On the definition of tubercle / by James Ross, M.D.

With the author's compliments

ON THE DEFINITION OF TUBERCLE.

By JAMES ROSS, M.D., Waterfoot, near Manchester.

The following attempt to define tubercle was made for my own personal satisfaction after reading the memorable debate at the Pathological Society, "On the Anatomical Relations of Pulmonary Phthisis to Tubercle of the Lung." No one will deny that the addresses delivered upon that occasion were characterised by great ability, but after a careful perusal of them, there was left in my mind a sense of vagueness almost amounting to confusion. I should have thought that the fault lay entirely with myself, had I not found that most medical men with whom I came in contact at the time gave expression to the same sense of bewilderment amongst the mass of details, and the apparent contradictions between the different views entertained. A careful study of that debate convinced me that the differences of opinion arose, not so much respecting the facts,—not even entirely regarding the interpretation of facts,—but in great measure from want of a mutual recognition of the exact meaning of the terms employed. I am not so presumptuous as to think that the following definition will be generally accepted, nor is it advanced as containing new views regarding the nature of tubercle; but a careful attempt to define the term, however unimportant it may be in itself, will be attended with considerable advantage, and may help to evoke more order in our mode of conceiving the subject. Even on the supposition that the definition is objected to in its entirety—in this instance a large portion of it is borrowed from such good sources that this is not likely to happen—I should still be entitled to ask my opponent upon what principle the objection is made; and if he succeed in enunciating an intelligible principle for our guidance in framing

the definitions of pathological morphology, it will be a clear gain to the science. If, on the other hand, some of the elements of the definition only are objected to, these may be modified, or omitted and replaced by others, so as to bring the definition finally into conformity with the highest knowledge we possess of tubercle, and a definition, however perfect it may be, can never be in advance of our knowledge of its subject-matter.

What, then, is tubercle? Is it a growth? Even upon this simple point there is by no means unanimity of opinion. But the difference of opinion in this instance manifestly arises from want of agreement regarding the definition of the term "growth" as employed in pathology. Some appear to think that in pathology *growth* is only applicable to cancer, sarcoma and to tumours generally; and, if this be the accepted meaning of the term, to call tubercle a *growth* is to affirm that it has greater affinities with tumours than with inflammatory products. It is very apparent, however, that those who maintain that tubercle is a *growth* give to the latter term a much more extensive meaning; but, since I do not know the exact sense in which it is used by others, I must proceed to define it for myself.

Anything is said to grow when it increases in size, and whatever grows by the addition of new material may etymologically be called a growth. In this sense, therefore, there is a pathological growth whenever a diseased part or a diseased product increases in size by the accumulation of new material. This definition, however, is not sufficiently precise. Passing over the term abnormal and its correlative normal as sufficiently definite for our purpose, the definition does not exclude inorganic concretions within the body, and great confusion would arise were these admitted into the list of pathological growths. Inorganic concretions may, however, be excluded by saying that a pathological growth is an abnormal increase of the size of a part of the body through the accumulation of *organic* material. But in tubercle, though there is an accumulation of organic material at certain localities, there is often little or no increase of bulk. If, therefore, tubercle is to be called a growth we must leave the increase of bulk out of the definition, and consider any abnormal accumulation of organic

material in a certain locality a growth whether it be or be not accompanied by augmentation of bulk. This amendment rescues us from one difficulty only to land us in others. When the stomach is overloaded by food there is an abnormal accumulation of organic materials, but no one would be inclined to call this a growth. In hæmorrhagic effusions such as pulmonary apoplexy there is an accumulation of organic material at a certain locality, but this also is not a growth in the general acceptation of the term. But if we say that a pathological growth is an abnormal *assimilative* accumulation of organic materials at a certain locality of the body this difficulty will be met; since neither excess of food in the stomach, nor hæmorrhages, are the result of a process of assimilation, while, on the other hand, there is a distinct process of assimilation in the formation of tumours, tubercles and all inflammatory products. But should not the meaning of the term be restricted still further?

