

The coexistence of tubercle and cancer / by D. Rutherford Haldane.

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THE
COEXISTENCE
OF
TUBERCLE AND CANCER.

BY
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COEXISTENCE OF TUBERCLE AND CANCER.

WHETHER or not cancer and tubercle can coexist in the same organism, is a question which has been frequently discussed, but which can scarcely be said to have been satisfactorily solved. Some pathologists, perhaps the majority, have maintained that the two diseases are mutually exclusive, that they depend upon different or opposite constitutional conditions, and that the existence of one indicates the impossibility of the simultaneous presence of the other. Others, again, have not considered cancer and tubercle as of so decidedly specific a character; and, while allowing that the two are seldom associated, are quite prepared to meet with cases where they shall be found to coexist. It is not my object to endeavour to solve this question in an absolute manner; but a case which lately came under my notice has led me to bring together a few general remarks on the subject.

In speaking of the possibility of the coexistence of tubercle and cancer, it must of course be premised that the only cases to be referred to are those in which both diseases are in an active condition, for that one may succeed the other is perfectly well known, and universally acknowledged. The order of succession is not, however, indifferent, for, in the great majority of cases, tubercle is the original, cancer the secondary disease. This mode of sequence probably depends upon the circumstance that tubercle is generally a disease of early, cancer of mature or advanced, life. In no small proportion of cases where cancer has been the cause of death, cretaceous concretions, or tubercle in a retrogressive or stationary condition, may be found in the upper part of the lungs. These cases, however, are not available in assisting us to answer the question proposed, for it is quite intelligible that the tubercular diathesis may have been recovered from, and that therefore there was no impediment to the development of the cancerous.

A priori considerations would certainly lead us to believe that the presence of the one morbid condition is incompatible with the simultaneous existence of the other. Neither tubercle nor cancer can be looked upon as a mere local condition; for even granting that either may be in the first instance generated by external causes, it cannot be denied that when the dyscrasia has been once

established, the manifestations in the two conditions are of a different character. Our views on this subject, however, must be regulated by the opinions we entertain as to the mode of origin of new growths,—a question which lies at the very foundation of pathology.

The doctrine which, till lately, was universally accepted was this : owing to certain causes, known or unknown, an exudation from the bloodvessels takes place ; in healthy persons, the matter poured out assumes more or less of the characters of the tissue in which it is effused, becomes converted into connective tissue, or degenerates into pus ; while, if the system be under the influence of the tubercular or cancerous cachexia, the effused material is converted, under the influence of the constitutional condition, into tubercle or cancer, as the case may be. Granting this view to be correct, it seems impossible that cancer and tubercle could coexist, for we cannot well imagine that the system could be under the influence of two such different dyscrasiæ at the same time. Arguments, however, are not wanting to show that such a mode of viewing the subject is erroneous. Did new formations take place in the manner alluded to, every exudation in a tubercular individual would necessarily be tubercular ; but everyday experience testifies to the contrary. Pleurisy, in a patient suffering from phthisis, is not necessarily or even generally tubercular ; connective tissue is organized, and adhesions are formed in precisely the same manner as in an individual in whom there is no constitutional taint. It is indeed said, that as the blood is continually undergoing changes, an exudation at one time may be very different from what it was at another ; and that even when the constitution is thoroughly cancerous or tubercular, simple exudations may be poured into tissues as the result of recent wounds or injuries.¹ This, however, would not explain another circumstance which is frequently met with. In cases of tubercular pleurisy, pericarditis, or peritonitis, the organized exudation will generally be found to consist of two parts, one portion being manifestly composed of tubercle, the other of ordinary, or what we may call healthy, connective tissue. Here the matter forming the new structures must, according to the exudation theory, have been poured forth from the same bloodvessels, into the same tissues, at the same time, and under the same constitutional circumstances, and it is inconceivable that if differences in the product depended exclusively upon differences in the inherent composition of the exudation, two such different materials could have been contemporaneously developed.

Another argument to the same effect is derived from what is seen in cases of constitutional syphilis. The system is here under the influence of a peculiar dyscrasia, which manifests itself by deposits or exudations of a particular kind, and by influencing in a peculiar manner certain of the vital processes. On the hypothesis we are

¹ Bennett's Principles and Practice of Medicine, 3d Edition, p. 151.

now considering, any healthy action should under these circumstances be impossible, every exudation should bear the special syphilitic stamp. This, however, we know not to be the case; wounds may heal, and fractures unite, as rapidly and as soundly in the syphilitic as in the healthy.

