

SECTION OF PATHOLOGY.

THE FRINGES OF THE CANCER PROBLEM.

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BEING connected with a hospital where for over a century there had been every opportunity for observing cancer, as it contained wards for inoperable cases, which could remain until released by death, I think it would be more interesting to those present, and it would be more congenial to myself, if, instead of embarking on the sea of speculation, I brought before them some observations which I had been able to make, and left them to do the speculating thereon. I believe that the cancer problem is best approached by tackling its fringes, rather than by a frontal attack on its central mystery. I would, therefore, speak mainly on dissemination. Until a few years ago the theory which held the field was the embolic theory, according to which cancer particles, passing along the lymphatics, got into the blood stream, and were carried all over the body, and gave rise to a crop of metastases. There was reason to believe that this theory, while containing an element of truth, was on the whole erroneous, and I have attempted to bring forward evidence in favour of what I call the permeation theory. By permeation I mean the growth of cancer along the lymphatic vessels as

a continuous line of cells, the cells growing just like tendril shoots by their own power of growth. The process of dissemination were best seen in the parietes, where they were most easily watched. The main highway of dissemination was the lymphatic plexus. My view is that the growth extends centrifugally in all directions independent of the lymph stream, growing along the fine lymphatics of the plexus. They would notice that although the cancer cells might be embolised in an early stage along the trunk lymphatics to the axillary glands, yet I believe that those cancer cells were destroyed when, after passing through other glands they reached the blood-stream. That view had received support from the work of Schmidt, who described the destruction of cancer cells in the small arteries of the lungs. Although embolism could not carry cancer cells out of the area in which they originated, permeation was capable of doing so. The fact that permeation could cross the boundaries between adjoining lymphatic areas place the whole body at the mercy of the process if time enough was given. I show a slide of a microscopic section of a permeated lymphatic taken from the deltoid region of the arm in a case of breast cancer. Turning to particular forms of growth, I may direct attention to melanotic sarcoma considered as the type of a malignant growth disseminated by the blood stream; but even in that form of growth, lymphatic permeation played a very important part. The black colour of the growth dispensed with any artificial stain in demonstrating permeation. The growth started from the chromatophores, branching connective tissue cells full of pigment. It really was a sarcoma, and not a carcinoma, as was thought a few years ago. I may mention a case of melanotic sarcoma of the heel in a woman aged thirty-five. The primary growth had been excised, and did not

return; but very soon a mass of glands developed in the inguinal region, and soon afterwards nodules made their appearance on the skin around the inguinal glands, and spread in every direction. One might consider the earliest secondary deposit in the inguinal region as a primary growth for the purpose of finding out how the dissemination occurred. I took a strip down the thigh, and froze it, and cut it into slices, and obtained the specimen from which the slides were made. The larger nodules were on the end of the strip nearest the inguinal glands. They became smaller until finally, at the other end of the strip, they could only see a network of black lines. These were permeated lymphatics. At the farthest end of the strip there was no invasion of the blood vessels, but nearer the glands they found the veins invaded, and then the arteries. That invasion took place because the lymphatics ran in company with the veins, and when the lymphatics were infected, it was only a matter of time for the veins, and later the arteries, to be invaded. To demonstrate the process of permeation, and in order to show that what I pointed out as lymphatics were really lymphatics, and not blood vessels, I show a slide with a cord of black growth accompanying the artery and vein, the latter being perfectly normal, which shows that permeation of the lymphatics preceded the invasion of the veins and arteries. After a time the growth distended and ruptured the lymphatics, and the melanotic growth infiltrated the vein. When the vein was once invaded it was very likely that the lymphatic permeation in melanotic sarcoma had done its most important work, and that the growth then disseminated by the blood stream; but sometimes the distribution of the metastases showed that lymphatic permeation was the important agent practically all through in distributing the growth.