There is a very general undercurrent of belief that a new growth should have a certain degree of individuality and coherence. If these elements are added to the definition most inflammatory products will be excluded. The disadvantages of this proceeding are, not only that tubercle will be included and pus excluded from the definition, and thus separated from their natural connections, but that what are called chronic inflammatory exudations and pus will also be separated from each other. I see no alternative, therefore, but to leave individuality and coherence out of the definition. A *growth*, therefore, according to this definition, will include tissues having incoherent units like pus as well as those having coherent units like cancer, and pus will come within the range of this definition when it is formed even on a free surface, since not only is the tissue from which it is formed tumefied, but, however little pus may adhere to the surface, it is still an assimilative accumulation of organic materials. And if pus is included in the definition, there is no reason to exclude the tumefactions of erysipelas, the pustules of small-pox, and even the minute red points of scarlet fever. I shall define a pathological growth, therefore, as an abnormal assimilative accumulation of organic material in a certain locality of the body, and it is only in this enlarged

sense of the term that I could consent to call tubercle a *morbid growth*. Our problem now is to differentiate tubercle from other kinds of growths.

The growths which come under the usual denotation of tubercle have loosely adherent units, so that if they formed upon the surface of the body they would soon become detached. It may, therefore, be expected that a tubercle cannot form upon either the external or internal surface of the body ;—I say, as a general rule, because, although it would be impossible for a tubercle to maintain itself upon a surface of the body which is freely exposed to external incident forces, yet there are certain infoldings of the surface in which this would be quite possible. In the bronchioles for instance, which are lined by infoldings of the membrane covering the internal surface of the body, it might be possible for growths similar to tubercles to maintain themselves. And, indeed, bodies are found in the alveoli of the lungs so similar to the growths which are by common consent denominated tubercles that they can scarcely be distinguished from each other. Must the morbid bodies found in the alveoli be included in the definition of tubercle? It is generally admitted that on clinical, ætiological and anatomical grounds it is better to exclude these alveolar accumulations. It may be said that the alveolar accumulations are mere mechanical aggregations of units, and are, therefore, not growths within the range of our definition, and if not growths they cannot be tubercles. If this is true there is no occasion to make a special provision in our definition to exclude them. The distinction is, however, too refined and too hypothetical for practical purposes, and it would be unsafe to trust to it. If we say that tubercle is a growth which forms in a tissue which has descended from the serous layer of the embryo, this will exclude the alveolar accumulations, since they are of an epithelial character. But, according to the researches of Dr. Burdon Sanderson and others, the localities in which tubercle occur are characterised by the presence in health of lymphatic or adenoid tissue. If this opinion should be confirmed by future researches, it constitutes a real and important discovery, and will aid us very materially in giving a definite connotation to tubercle. I shall, in the mean-

time, accept Dr. Burdon Sanderson's views, merely remarking that, if they are not confirmed by subsequent observations, the definition must be modified accordingly. According to these views, then, tubercle is an *adenoid* growth. It is not meant by this that tubercle is a growth more or less similar to lymphatic or adenoid tissue, but that it grows in that tissue, and that, in the terminology of Virchow, it is not a *heteroplastic*, but a *hyperplastic* formation. This part of the definition, therefore, not only excludes the alveolar accumulations, but all other growths which do not occur in a locality which is characterised in health by the presence of adenoid tissue. But the most opposite kinds of growth may occur in adenoid tissue, such as pus, lymphomata, and cancer as a secondary formation. The definition must now be framed so as to exclude all these.

If tubercle is compared with cancer and other growths, such as tumours, which have high powers of self-maintenance, we find that the former is characterised by being composed of cells similar to lymph and white-blood cells, while the latter have cells which are very considerably differentiated from such elementary units. If we now say that tubercle consists of lymphoid cells, this will sufficiently distinguish it from those growths which have a distinct individuality, like cancer and from tumours generally. By *lymphoid cells* is simply meant that the units of which the growth is composed are more or less similar to lymph cells, and it involves no theory of their derivation. It is equally descriptive of tubercle whether its units are derived from proliferation of pre-existing cells, or from migration of white blood-corpuscles. It may also be added that *cells* are used here subject to the recent change in the theory of the nature of these elementary bodies, and that it is not meant that they are made up of cell-walls and contents. With this addition, the definition is, that *tubercle is an adenoid growth consisting of lymphoid cells.*