The other doctrine as to the genesis of new formations, has been most clearly enunciated by Virchow. Its supporters maintain that an exudation is not poured out directly from the bloodvessels, but that every new growth takes its origin from the tissues themselves. Cells can no more arise in situations where no cells previously existed, than new organisms can be produced by spontaneous generation. It can scarcely be doubted that in the physiological renovation of tissues the principle of *continuous development* holds good; and the best investigations go to prove that pathological formations obey the same law. There is now an overwhelming mass of evidence with regard to the origin of pus; and the evidence is scarcely less strong in the case of tubercle and cancer. Why the new tissue should assume a peculiar form, we do not know. We know that when all is going on normally, the process of decay is exactly balanced by the process of repair; although the elements of the tissues are constantly undergoing change, this change takes place so silently, and so continuously, that the parts appear to remain always the same. But now, let an irritant be applied to the tissue where everything was going on so smoothly. A tumultuous process is immediately set up; there is rapid destruction of tissues, but equally rapid repair; as Mr Simon has well expressed it, "*the appreciability of the opposed results* is in itself a differential mark of inflammation."¹ The results even in the most healthy inflammations are, however, far inferior to the reproduction of tissue which goes on in health. The type of inflammatory products is invariably low; the higher tissues, such as nerve or muscle, skin or cartilage, are incapable of being thus produced. Now it is perfectly conceivable that the nature of the irritant may determine the character of the future product. Of this principle we have already some undoubted examples. The bite of a poisonous snake occasions an inflammation which runs on rapidly to gangrene. The irritation of a short hot pipe is believed to lead to epithelioma of the lip; while the frequent contact of soot leads to a similar affection of the scrotum. It is probable that this principle has wider applications than we are yet aware of, and that special forms of disease are often to be explained by something special in their causation.

No doubt there is a difference in the character of the tissues themselves which explains their greater or less liability to particular forms of disease. The tissues of the soundest and healthiest individual are susceptible of inflammation, but it is questionable whether the same can be said with regard to tubercle. It is doubtful whether the ordinary causes of tubercle, such as insufficient food

¹ Holmes' System of Surgery, vol. i., p. 6.

and clothing, damp, cold, impure air, and deficiency of light, can develop the disease in a sound constitution, without the slightest hereditary taint. Virchow, indeed, believes that every dyscrasia has a local origin; in other words, that there is first a local disease, that *it* is the cause of the poisoning of the blood, and that when the poisoning has once taken place, various secondary phenomena, manifestations of the now established dyscrasia, show themselves. He denies that certain changes can persist in the blood considered as an independent fluid, but maintains that, for the keeping up of a permanently morbid condition, there must be a permanent supply of noxious material from other sources. In pyæmia, for instance, the constitution of the blood is generally altered in two ways: there is the presence in it of small masses of fibrine derived from the disintegration of thrombi, and giving rise by embolism to metastatic deposits; and there is absorption of putrid juices, causing unhealthy and gangrenous inflammation. It cannot be questioned that there is much truth in this doctrine, and it is possible that future researches may show that it is of general application; but in the present state of our knowledge this cannot be said of it, for there are various constitutional conditions for which we have hitherto been unable to discover a local origin. This is especially true with regard to tubercle, for very often, before there is the slightest manifestation of local disease, a peculiar condition is established, which physicians have designated as the pretubercular stage of phthisis. The same is probably true with regard to cancer, though to a less extent, as the disease is less strikingly hereditary, and the early stage of the diathesis is less strongly marked. But although there be an early stage of constitutional affection previous to the development of the local disease, it does not follow that the first stage is to be considered as special—that is to say, as the manifestation of a specific dyscrasia. It may, in fact, be nothing more than a condition of generally impaired nutrition and constitutional weakness (which may or may not be hereditary), which makes the individual more susceptible to the exciting causes of the particular disease.