In breast cancer the clinical evidence of dissemination in the superficial layers was the presence of subcutaneous nodules. They used to be said to be due to embolism, but there was one fact which practically disposed of that contention—that was, that they always appeared first close to the primary growth, and spread from it centrifugally. They recalled the mode of spread of a tertiary syphilide, but it was entirely unlike the chance distribution of secondary deposits by a random process of embolism. (A slide was exhibited which showed the nodules practically all included in a circle from the centre of distribution.) Particles of clot containing septic organisms distributed by embolism were apt to find a lodgment in the arteries of the limbs, and if cancer were distributed by embolism it might be expected that secondary deposits would not infrequently be found in the distal portions of the limbs. But the freedom of the limbs from secondary deposits was practically an invariable rule in breast cancer and in other forms. (A slide showed that the secondary deposits near the primary growth were older than those farther away, as indicated by their ulceration.) The same rule applied to secondary deposits in bone : they never occurred below the elbow and knee. I have only found one exception, in which the knee was ankylosed, and the growth extended by continuity from the femur to the tibia. Such evidence was, however, only *primâ facie*. The question could only be settled by sections taken in various directions radially from the primary growth. (Several such slides were then exhibited.) The deposits at the level of the nipple could be traced a long way down upon the deep fascia, much farther than they could be traced on the skin. That was a strong argument against thinking that the cancer spread in the plane of the skin, and a strong argument in favour

of removing rather less skin and considerably more deep fascia than formerly. I exhibit slides of the microscopic growing edge of carcinoma, which I do not think had been previously detected, situated in the region beyond the remotest visible nodules. It was purely microscopic, and in the region where it lay there was no interstitial invasion of the tissues by cancer cells. The microscopic growing edge of a breast cancer was situated in the deep fascia, simply because the easy highway of growth lay there. (A slide was shown demonstrating permeation which spread against, as well as with, the lymph current, and then invaded the net work of capillaries.)

There was one fact in studying permeation which baffled me for a long time. Although I could find the permeated lymphatics at a long distance from the growth, yet at points nearer to the growth I could not find any such permeated lymphatics. I think that was why the importance of permeation failed so long to be recognised. But I have been able to trace out the reason, and to demonstrate a series of changes by which a permeated lymphatic was ultimately changed into a fibrous cord containing no cancer cells. I show a slide giving a cross section in the abdominal region in a case of breast cancer, close to the growing edge, almost the remotest deposit. The lymphatic was not distended. There were no inflammatory cells around it. The small tributary lymphatic was also free from cells, and obviously the reason was because the cancer found it easier to grow along the main route rather than turn up the side stream for the time being. Another slide shows similar permeated lymphatics with a normal blood vessel between, and no infiltration. As one passed up towards the primary growth, it was found that the permeated lymphatics looked larger, because they were being distended by the continued growth of the cells.

Other slides show varying degrees of distension, until the lymphatics became so distended that the cancer cells found it difficult to nourish themselves. Coincident with the degeneration which took place, a few inflammatory round cells appeared in the neighbourhood of the permeated lymphatic. The distension could not go on indefinitely, and the mass of cells finally burst the lymphatic. Then the mass of inflammatory cells organised into fibrous tissue, and they saw a mass of degenerate cancer cells enclosed in a layer of newly organised fibrous tissue. Such tissue contracted down on the degenerate cancer cells, and finally squeezed them out of existence. (Slides were shown of varying degrees of this process which he called perilymphatic fibrosis.) It accounted for many things in connection with cancer—for the absence of permeated lymphatics from the region immediately round the primary growth, and also for the whole train of symptoms due to puckering around the original growth. It accounted for the contraction of the nipple, for the small size of the affected breast, and for the brawny arm of breast cancer which was due to the entire separation of the lymphatic system of the arm from the lymphatic system of the rest of the body. This could not be brought about merely by blocking the lymphatic trunks, for a collateral circulation would take place; but if in the whole district all the lymphatics had been turned into fibrous cords, the lymph could only return slowly by percolating the tissue spaces.

