest capacity for the highest phases of vital action. As we pass from the general to the special, this power dies out, and at length there is only the power, and this to a limited extent, of self-maintenance. In the qualities in which cartilage can be said to be above bone, all young structures are above adult ones.

I suppose it must be admitted that the present classification of tumours is not altogether a satisfactory one; but it was undoubtedly a great step onward when those tumours which, although not cancer proper, possess some of the worst features of malignancy, and which, as a class, are distinguished by the obstinacy of their disposition to recur, were brought together into one great group under the title of sarcoma. The title itself is an unfortunate one; but, nevertheless, our knowledge of the subject of tumours becomes clearer if we understand the chief marks of distinction, both pathological and clinical, between cancer and sarcoma, even without reference to the doctrine of their respective origins from epithelial and connective tissue, or rather from structures derived from the epiblast and hypoblast on the one hand, and from tissues derived from the mesoblast on the other. But under the term sarcoma is included a large class which may be very fairly subdivided into orders that for the most part differ strongly from each other; and this must of necessity be so if the view on which I have ventured to insist be well founded; for the sarcomata, in truth, represent the several connecting links

which pass between the two extremes of cancer on the one hand, and quite innocent tumours on the other. The worst of the sarcomata are almost or altogether as bad as the worst cancers, and in their structural elements they very closely resemble them; nay, in some instances they overlap or even pass to the other side. The clinical history of some forms of melanotic sarcoma is far worse than that of some forms of epithelial cancer; while some of the outgrowths which still fall within the class of sarcoma, as, for instance, the common nasal polypus, or myxoma, as it is called, may fairly claim, by its behaviour, to be ranked amongst tumours which are innocent. And as in the clinical history, so in the structural elements of sarcoma, the same gradation prevails. In this class, we pass through all degrees, from the scarcely altered cell, or fragment of protoplasm, through oval, spindle, and fusiform cells, to the fully formed fibre.

These three great classes of tumours, then, are distinguished by the grade of development of the structures which constitute them.

Those tumours which are recognized as innocent ones are constituted of elements which, for the most part, are on a level, in grade of development, with many of the fully formed or adult tissues of the body, and therefore in physical characters they are identical with them.

Those tumours which are included in the class sarcoma are constituted of elements of various grades of development, being on a level with the successive stages of formation of some of the normal tissues.

And those tumours which form the most malignant cancers are constituted of quite rudimentary elements, those of the lowest grades of development being but

on a level with the embryonic stage of normal structures.

With reference, however, to this classification, it must be remembered that some tumours are of, what may be called, mixed or compound constitution; that is to say that they consist of different structures in different parts. In some parts they consist of tissues like the mature normal structures, in other parts of more or less rudimentary forms; and, of course, their clinical characters will vary accordingly. Hence, unless an examination of such a tumour be very thorough and complete, any inference drawn from it may be very erroneous. Perhaps most tumours present, in some degree, differences of this kind. But then, when structures of some low grade of development are discovered, the question, which is of cardinal importance, still remains to be answered: whether these are on their way to further development, or whether they have already reached their level, and live only to multiply and invade.

Another point of importance in reference to such a classification is, to beware that we do not confound mere shape or form of these structural elements with their nature and attributes, or rather to be cautious in drawing any inference of the one from the discovery of the other. For example, epithelioma of the lip and carcinoma of the breast are both composed essentially of what are called cells. But most of the cells of epithelioma are properly so-called. They are more or less mature. But the so-called cells of carcinoma are, as I have said, but fragments of protoplasm, and never reach to the level of true cells. To be sure, the grade of development in each case is low enough, and therefore both kinds of growth are malignant. But still there is

a marked difference of grade in the two cases, and therefore an obvious difference in degree of malignancy.

I would venture to insist on the significance of the fact, that the present classification of tumours, which has been gradually worked out as the result of long and patient investigation, but without any reference to the principle I have been endeavouring to set forth, should nevertheless be in such accordance with the laws which govern the phenomena of life in general. It is suggestive enough that two paths of inquiry, separately pursued—that of clinical study, and that of histological research—should lead at length to the same conclusion; that different degrees of malignancy of character should correspond with different grades of development of structure; that in morbid structures, as in normal forms of life, there should be an inverse relation between the capability to increase and extend, and the power of passing, by development, from the general to the special.