The definition, however, does not draw any distinction between tubercle and leucæmic growths and lymphomata. The most obvious differences between tubercle and these growths are that, in the former, the cells are more aggregated than in the latter; and that in tubercle the circulation is obstructed, while the other

growths are vascular. Which of these characteristics shall we select as a means of differentiation? Or is it necessary to include both differences in the definition of tubercle? If we say that tubercle is an adenoid growth consisting of closely-aggregated lymphoid cells this will undoubtedly serve, to a certain extent, as a distinguishing mark between tubercle, on the one hand, and leucæmic growths and lymphomata, on the other. It may, however, be asked how close must the aggregation be to constitute tubercle, and a difference in degree is too indeterminate to serve as a good characteristic in a definition, unless, indeed, we can give it a quantitative expression, which is impossible in this case. If we now turn to the other distinction, and say that tubercle is a non-vascular adenoid growth, this of itself will be amply sufficient to distinguish it from the other growths, and it will be perfectly superfluous to add that the cells of which it is composed are closely aggregated, since this is implied in its other characteristics. The only objection is that in its very early stage tubercle may not be absolutely non-vascular, but the vessels become obliterated so soon that non-vascularity is as good a characteristic as it is possible to obtain in order to distinguish between growths which in their early stages merge almost insensibly into one another. Our definition now is, that *tubercle is a non-vascular adenoid growth consisting of lymphoid cells.*

This definition is still very imperfect since it does not distinguish between tubercle and a circumscribed abscess occurring in adenoid tissue. What now is the most distinguishing characteristic between tubercle and pus? When pus occurs upon either the internal or external surface of the body it cannot be confounded with tubercle. The former can only be mistaken for the latter when it occurs in a locality characterised during health by the presence of adenoid tissue. But when pus does occur in such a locality both it and tubercle are non-vascular, both consist of lymphoid, and even of closely aggregated lymphoid cells, and it is possible for both to be similar to one another in outward form. How can they be distinguished in such circumstances? The most obvious distinction is that the cells of pus are moveable upon one another, while those of tubercle cannot be so moved

without destruction of the growth; the cells of the former are incoherent, and those of the latter coherent. Tubercle, therefore, as we now regard it, *is a non-vascular adenoid growth consisting of coherent lymphoid cells.*

There is one other characteristic which should not be left out of the definition of tubercle. One of the prominent features of the growth is that it is disseminated through the body. Whether the disease spreads through infection, or through the mechanical irritation caused by the absorption of small particles of decaying matter during the softening of the growth, is not yet determined. And although my own opinion is that the disease spreads, like pyæmia, by an infective process, it is necessary to avoid the inclusion of a theory of infection in our definition. The essential facts will be included if we say that the growth tends to become multiple, or, in short, that it is *generally multiple.* I say *generally* because it is possible for a growth to be tubercle, even when it is not multiple. The disease must have a starting point, and the first growth may be tubercle even before there is a second, although this is by no means always the case. The definition as thus amended is, that *tubercle is a non-vascular, generally multiple, adenoid growth, consisting of coherent lymphoid cells.*

But, although this definition serves to mark off tubercle more or less clearly from other growths, it is essentially defective. It fails to convey an adequate conception of all the growths which are usually called tubercular. This definition is descriptive of grey tubercle, and is only very partially applicable to the other forms of the growth. We must now endeavour to amend our formula so as to embrace, as far as possible, all the forms of tubercle. If we take a wide glance at the series of morphological changes undergone by organisms during the entire time of their individual existence, we shall find that they may be divided into three principal stages. The first is the stage of simple growth, which is usually accompanied by a process of differentiation; in the second stage, which represents the mature condition of the organism, the increase in size either ceases entirely or becomes very inconspicuous, while the changes which take place are repre-