As to visceral dissemination, how did breast cancer reach the interior of the body? I think it went by one of two routes, either by infiltrating the chest wall immediately under the growth or by infiltrating the epigastric parietes at a point immediately under the ensiform cartilage. That was suggested to me first,

because there were so many cases in which after death secondary deposits were present in the abdomen and not in the chest. That was a condition of affairs which the embolic theory failed to account for. It seemed to me that possibly the solution might be the direct infiltration of the parietes, and I was able to prove that such was really the case. (Slides were demonstrated showing the various stages of this process.) The extension of permeation in the fascial plexus led to the formation of nodules upon the rectus sheath in the epigastric angle. Next the muscle itself and the fibrous tissue of the linea alba were infiltrated by the growth, which was thus carried to the subperitoneal fat and to the subperitoneal lymphatic plexus. Cancer cells then escaped into the general peritoneal cavity, and implanted themselves upon the liver, or falling into the pelvis there gave rise to secondary deposits.

With regard to stomach cancer, sometimes it invaded the parietes at the umbilicus. I show a slide from the case of a young man in whom malignant disease was diagnosed because of the presence of three tiny nodules close to the umbilicus. In another slide the centrifugal spread is manifest, the assumption being that it spread, like breast cancer, chiefly by permeation. It was difficult in stomach cancer to trace permeation, but I have been able to overcome the difficulty in some degree by employing a stain called mucicarmine, which was a specific stain for mucus. (A slide was shown which demonstrated cancer cells.)

I should have liked to go into the question of the natural cure of cancer. I think the most important point of my observations, from the practical point of view, was that they showed the presence in cancer of processes of cure going on along with the advance of the disease; and the

same tendency of cancer to spontaneous cure in a centrifugal manner could be traced in the primary growth, which, after ulcerating, was sometimes replaced by a mere scar.

PROFESSOR O'SULLIVAN moved a vote of thanks to Mr. Handley, expressing the obligation of the Section for a clear statement of views illustrated by beautiful examples. He thought the doctrine of the permeating spread of cancer was not a very recent one. It was held by Weigert, who had said that cancer went by direct extension along the lymphatic paths. What had been shown, however, as to the spread of melanotic sarcoma was entirely new to him. One of the most interesting specimens was, perhaps, the one showing the sarcoma filling the lymphatics, the artery and vein being unaffected. Mr. Handley had arrived at a very interesting conclusion relating to the way in which a cancer was disposed of in the immediate neighbourhood of the primary growth, which had almost a terrible interest both to the surgeon and also to the histologist, who had to discover if the operation had been carried sufficiently far. It suggested that it would be necessary for them, instead of examining for traces of cancer on the outskirts of the portion of tissue removed, to see whether there were traces of fibrosis of the lymphatics, which would be a much more difficult thing to be sure of. What they had been told threw a good deal of light on the question of what was sometimes called fibroid change in the wall of the stomach. Views had been put forward to the effect that a good many of those pyloric obstructions were due to inflammation, and had nothing to do with cancer. His experience had gone the other way. One often had to search a long time before finding any cancer cells at all in scirrhus cancer of the stomach. If they found such difficulty, was there any reason why they should not find it impossible? The fibrous portions of the stomach wall might be places where all the cancer had disappeared by the process described.

DR. WALTER G. SMITH, in seconding the vote of thanks,

said a physician was necessarily, by his vocation, less concerned with the cancer problem than the surgeon. The physician's cases fell into two groups—those in which the disease could not be got at and was inoperable, and in which the physician's duty was little more than a meditation on death; and those in which the cancer might be judged possibly suitable for operation, in which case the physician had to mark down the game to hand it over to the surgical sportsman. When they considered the twin scourges of humanity, tuberculosis and cancer, it seemed that at present in their investigation they had to rely on the microscope and the experimental inoculation of animals. He was afraid they could not look to the allied science of chemistry to throw any light on either problem. So far as he knew, no chemical substance had been isolated from, or detected in, malignant growth, yet malignant growths carried their chemistry to distant parts of the body. Mr. Handley's observations appeared to him to be, if not inconsistent with, at least to throw great difficulties in the way of regarding cancer as a disease due to a specific organism. It had been frequently sought for and ascribed to animal and vegetable origin; and there was another possibility, that in that case, and also in yellow fever, the parasites were ultra-microscopic, and so eluded research. It was a great pleasure to him to second the vote of thanks to Mr. Handley, for he had not only given them an intellectual treat, but had lit a lamp which had thrown light on some of the dark corners of one of the gravest problems of pathology.