And in the examination of a tumour, with the view of forecasting its clinical history, it appears to me that this is the chief question which should be taken into consideration. It will assist us less to know that any given tumour belongs to this or that particular class and order, than to ascertain its own exact nature from a thorough investigation of its substance. Of course, help in this, to a greater or less degree, may be derived from all the circumstances which pertain to it; not only by considering it in reference to the group to which it may belong, but also by reviewing its own previous history. But withal, when corrected or adjusted by such considerations as these, and others, too, such as its situation and mode of growth, and the local and general conditions to which it is subject, the first place may be given to a complete investigation

of its anatomy. I say complete investigation, because of the fact, already referred to, that some tumours are of mixed characters, and their potency for mischief has perhaps to be estimated by the worse rather than by the better parts of them. I think if, in a doubtful case, I had to depend for prognosis on one source of knowledge only, I should choose to have this. The family and personal history of the patient; his or her own age or period of life; the physical characters of the tumour, and its relation to surrounding structures; its place and previous history; especially its rate of growth; and, beyond all, its disposition to affect neighbouring and distant parts—of course, these together, and some of them alone, oftentimes speak clearly enough; and would, and should, with our present knowledge, outweigh any evidence derived from anatomical characters only. But when serious discrepancy occurs, as, indeed, it sometimes does, between clinical and anatomical evidence, this is due, I venture to think, rather to deficient examination or defective interpretation of what is seen, than to any fallacy of the principles involved in it.

It is in accordance with our knowledge of the relation of the lowest individuals to the conditions under which they exist, that malignant tumours should be very largely influenced by these. Look for instance, at epithelioma of the tongue. Epithelioma, as a rule, is not reckoned as the most malignant form of cancer; and yet, what a terrible history is that of epithelioma of the tongue! And may not this, at least in great part, be explained by its place, and the conditions to which it is exposed; to the great vascularity of the tissues among which it lives; to the warmth, moisture, and continual motion; to say nothing of repeated, though perhaps slight, injury, and

inevitably frequent irritation? Yet, after all, what is the sum of the effect of these causes here upon diseases of a totally different nature? Surely the life-history of cancer, as of any normal individual, is determined, in the first place, by its own endowments, which are the outcome of its structure.

Tumours are living structures, distinct outgrowths in some part or other, of the body; local, or limited to a particular place, in inverse ratio to the capability of their elements to adjustment to different conditions of life. Like the natural structures and organs, they have an independent life of their own, which is more or less influenced, modified, and controlled by the life of the body. Like natural structures, they have an inherent power of maintenance, but this power is regulated by the condition of the body in general. Tumours, by certain members of their class, approach very nearly to normal structures; and, indeed, between some of these, and what may be fairly called local hypertrophies of tissue, no well-defined line of demarcation can be drawn. Some of the chronic mammary or glandular tumours illustrate this. But, even in such outgrowths the first departure from normal type is shown, not only in the formation of their substance, but also in the fact that they are not in such close physiological relation with normal structures as these are with each other. The sympathy which universally prevails between the several structures and organs of the body, and which is maintained either through the blood or by the nervous system, or in both ways, varies in degree among natural structures; but between all these and tumours, a far wider divergence is found. They rise and fall less with the ebb and flow of general life, and they are less affected by changes in other structures.

