OBSERVATIONS ON THE STRUCTURE OF TUMOURS: IN RELATION TO THEIR CHARACTER AND CLINICAL HISTORY.

BY WILLIAM S. SAVORY, F.R.S.,
Surgeon to St. Bartholomew's Hospital.

It must be confessed that it is no light task for a student to grapple with our present knowledge of the great subject of tumours. We may be, and no doubt are, nearer to the truth than we ever have been; but, as the matter was taught and understood a few years back, it was certainly easier of comprehension than it is now. It is by no means easy to follow the literature of the subject, but just now the chief difficulty is to reconcile the results of pathological research with clinical observation. The clinical history of tumours points very plainly to the two great classes of innocent and malignant growths; for the distinction is marked strongly enough in typical instances, although, as we ought to anticipate, they gradually pass into each other by intermediate forms: we all are familiar with recurrent tumours. And so, but a few years ago, morbid anatomy or pathological histology seemed to be fairly in accord with the results of clinical study. Although it was never generally admitted that a cancer-cell could be accurately defined or always clearly recognised, yet it was allowed by those who had given most attention to the subject, that the structure of tumours pointed to a classification in harmony with that suggested by their clinical history. Microscopic investigation claimed to be in strict accord with clinical observation. But this cannot be asserted now. It will be so; it must be so hereafter. No doubt we were in error in the past; but at present there is no doubt either that we are in some confusion. And the present state of confusion has arisen with the introduction of a class of tumours called sarcomata, which we owe especially to the ability and influence of Virchow. But I would not on this point be misunderstood for a moment; I am not suggesting that we have moved backward in our work; I am only endeavouring to show that the subject has thus become for a while more complex and intricate. Truth emerges from error sooner than from confusion, says Bacon, but oftentimes truth can be educed from error only through confusion.

The one objection I would urge now is to the term sarcoma, which is very unfortunate: unfortunate as the revival of an old term once upon a time most vaguely employed to all sorts of tumours, about which nothing was known; and unfortunate, as now either meaningless, or, as it implies anything, tending to mislead.

If the view derived from histology which is now current concerning the distinction between sarcoma and carcinoma be established—I mean, of course, the view of a different structural origin—then assuredly, whatever temporary difficulty may have been created by it, it is a distinct step forward, and must inevitably, sooner or later, aid and enlighten bedside work. But the temporary difficulty is this: put a tumour into the hands of the pathologist, and an examination of its structure will, with very few exceptions, enable him to assign to it its proper place in his classification, and he will for the most part have plain and intelligible grounds for the conclusions he draws. So far all is clear enough. The surgeon, too, though with far more numerous exceptions, and in many cases with much doubt, will, after the clinical study of a tumour, be able to forecast his patient's fate. But between the two there is this interruption: the surgeon fails to recognise the full force of the distinction between carcinoma and certain forms of sarcoma. They both to him are intensely malignant diseases, and their clinical history, so far as he at present knows, presents no contrast corresponding to that which is pointed out by their histology. I am not overlooking the difference of clinical features to which attention has been called, such as the far greater disposition of carcinoma to affect lymphatic glands; but, even allowing the most to these, they are not enough. But then the pathologist will say, Why not accept the two forms of malignant tumours—carcinoma and sarcoma? They admit of distinction by their structure at all events. True, it may be replied; but the pathologist, in his present classification, puts under the same order of

structure tumours possessing the utmost possible diversity of clinical history; for a sarcoma may be almost or altogether innocent,* or most malignant. And if, once more, it be urged that this difference between sarcomata is declared by their structure, and that, although, for morphological reasons, they are placed under one head, yet nevertheless their individual characters are for the most part marked to the histologist; it must be allowed that the surgeon is still justified in withholding his unqualified assent to a classification which groups together under one head tumours so widely separated in their life and action.

Under pressure of this difficulty, and in misgiving of the security of the step which, in our present classification, pathological histology has taken, I still seek for some clue to a better understanding of the relation which the character and clinical history of any tumour bears to its structure. Meanwhile, may we not find in tumours a striking instance of the light which physiology can throw on pathology? In the study of the various members of the organic kingdom, the law is revealed that the power of multiplication or reproduction is in an inverse ratio to their grade of development, or to the degree of change which they have passed through. In other words, the power of metamorphosis appears to be opposed to the power of reproduction.

Now that which is true of different members of the animal kingdom is true also of individual parts of the same member: as with the body itself, so with each of the tissues of the more complex forms—that which is originally developed in the simplest way, through the least degree of change, can be subsequently most readily and completely reproduced. In other words, that which in the adult condition is removed furthest from the embryonic state is least capable of reproduction. As, then, with animals so with their tissues—the simplest multiply the fastest. Witness, in illustration of this, the degree in which they severally possess the power of repair; from complete reproduction, as in fibrous tissue, to the utter want of it, as in muscle.