One who holds, though even in a somewhat modified form, the views of Virchow, has much less difficulty in acknowledging the possibility of the coexistence of tubercle and cancer, than one who clings to the exudation theory. I fully believe that both tubercle and cancer are to a certain or even to a great extent constitutional, and that the constitutional conditions connected with them are of a different character; still I have no difficulty in believing that the two morbid conditions may occasionally coexist. It is, however, only by an appeal to facts that a question of this kind can be decided, for no pathological laws are as yet sufficiently established to enable us to refer to them for a solution of such problems. So far as my own experience goes, I have never met with a case where I was satisfied that cancer and tubercle coexisted in an active

form. Such cases have undoubtedly been recorded, and some unquestionably may have been instances of the kind; but I am satisfied that not unfrequently the observers were mistaken; in some the characters of the morbid products having been misunderstood, in others the tubercle having certainly been in a state of obsolescence. In illustration of the fallacies to be guarded against, I subjoin a case in which a mistake might readily enough have been committed.

Mary L., aged 40, was admitted, on account of cough and debility, into the Royal Infirmary, under the care of Dr Gairdner, on the 22d of April 1862. She stated that, though not robust, her health had been generally good, but that since the birth of her youngest child (four weeks before admission) she had suffered from cough, accompanied with febrile symptoms. She stated that she had never had hæmoptysis, and had never suffered from pain in the chest.

When admitted she was in a feverish condition, the skin was hot, the tongue dry and cracked. There was much cough, with rather scanty muco-purulent expectoration. On physical examination, there was no dulness on percussion, but the auscultatory signs of bronchitis were present, chiefly on the right side of the chest. About ten days after admission, percussion was found to be markedly dull over the right side. The following was her state on the 3d of May:—

Countenance pallid, no lividity, no flush. Voice broken and hoarse. Respirations, 36. No very marked dyspnoea; lies equally well on either side, or on the back, the latter being her usual position. When closely interrogated, could hardly be brought to admit any pain during the course of her complaint; but after leading questions, referred to the right side as the seat of a little uneasiness. Percussion quite dull over the right side of the chest from above the clavicle to the level of the nipple. Little respiratory sound in front, except above the clavicle, and there chiefly tubular. Sputum muco-purulent; mucus and pus about equally mixed; pus in flakes, not decidedly globular.

On the 2d of June her condition was the following:—

Patient has occasionally tried to get up of her own accord, but has generally been obliged to lie down again soon. Is now very feeble and pallid; there is scarcely any flush whatever; febrile symptoms much less distinct than formerly. Tongue almost perfectly natural, but retaining marks of former cracking. Has still no complaint of pain; chief cause of suffering is cough, which is fully more severe than ever. The dulness or percussion over the right front is diminished, being replaced in part by tympanitic or dull tympanitic resonance. Auscultatory signs, pretty distinctly these of progressive excavation of right front. Expectoration has been increased in quantity, and has become more and more purulent, but is still frothy, and not distinctly globular in character. Last night, for the first time, the sputa were tinged with a little blood. Has had very little diarrhoea.

She became gradually weaker, and died on the 10th of June.

The opinion entertained of the patient's case during her life was that she was suffering from acute phthisis, causing rapid breaking down of the substance of the right lung. The following were the appearances found on dissection:—

Surface of body very pale; abdomen wrinkled.

On proceeding to remove the right lung, firm pleuritic adhesions were found over the upper two-thirds of the organ; in separating these, a very superficial cavity in the anterior part of the lung was opened into. The upper and middle lobes of the right lung were found occupied by numerous communicating cavities exactly resembling such as result from the breaking down of tubercular matter. The walls of the cavities were irregular, coated with a soft yellowish matter, and in many places were crossed by fibrous cords, the remains of obliterated, or nearly obliterated, bloodvessels. In the pulmonary tissue

between the cavities were numerous small, opaque, yellow masses. The lower lobe of the lung was in a condition of solid œdema, but contained no deposit. In removing the lung, its root was found to be much thickened by a deposit which surrounded and separated the normal structures. This infiltrated matter was of a pinkish white colour, slightly translucent appearance, of softish consistence, and presented all the physical characters of cancer; on scraping it, an abundant creamy juice, readily miscible with water, exuded. The growth was found to consist of degenerated bronchial glands, which started from the bifurcation of the trachea and followed the root of the right lung; it extended for about half-an-inch into the substance of the lung, and there ceased abruptly. The normal structures forming the root of the lung were much compressed; the bronchus was converted into little more than a slit, and the pulmonary artery and veins were much diminished in calibre.