sented mainly by processes of differentiation. The most marked feature of the last stage is a degenerative process, which is sometimes, but not always, accompanied by a decrease of size. These three stages—the *Aufbildung*, *Umbildung* and *Rückbildung* of Haeckel—may be traced not only in the life-history of physiological individuals (with very rare exceptions), but they may be equally noticed in that of the groups of individuals which constitute races, kinds, and species, and in the parts of individuals which constitute organs and tissues, and even frequently in the life-history of the individual cells of which the tissues are composed; and these three stages can be more or less distinctly traced in the transformations of tubercle. The most marked feature of the first stage of tubercle is the rapid multiplication of cells which take place—a multiplication so rapid that the capillaries of the part are pressed upon and obliterated. The stage of growth is, then, very distinctly marked. The stage of differentiation is, however, very inconspicuous; and this is only what might be expected, considering the rapidity of the growth. Other things being equal, there is an inverse ratio between growth and differentiation. When an organism is highly differentiated the growth is slow, and *vice versâ*. There is no organism so highly differentiated as man, yet there is no organism which grows so slowly. But, although the stage of differentiation in tubercle is not well marked, yet there are slight indications that it is not entirely absent. The formation of the reticulum, in which the cellular elements of the growth become embedded, is, to some small extent, a process of differentiation. Even the absorption of the fluid of the growth which occurs at this stage is some evidence of a similar process, although there is some reason to believe that such absorption attends the incipient stage of degeneration. Processes of differentiation are, upon the whole, accompanied by consolidation of tissue, a rule which is well exemplified by the fact that the chrysalis during its transformation loses weight and bulk. The consolidation of the tubercle which occurs at this stage may, therefore, be taken as an indication of a process of differentiation. The change which tubercle undergoes at this stage has been called the fibroid degeneration; but, although I do

not deny that degenerative changes do take place at this stage I shall simply call it the fibroid change, a term which involves no theory of the process. But if the stage of differentiation is hardly discernible in the life-history of tubercle, the stage of degeneration is probably the most conspicuous and important of all. The fatty degeneration of tubercle, with its subsequent softening and ulceration, are so well known that I need not describe them here. I shall only remark that, other things being equal, the time occupied by the stage of degeneration bears a direct ratio to the time occupied by the stage of growth. The more rapid the growth the less conspicuous will be the stage of differentiation, and the more rapid will be the stage of degeneration. The longer the stage of growth the more marked will be the stage of differentiation, and the slower will the degenerative changes be in leading to the destruction of the growth. It is, therefore, apparent that the rate of progress of the primary stage of growth may lead to an almost endless diversity in the morphological appearances of tubercle.

These remarks show that the changes which tubercle undergoes are strictly analogous to the changes which take place in the life-history of organic individuals, of parts of individuals, and of groups of individuals; and this brings the morphological changes which occur in the life-history of tubercle within the scope of a very wide generalization. We might, therefore, content ourselves with summing up the results obtained in the briefest possible language, and adding them to our definition. But before we can give complete unity to our representation, we must not only know that changes do occur in tubercle in a certain order, but we must also know *why* they occur in this order, and *why* strictly analogous changes fail to be recognisable in allied growths. Before these questions can be satisfactorily answered we must regard tubercle not, as hitherto, in its statical, but in its dynamical relations,—not its morphology, but its physiology,—employing the latter term in its ~~the~~ widest acceptation ~~of the term~~. From the bare contemplation of the *product*, we must now pass to the consideration of the *process* which underlies its formation.

When a living tissue is irritated its cells begin to proliferate,

and it is now proved, that, under these circumstances, there is not only a multiplication of existing units, but also a migration of other units to the locality. Starting from these facts, without waiting to ask if an explanation of them is possible, we may notice the similarity of this process to what takes place in a certain district of a social organism under the stimulus of a sudden prospective increase of production. Not only do the individuals who already live in the district marry earlier and multiply more rapidly, but immigration takes place from other parts of the social organism. But whenever the units of a locality, whether of the individual or of the social organism, increase in number, no matter from what cause, it is evident that the required nutriment and the mode in which it is distributed and expended must undergo corresponding changes. If the regulative and distributive agencies undergo adaptive modifications corresponding to the increase in the number of the units which expend the nutriment, then the locality may become organised as an integral part of the whole. But if the structure of the part fails without being replaced by new structure, the molecular motion expended by the units cannot be balanced by an equivalent amount from absorbed nutriment, and consequently the units must either migrate or starve. The units may be said to *migrate* either when they disperse through the organism or when they become detached while living, no matter what may be their subsequent history; and they *starve* when the forces expended are not replaced by equivalent forces from absorbed nutriment, and it is needless to add that the latter condition when prolonged must be accompanied by a high rate of mortality. These remarks are as applicable to the units of which an individual is composed, as they are to the individuals which compose a social organism. Let us now confine our remarks to the *cell* or unit of which the individual organism is composed.