Now this great law does not appear to be limited to healthy structures; for morbid growths are but deviations from natural tissues; they are derived from these, and we might, therefore, reasonably be led to the conclusion—to which indeed the facts within our knowledge point—that their life is governed by the same laws. These laws prevail within the domain of pathology, and govern the growth, development, degeneration, and decay of tumours.

For example, how apt is fibrous tissue, in its several varieties, to produce tumours; and the various forms of fibroid, fibrocellular, and fibroplastic tumours which are now included under the head of sarcoma differ widely in their clinical history; but then, in their structure, these different forms exhibit elements representing various stages in the development of fibrous tissue; and it may be said generally that, in proportion as their elements retain their embryonic character, so does the tumour betray the features of malignancy.

Thus, in the common spindle-celled sarcoma, the forms are those of granulation tissue at a certain period of its development; but, in the tumour, these forms, instead of passing on into adult fibrous tissue, become exceedingly multiplied. The worst of it is, that, instead of transformation, there is reproduction. In other so-called sarcomata, the round or oval celled—of the gravest malignancy, more rapidly destructive than the spindle-celled, and perhaps more apt to infect lymphatic glands—the “cells” are still more embryonic, like those in the earliest stage of granulation tissue.

The tendency to recurrence, then, which is so characteristic of the sarcomata may be associated with the fact, that they are tumours composed of immature cellular tissue, of cellular tissue which does not attain the adult form, but whose development has failed at some previous stage.

In carcinoma, I think, we have an illustration of the same law. It has been often said of cancers that their structure does not resemble any of the natural structures of the body; but is it not more correct to say that, of all tumours, the essential elements of carcinoma most obstinately retain the embryonic form. Their cells or the masses of protoplasm resemble most closely those commonly seen in the earliest stages of natural tissues. Witness, for example, the resemblance between cancer-cells and the cells in the brain of the foetus.

The difference between homologous and heterologous growths is this: that in homologous growths the development is normal, but is carried out in the wrong place, and under abnormal conditions; in heterologous growths, there is more or less wide deviation from normal development. But there is no defined line of demarcation between the two. The whole difference turns upon the direction development takes, and the degree to which it proceeds.

* “Almost or altogether innocent”, for the term “sarcoma” is not used, even by the best pathologists, always in the same sense; while by some it is limited to tumours which are recurrent, by others it is extended to all tumours of a fibrous structure.

But, with regard to cancer, there is another question perhaps worth more attention than it has yet received. The existence of a "cancer-juice" is always recognised; but the cells are spoken of as the active agents, and to their account all the mischief is placed. Now if, as I suppose, the cancer-juice represents the formless protoplasm out of which the cells arise, may not that, rather than the cells even, be the prime source of mischief? I know no way of practically proving this. The juice may be in this respect altogether neutral, and the forms which spring out of it, or, if we will, exist in it, may be the starting-point of mischief; but, looking to analogy in the development of natural structures, and to the wide and vague view which must be and now is taken of a "cell", it may be that, in the formless protoplasm which after death or removal appears as cancer-juice, lies the idea of cancer.

No doubt exceptions may be mentioned to this law of relation between the want of development in the structures of a tumour and their tendency to multiply; but are they real or apparent? It is not always practicable to decide between immature and adult forms. An elementary tissue virtually adult may yet present an embryonic form, just as in normal structures the character of a tissue, in this as in other respects, may be determined with far more certainty by its physiology than by its anatomy. In two forms of tumours, for instance, this distinction between apparent embryonic form and embryonic character is very marked. In the fatty tumour, the fat-cell, seemingly simple, is, as we know, to all intents and purposes an adult form, and in the tumour it discharges a function precisely similar to that of the normal fat-cell. Still more strikingly is this shown in the glandular tumours, as, for example, in that of the breast, the chronic mammary tumour. The cells which are so abundant might, when isolated and free, be easily interpreted as cells of some malignant growth; that is, so far as their general structure is concerned, without relation to any special characteristic which an educated eye may detect; and yet they are truly adult forms—structures which have no doubt reached a degree of development equal to that which they attain in the normal gland; sometimes indeed even, like them, secreting milk; and the key to the true interpretation of their nature is given by their arrangement in, and relation to the acini. Yet these tumours, innocent as they usually are, occasionally prove recurrent; and there is not wanting evidence to show that this recurrence may be due to the persistence in some portion of the tumour of elements in a more embryonic form.