The left lung was perfectly healthy, containing no trace of abnormal deposit; the bronchial glands at the root of this lung were also natural.

The liver was healthy. The kidneys were of normal size; in each were several small rounded masses, about the size of pepper-corns, of pinkish colour and rather soft consistence. Other organs natural.

On *microscopic examination* of the creamy juice squeezed from the matter in the root of the right lung, it was found to contain an enormous number of naked nuclei, about $\frac{1}{2000}$ th to $\frac{1}{1500}$ th of an inch in diameter; there was a comparatively small number of rounded or oval cells, pale, but tolerably distinct, and each containing a nucleus similar to those floating loose; finally, there were a few compound granular corpuscles, and some granular matter. On the addition of acetic acid the cells became still paler; the nuclei, on the other hand, were rendered more distinct, but appeared somewhat diminished in size. On examining some of the soft yellow matter from the right lung, which to the naked eye bore a strong resemblance to tubercle, no distinct cells or nuclei could be seen; it appeared to consist entirely of broken down matter, mostly granular, but in some places having a tendency to obscure fibrillation, with some compound granular corpuscles. The structure of the nodules in the kidneys was found to be precisely similar to that of the degenerated bronchial glands in the root of the right lung.

It must be allowed that this case was in some respects a very deceptive one. Without speaking of the symptoms, the appearances presented on dissection were at first precisely such as are found in tubercular disorganization of the lung,—adhesions of the pleura, a large cavity broken into during removal, the walls of which were lined with a soft cheesy matter and crossed by obliterated bloodvessels, seemed to leave little doubt as to the nature of the case. But when the root of the lung came under observation, its condition was evidently due to a cancerous affection, beginning in the glands, and extending into the substance of the lung. Was this then a specimen of conjoined cancer and tubercle? I think not. The microscope showed distinctly the cancerous nature of the glandular disease, but threw no more than a negative light upon the condition of the lung. It must, however, be borne in mind that the histological characters of tubercular deposits are frequently ill-defined, particularly where considerable disintegration has taken place. Accordingly, as the absence of the so-called tubercle-corpuscles could not be considered sufficient evidence of the non-tubercular character of the deposit, its nature had to be decided upon from other considerations. And here a point of great importance was the absolute limitation of the deposit to a portion of one lung. We not uncommonly find one

lung in an advanced state of tubercular disease, while the other is comparatively unaffected, but it would, so far as I know, be unprecedented, to have *absolute* freedom from disease in one lung, while the other was in the condition observed in this instance. Under these circumstances, and as there was no trace of tubercle either in the lymphatic glands or in the intestinal mucous membrane, I had no hesitation in coming to the conclusion that the affection of the lung was non-tubercular. If not tubercular, what then was it? The idea of cancer naturally suggests itself; but this too, I think, must be negatived. In a pretty extensive experience of cancer of the lung, I have never seen it produce destruction of the character met with in this case. Cancer is generally found in the lung in the condition of nodules or of infiltrated masses; in but few cases is softening found to have taken place, and when met with, it has been rather the result of a process of sloughing than of a comparatively slow and gradual disintegration; softening of cancer when it does occur, takes place too rapidly to allow the neighbouring bloodvessels to be sealed up. The microscopic appearances were also opposed to the identity of the deposits in the root of the lung and in its substance. Had the growth in the lung been cancerous we should undoubtedly have found cells, or more probably free nuclei, to testify to what had been the original character of the lesion.

On the whole, I came to the conclusion that the disease in the lung was the result of a low form of inflammation, determining the presence of a fibrinous material which subsequently underwent disintegration. It is now generally recognised by pathologists that all cases of so-called pulmonary phthisis do not result from tubercle, but that some are occasioned by a low grade of the inflammatory process. I believe that this was the case here, and that the pressure upon the important parts in the root of the lung was the determining cause of the lesion. I have more than once seen cases where the pressure of an aneurism on the root of a lung has been connected with very similar appearances, and where the entire absence of tubercle from other organs rendered it highly improbable that the deposit was specific. The absolute character of the lesion is, however, of secondary importance, provided it be admitted that the pulmonary disease was not tubercular; if this be correct, the case narrated will have no bearing upon the question of the coexistence of tubercle and cancer, but it may serve to show how readily, under certain circumstances, an error of observation may be committed.