Thus, by the most innocent and homologous tumours, is the first step taken towards an independent life; and, it may be observed, that this independence gradually gains strength, and becomes more marked as we pass from the most innocent, through tumours of varying degrees of malignancy, to the very worst; and, as we have seen, it is to the comparative independence of their life that the most deadly of their attributes belong. And while tumours, by the most innocent, touch and indeed pass into natural structures, by the most malignant, they touch, if they do not actually pass into, the class of parasites. Parasites are living forms, having, too, in various degrees, a power of independent life. For the most part, they can flourish only in the living body; and while there, they too are within the pale of the laws of its natural life. But, within this, they have an individual life, more independent of that of the body in which they live than tumours possess; and, moreover, they can, for a longer period, maintain life altogether apart from the body they are prone to infest. They can maintain a separate life in some of its lower grades; but they can exhibit their full vital endowments only in the body to which they belong. Now at present it must be confessed, that experiments on the grafting or inoculation of tumours, even of the most malignant, have not been attended by success. We cannot yet say that cancer can be thus propagated. Still there are some curious facts in reference to this. In certain cases, it has been observed that, when a cancerous mass has been allowed, for some time, to lie in contact with an apparently healthy surface, this healthy surface has at length become cancerous; and, in this manner, cancer seems capable, after the fashion of a parasite, of passing from part to part. From part

to part of the same body only; but I wonder what would happen if such an experiment could be fairly tried between different bodies. May not the experiments on inoculation hitherto have failed because of the crude conditions under which they have been performed? But be this as it may, and setting aside this conjecture, it would really appear that the interval between the worst cancer and certain parasites must be a very narrow one. Through the various kinds of parasites we pass to altogether independent forms of life; and I cannot help thinking that, from this point of view, much interest must be attached to tumours, as indicating the first steps towards the assumption of a separate and independent existence.

But, until it can be shown that tumours may be transmitted from one person to another by grafting or inoculation, it must be acknowledged that there is this sharp line of distinction between all of them and parasites. Parasites come always from without; tumours arise only from within; from some part or natural structure of the body itself. And it may be said that, after all, nothing more is known of the origin of tumours than this. Once started, we may perhaps see something of the laws which regulate their existence, but concerning their origin we are altogether in the dark. Yet, still recognizing in this darkness an obscurity which enshrouds also some of the largest facts in physiology, we may perhaps be able to discern the direction in which light must at length come.

While tumours, then, appear to be bounded by the lower and simpler forms of parasites on the one hand, they are approached by what are regarded as abnormal conditions of nutrition on the other. The process of nutrition in its simplest state is one of mere maintenance. The bulk

and weight of a structure or organ are preserved, in spite of constant wear and tear. In growth, there is increase either of bulk or of weight, or of both. But why, at a particular point, growth should cease, we do not know. We can only speak of it as a natural law. It is the same with regeneration or repair after injury. There is reproduction up to a certain point, and then this, like normal growth, closes. But, within limits, the growth or natural increase of a structure or organ is regulated by the conditions under which it exists. Some of these conditions are healthy ones, others are morbid; and thus we speak of overgrowths or hypertrophies as conservative or pathological. Now, the hypertrophies which are morbid in their nature seem to lead us on to tumours. The morbid hypertrophies, as a rule, affect, more or less, the whole bulk of an organ, as in the instance of the prostate or thyroid gland. But the more or less is a very important fact for us, for sometimes the overgrowth involves only a portion of the structure, leaving the rest unchanged. This is abundantly illustrated in the two organs just mentioned. Only a particular part, as a single lobe, may become overgrown, and the limit to such extension we can hardly indicate. Again, the excess of substance may be produced in one or both of two ways; either by a simple enlargement of the already existing elements of the organ, or by the development anew of additional elements. The organ may become larger by an increase in the size or in the number of its elementary structures. Thus, we have what is called simple hypertrophy, and what is called numerical hypertrophy or hyperplasia; and I think there can be little doubt that increase by hyperplasia is at least the more common process. In many cases, this is clearly revealed,

as in epithelial structures generally, and glands more particularly. Now, surely, the transition from a local hyperplasia to a distinct tumour is not a very abrupt one. Nay, is it not, I repeat, sometimes very difficult, if not impracticable, as in the instance of certain masses in the mammary or prostate gland, to draw any line of distinction between them? The mystery, then, which enshrouds the origin of tumours appears to envelope also other eccentric modes of vital action, which are nevertheless more akin to some of the normal processes of life. Before we shall ever be able to answer the question why or how do tumours form, it seems to me that we must be able to solve the problem of normal growth and development, and to answer the question why or how it is that these continue up to a certain point, and then suddenly cease.

Pardon and Sons Printers, Paternoster Row, and Wine Office Court, E.C.