In fact, recurrence is occasionally exhibited as a feature of any form of tumour, even apparently the most innocent; and this it is not difficult to understand if recurrence depend on the persistence of rudimentary or embryonic forms. And, while in practice we may be apprehensive about the future of any case in which a tumour consists of very immature structures, we can never be quite sure that any tumour, even though in structure apparently the most innocent, may not contain within the visible mass undeveloped forms.

And in relation to this there is another matter of importance. Many tumours are composed of various elemental forms, and exhibit in different parts very different structures. And these mixed tumours are, perhaps, of more frequent occurrence than is generally believed. Now, although in such a mass one structure may largely predominate which is very innocent in its nature, yet the tumour may prove to be recurrent from the presence of other structures which formed but a very small portion of the original mass. Thus the chief importance of a tumour—that is, its worst feature—is not derived from the predominant structure. It is well known that, when recurrent tumours are frequently removed, each successive tumour is apt to show a greater abundance of more immature forms. The structure of the first growth may hardly have been suspicious, whereas the structure of the last tells plainly enough a tale of mischief.

From this view of the subject, there is a curious fact about cartilaginous tumours. As every one knows, the majority of these are innocent, and yet, as is well known, too, a cartilaginous tumour occasionally behaves like a malignant one, and new growths of the same structure spring up in distant and various parts; nor do I know that these malignant tumours present any visible peculiarity of structure whereby they may be distinguished from the innocent ones. To be sure, these more mischievous tumours usually grow unconnected with bone; in strange parts, as the testicle; but then, again, cartilage sometimes enters in abundance into the composition of tumours which do not recur, as, for example, into gland-tissue over the parotid. But then let us remember that, curiously enough, there are different forms of normal cartilage; not only various kinds that differ in their structure, but also forms which differ in their life; notably in their tendency to pass into bone, as temporary and permanent cartilage. Nor is there, let it be observed, in point of structure alone, any means of distinction between the two. Now, is there anything analogous to this in

cartilaginous tumours? Are those which are innocent of the nature of cartilage which tends to reach the final term of its development, while others, lacking power in this direction, tend to increase and multiply? This question, indeed, in the case of all tumours, needs consideration. Granted the presence of immature forms—which of course must exist in every growing tumour—what is their prevailing tendency? Are they, or are they not, in process of development? But, with regard to this exceptional character of cartilaginous tumours, there are other significant facts. Thus, in structure, combination, and mode of development, they strikingly resemble foetal cartilage; they often grow very rapidly, and attain an enormous size; they are often multiple, sometimes hereditary; in their structure, they are apt to exhibit a strange and almost endless diversity of elementary forms; they are often mingled with other tumours, and sometimes with cancer; in certain instances at least, their dissemination has been associated with the extensive growth of the original tumour in the interior of lymphatics or blood-vessels.

It is interesting to note, with regard to this relation between the structure and character of tumours, if it exist, that, with the development of more perfect tissue, there is usually more definite form. Circumscribed and uniform tumours are more likely to be composed of adult tissue; infiltrations, of embryonic or rudimentary elements. Nor are the real exceptions to this so numerous as the apparent ones; for oftentimes, as every one knows, when a malignant tumour appears to the naked eye to be circumscribed, or even encapsuled, a more minute examination will detect its extension in all directions into the tissues around.

Attempts have been made to explain the character and clinical history of a tumour by its construction; to account, on the one hand, for the limitation of its growth to a single part by the mode in, or the degree to, which its elements are bound together; and, on the other, for its dissemination by the slight bond of connection existing between them. But I submit that a low grade of development is far more important in relation to transference and dissemination, or malignancy, than the mere want of coherence among the elements of a tumour. A glandular tumour, like the chronic mammary, is innocent, not because of its construction, but because its cells are comparatively incapable of separate and independent life. When detached, they speedily perish. A cancer is malignant, not because its cells lie loosely in alveoli, but because they consist of indifferent substance. These cells being less highly developed, less specialised, have a more enduring power of individual life; they are more independent of their environments.

And herein, I think, is a clue also to the difference between local recurrence only and malignancy. The simple elements of a recurrent tumour may grow actively, spread widely, and be reproduced easily, but they are not so capable of sustaining an independent and isolated life as are the elements—being of a yet lower grade—of cancer.

The character of a tumour, then, is determined by the nature rather than by the mobility of its elements or its position. I do not deny the influence of these and other conditions such as vascularity, warmth, moisture, and movement; but I think it is a subordinate one.