When a tissue is subjected to great irritation the subsequent multiplication of units is so great that the original structure of the part disappears, and the organised tissue is replaced by pus, a tissue which consists of freely moving units and destitute of structure. The implication is that the part has absorbed a large part of molecular motion, all of which is devoted to multiplication,

and none to that orderly arrangement of units into a coherent whole which constitutes organisation. What is the subsequent history of this tissue? When the pus forms upon a free surface its units become detached almost as soon as formed, and with this emigration from the parent organism ceases their interest for our present purpose. Again, when pus forms within the body it generally makes its way to the surface ~~of the body~~ by an extension of the process which first produced it, and by its units as it were feeding upon their more orderly neighbours. But no matter how the units make their way to the surface, they may be said, when the abscess bursts, to emigrate in a body, and their subsequent history does not concern us at present. But either some or all of these units may disperse through the organism. Passing over the condition of the surrounding textures which facilitates this dispersion, I shall briefly notice the kind of pus whose units become easily distributed. Along with the disintegrating process involved in the formation of pus there goes a corresponding absorption of molecular motion. When the irritation is excessive the disintegrating process will be rapid, and there will also be a correlative absorption of molecular motion. Under such circumstances a tissue forms which is fluid, with very incoherent units, showing a large amount of mobility; one in which the multiplication of units is rapid, and consequently their bulk diminished. It is scarcely necessary to add that this fluid tissue with small rapidly multiplying units may easily become dispersed throughout the organism. The laws of distribution of such tissues and the effects they produce upon the organism may be passed over at present. Their subsequent history belongs to pyæmia and septicæmia. It is obvious, however, that, when the units become detached or dispersed throughout the organism, the morphological stages of differentiation and degeneration cannot become developed in the locality primarily affected.

But the units of pus and allied tissues do not at all times either separate or dissipate. What becomes of them in that case? When pus forms in the tissues the growth is so rapid that the regulative and distributive nutrient agencies, the nerves and blood-vessels, disappear; and consequently if the units are not sufficiently

active to migrate, or to feed themselves by breaking down surrounding structure and thus making their way to the surface, their subsequent history may be summed up in one word—starvation. When pus forms within the body the proper tissues of the part become pushed aside; and as the units of the pus increase in number they become further removed from the nutrient juices, so that by-and-by whatever amount of molecular motion is expended by them is not replaced by the absorption of a corresponding amount from the surrounding medium. What, then, must be the morphological change which corresponds to this necessary molecular change? The first loss of molecular motion declares itself by the drying of the pus, which is accompanied by an approximation and shrinking of its units. This external change is in all probability accompanied, and in great measure caused, by a deeper chemical change. The proteinaceous substance which forms the protoplasm of the pus-corpuscle falls into a lower isomeric state,—a portion of water is thus set chemically free which is absorbed by the surrounding tissues. When the morphological changes in the life-history of tubercle was under consideration it was noticed that the consolidation of tissue which occurs was some evidence of a process of differentiation, but the drying of the pus can scarcely be regarded in this light. Everything points to the conclusion that the stage of growth gives place to that of degeneration without the intervention of a stage of differentiation. Subsequent to the drying of the pus loss of molecular motion declares itself by fatty degeneration. Without entering into the details of the chemical changes which accompany this transformation, the great point for us to notice is that the high molecular complexity of the proteine of the protoplasm is in great measure replaced by the lower molecular complexity of a hydrocarbon. If fatty degeneration proceeds rapidly before the pus has lost a large part of its fluid, the living units completely break up, and the product is converted into an oleo-albuminous fluid which Virchow calls "pathological milk," which is subsequently absorbed. If, on the other hand, the fatty transformation proceeds more slowly, while the pus has previously parted with a large part of its water, the units may retain more or less of their form, and this gives rise to what is called *caseous* pus.