It will be said, even by those who will allow that there is some truth in this view, that, after all, the best way to forecast the future of a case in which a tumour has been removed is to determine, by its examination, the class to which it belongs, and then to found our prognosis upon what is known of the clinical history of that class. No doubt in this way much useful knowledge is attained. This, indeed, is the great, nay, has hitherto been the sole way; and indeed, within certain limits, it would do all that is desired, if only the different classes of tumours were distinct, and if the structure and clinical history of each class were clear and defined. When these conditions are even moderately fulfilled, we become tolerably well informed. Take, for example, a case of scirrhus carcinoma of the breast. When we have determined its nature with the assurance which may be derived from the means at present at our command, how far and very clearly we can look into the future. But even here after all how much is left uncertain. How widely the clinical history of scirrhus varies. Even in this one kind may be traced all degrees of malignancy. And, when we pass to other classes of tumours about which our knowledge is still less clear and defined, what admission must be made here? At least this: that no line of demarcation can be drawn between innocent and malignant growths.

And then, lastly, even from a pathological point of view, how vague and untrustworthy are the distinctions in structure between different tumours, as, for example, between a "round" or "oval-celled" sarcoma and a lymphoma. Looking back now for some years over the admirable work which has been done in this subject, I confess I am not sanguine of the stability of our present classification. Even apart from the chief fact, that it does not naturally come into harmony with

cinical work, when tried solely on its own ground, that of histology, the data from which distinctions are drawn appear to be too trifling or insecure. Malignant sarcomata, for example, are classed with comparatively innocent growths, and separated from carcinoma, on the ground that, while both are composed of cells, the cells of carcinoma are of an epithelial type, while those of sarcoma spring from connective tissue. I do not say that this is the sole ground of distinction. There is the very subordinate difference, probably dependent on this, of arrangement of those elements. But this, I take it, is the radical distinction; yet of what after all consists the line of demarcation between connective tissue and epithelium? Is it strong enough—that is, physiologically distinct enough—to be the durable basis of such a classification?

But, at all events, if hereafter a more stable basis for the arrangement of tumours shall be devised than any which is founded upon the character of their elements, in the meanwhile I would suggest that, in structures of a doubtful kind, in tumours of no definite description, in growths of a mixed nature, and as an aid to, or in criticism of, conclusions drawn from current views, more attention than heretofore might with advantage be given to a study of the relation of a low grade of development to dissemination and recurrence.

In summary then:—The tissues which are simplest in structure and mode of development are most apt to form the substance of tumours, as, for example, connective tissue. The most elaborate tissue in these respects—striated muscle—is very rarely, if ever, found as a distinct morbid growth, and it is comparatively rare to find even unstriated muscle as a separate mass in the substance of tumours. In the elementary structures of tumours, there is an inverse ratio between the tendency to progressive metamorphosis and the tendency to reproduction. The less the structures of which a tumour is composed tend to change from their primary or embryonic form, the more abundantly will they multiply; so that those tumours whose structures retain most nearly their primary form are the most malignant. And, as the structures of a tumour are capable of transformation, so do they lose their power of repetition; so that those tumours which consist most completely of fully formed tissue are the most innocent.

LABORATORY NOTE: ON THE TENSILE STRENGTH OF THE FRESH ADULT FŒTUS.*

By J. MATTHEWS DUNCAN, M.D.,
President of the Obstetrical Society, Edinburgh.

THERE are almost innumerable laboratory experiments demanded in the present state of obstetrical science; for, while many important points in the mechanism of natural and of unnatural delivery may be admirably illustrated or explained by them, others can in no other way be made out or settled. To give a list of those which at once occur to the mind would be tedious and, to me at least, very tantalising, for I have been able to make very few; and this deficiency arises, in great part, from the want of material. Yet those acquainted with the recent progress of obstetrics can easily recall to mind some of the most valuable of our recent steps in advance, which have been attained through following that experimental method, the dawn of whose usefulness is as yet scarcely recognised by obstetricians.

The experiments which I am now about to describe were made with a view to arrive at correct ideas as to the force available in delivering a child footling; for example, in the operation of podalic extraction now extensively recommended in the conduct of certain cases of contracted pelvis. I knew that even among our best recent authors there has prevailed gross error on this point, the available force being absurdly overrated and the force that could be exerted in the alternative forceps operation almost as absurdly underrated. It would be easy, but it is unnecessary, to cite strong asseverations to this erroneous effect from the most recent authors, widely reputed as our best. Now the point is not of second, but of first-rate importance in the question; indeed, a fundamental matter. It is, therefore, well worthy of careful discussion, and fortunately it is easily settled in a quite conclusive manner.

I took a fresh newly-born child, and, after passing its body through an aperture so cut in hard wood as to represent the brim of a contracted pelvis, or after fixing its head below the biparietal diameter between two parallel bars, I applied above an ankle an apparatus consisting essentially of a hook, whereby to suspend the weights, which were to

be gradually increased till they produced disseverment of the body of the child.

As is well known, the disseverment in actual practice takes place, as it did in all my experiments, in the neck. The disseverment was, therefore, always decapitation.

The force effecting decapitation is in these experiments equal to the combined weight of the child beneath the line of disseverment, of the apparatus attached above the ankle, and of the special weights applied. But great nicety was not attempted, the increments of weight attached being made by several pounds at a time.

It was desirable to limit the time during which in each trial the weight was allowed to operate, and the term of a half-minute was adopted, the weight not being allowed to act longer than that time in one trial. A limit of this kind was necessary to bring the experiments into conditions somewhat analogous to the pains or force of labour and the efforts of the accoucheur in a difficult case in actual practice.

The decapitating force thus discovered is the measure of the tensile strength of the fœtus; and, of course, in podalic extraction, whether by the feet or by the Prague seizure, no greater force effective in delivering the head can possibly be applied, for the materials give way when the weight reaches the decapitating amount.

In actual practice, a greater dragging force may be exerted by the accoucheur and applied to the child. But such force, so far as it exceeds the decapitating amount, does not directly help the delivery of the head. It is either usefully spent in overcoming friction of some part below the line of disseverment, or uselessly or even banefully spent, because misdirected. In actual practice, however, when the head is fixed on the brim, the decapitating force must be very nearly an exact highest limit of the force that can be exerted by the accoucheur.

These remarks are made without regard to the life of the child, and with a view merely to the strength of the materials. The experiments to be narrated will show that the life of the child is compromised before the limit of the tensile strength of the fœtus is reached. This is easily explained by the destruction of the spinal column, which occurs under a force considerably less than the decapitating force; and this circumstance must be kept in mind when podalic extraction is compared with forceps-extraction; for, in making the comparison, it is supposed that the life of the child is not compromised. Neither operation would be selected as the best, if the securing a living child were hopeless.

Experiment 1. A fresh adult female fœtus, weighing 5 lbs. 6 oz., and measuring eighteen inches in length. The spinal column gave way under 90 lbs. Decapitation took place under a weight of 118 lbs. The disseverment occurred between the fifth and sixth cervical vertebra.

Experiment 2. A fresh adult female fœtus, weighing 7 lbs. 7 oz., and measuring twenty inches in length. The spinal column gave way under a weight of 120 lbs. Decapitation took place under 141 lbs. The disseverment occurred between the sixth and seventh cervical vertebra.

Experiment 3. A fresh adult female fœtus, weighing 8 lbs. 15 oz., and measuring twenty-three inches in length. The spinal column gave way under a weight of 122 lbs. Decapitation took place under 136 lbs. The disseverment was between the fourth and fifth cervical vertebra.

Experiment 4. A fresh adult male fœtus, weighing 5 lbs. 12 oz., and measuring twenty-one inches in length. The spinal column gave way under a weight of 91 lbs. Decapitation occurred under a weight of the same amount. The disseverment was between the fourth and fifth cervical vertebra.

Experiment 5. This experiment is not to be included with the former, as it was performed not on a newly-born child, but on one a fortnight old. It was fresh, and weighed 7 lbs. 5 oz., and measured twenty-two inches in length. The spinal column gave way under a weight of 147 lbs. Decapitation took place under a weight of 163 lbs. The disseverment was between the third and fourth cervical vertebra.

The dissevering or decapitating force in these experiments was 118, 141, 136, and 91 lbs. respectively, or, on an average, about 120 lbs. This is probably far from being what most obstetricians would regard as a great force; and it may be said with truth that, if we are to avoid premature decapitation, the force used should not reach this amount; should not, indeed, exceed a hundredweight. Such a force, if used only for a short time, if it cause no great contusion, and especially if it do not break the continuity of the mucous surface, may be safely used in repeated efforts in delivering. On this point, there is much inexactness from our ignorance as to how much and how long the soft parts will endure compression without great resulting evil to the mother.

This podalic dragging force of a hundredweight is considerably greater than any ever known to be exerted in propulsive efforts in natural parturition, and so also is the force of 100 lbs., which is about the limit of what is available without destroying the life of the child. Estimates of the force of labour-pains have, as is well known, been published, which make it much above a hundredweight; but such esti-

* Read before the Obstetric Medicine Section at the Annual Meeting of the British Medical Association in Norwich, August 1874.