If we carry these conceptions with us to the consideration of tubercle, we will not require to say much with regard to the mechanism of its transformations. We have just seen that in a circumscribed abscess the stage of the growth of the pus is succeeded directly by that of degeneration, while we have previously seen that in tubercle there is interposed between these a stage which, even if accompanied by some degenerative changes, is yet one mainly of differentiation. Why should a stage of differentiation appear in the life-history of tubercle, and not in that of pus, even when it forms in adenoid tissue? This depends upon the rapidity of the growth of the one, and the comparative slowness of the growth of the other. All the nutriment absorbed by the pus-corpuscles is devoted to their multiplication, hence the tissue breaks up into independent units; and the fact that the units of tubercle remain coherent shows that of the available nutriment a small margin is left which is not devoted to multiplication. And when the multiplication of the units of tubercle is checked by the pressure of the surrounding tissues and by the obliteration of the capillaries, the balance of nutriment which was not devoted to genesis is left to produce a slight process of differentiation. That the presence of the stage of differentiation depends upon the comparative slowness of the growth is further confirmed when we notice that this stage is the more conspicuous according as the growth of the tubercle is slow. So much is this the case that in the very slow growing tubercles the fibroid change which takes place is the most marked feature of their history. And even if we do not choose to extend the term tubercle to any growth in which the stage of fatty degeneration is absent, yet there are closely allied growths having a slow rate of progress in which the stage of degeneration either entirely fails or is not readily discernible. If the object of this paper were to discuss tubercle in all its relations, it would now be necessary to consider the various terminations of the growth; but, since the object is to arrive at a good definition, it is quite unnecessary to carry the discussion further. That tubercle ends in excavation, cretification or obsolescence, is a most important part of its clinical history; but the terminations of a growth have no right to be

included in its definition. A cavity, for instance, is neither tubercle nor an attribute of tubercle, and, therefore, has no legitimate claim to a place in its definition, and the same may be said with regard to the other terminations.

A consideration of the statics of tubercle has led us to the conclusion that the morphological changes of tubercle present three stages —one of growth, one of differentiation, and one of degeneration; and a consideration of its dynamics has confirmed and in great part explained this conclusion. The question we have now to determine is how best to include the transformations of tubercle in our previous formula. The formula was—that tubercle is *a non-vascular, generally multiple, adenoid growth, consisting of coherent lymphoid cells.* We have now to notice that this is only descriptive of tubercle in its first stage, and that it subsequently undergoes transformations, the first of which we may call the *fibroid change,* and, lastly, a fatty degeneration, which is generally called *caseation.* The definition, as amended by the addition of these elements, is—that *tubercle is a non-vascular, generally multiple, adenoid growth, consisting in its first stage of coherent lymphoid cells, and subsequently undergoing a fibroid change and caseation.*

In conclusion, I shall endeavour to remove one or two objections which may be advanced against this definition. Some may think that we ought to state in it that the growth is morbid; but a definition of a morbid tissue, in order to be adequate, ought to distinguish it from healthy as well as from other diseased tissues, and if our definition is not already adequate for this purpose it will not help us much to state that the growth is morbid. Imagine any one defining tubercle, with a view to distinguish it from cancer, by saying that it was a non-cancerous growth; and this is only a similar proceeding to that adopted by those who would distinguish between tubercle and healthy tissues by saying that the former is morbid, or, in other words, is not healthy. But the principal objection to this and to other definitions of tubercle is that it does not enable us to distinguish at all times between it and allied growths. But those who urge this objection seem to forget the nature of the facts with which we have to deal.

Objective differences never exactly correspond to subjective distinctions, and this is particularly the case in the present instance, since tubercle is surrounded on all sides by growths with which it is connected by transitional forms. Between tubercle on the one hand and scrofulous and leucocythæmic growths, lymphoma, pus, connective-tissue proliferations, epithelial accumulations in the alveoli, and fibroid on the other, there not only are, but there must be, intermediate forms in which it is impossible to determine whether a particular growth comes within the range of our definition or not. This difficulty, therefore, arises from the nature of the facts with which we have to deal, and no definition, however perfect, can ever entirely meet it. Similar difficulties of definition and classification are met with in all departments of biology. Botanists, for instance, meet with transitional forms which it is impossible to identify as belonging to a particular species, and if this be the case amongst organisms where the principle of natural selection has, to a large extent, produced extinction of the intermediate forms, how much more must it be the case amongst growths where no principle of the kind is in action.