PROFESSOR E. H. TAYLOR supported the motion. He had followed Mr. Handley's work for some years. Two years ago he had met him in Brussels at the Surgical Congress, where his views were warmly accepted by the greatest surgeons in Germany and on the Continent generally. From the surgical standpoint he thought that the views so forcibly put forward by Mr. Handley had done a lot of good. He thought there was no operation for cancer which had shown such a definite advance as that for breast cancer. Mr. Handley's name was associated with others in the evolution of the operation. For some years he had practised the

operation spoken of by Mr. Handley, which aimed at removing the disease widely. No operation was thorough unless it aimed at removing the deep fascia.

PROFESSOR METTAM also supported the vote of thanks. He said his experience of cancer was limited to domesticated animals. The movement of the cancerous growth against the lymph stream was of great interest to him personally, partly because he was very sceptical as to the correctness of the present description of the lymphatic circulation. His impression had always been that the new growth was centrifugal, and the ultimate destination, if the animal lived long enough, was the blood stream. They were informed that the tubercle bacillus was able to move against the lymph stream. In tuberculosis of the udder of cattle, one way in which they could explain infection was that the virus had moved against the lymph current. It was conceivable that the cancer grew along the lymphatics, but he did not quite follow how the bud was cut off from the centre. The picture indicated that as they approached the primary focus there was an infiltration of round cells, fibroblasts which gave rise to new granulation tissue. He accepted the dictum that the irritation set up eventually formed tissue which cut off the new growth. This showed that the new growth was not quite independent of the primary growth. In his own observations he had not observed the dissemination of the secondary new growth in the subcutaneous tissue of the lower animals. In cases of carcinoma of the liver, he would have liked to hear if the secondary new growth followed the blood stream or the lymphatic stream of the liver. The latter seemed to journey backwards. He thought some one should look into the matter of the lymphatic circulation.

The vote of thanks was passed by acclamation.

MR. HANDLEY, in acknowledging the motion, said nothing could illustrate better the complexity of the subject of cancer than the speeches which had followed his remarks. Each approached it from an entirely different point of view, and all were interesting and important. One person could only hope to tackle a portion of the problem. He had suspected that the fibrotic lumps in the stomach spoken of by Dr.

O'Sullivan were extinct carcinomata, and Dr. O'Sullivan's observations tended to confirm his suspicion. It looked as if cancer were not quite the incurable disease that it was thought to be. It looked as if there might be abortive cases of cancer which never obtained the clinical dignity of fully developed disease. He wished to disclaim having discovered the process of permeation. It had been known for a long time; but he was responsible for the name. It used to be called lymphangitis carcinomatosa, and was regarded as a pathological curiosity. The reason why its importance was not recognised was, he thought, that the fibrotic process had not been described or detected. Until that process was detected it was impossible by means of permeation to explain dissemination, because permeated lymphatics were absent from the region just round the primary growth, where it would seem they ought to be specially present. He was specially pleased to hear of Mr. Taylor's satisfaction with his operation for breast cancer. Referring to Professor Mettam's remarks, he did not think that one could transfer experience in human cancer to that in animals, or indeed *vice versâ*. There seemed to be great differences between the two. He was not an expert on the varieties of cells found in the blood and lymph, but his colleague, Professor Bonney, had confirmed his work, and he could appeal to him when he spoke of the cells as fibroblast. Professor Mettam had not observed such extensive subcutaneous deposit as he had; but, of course, in man such extensive deposits were rare, and he showed the cases which illustrated the spread more strikingly than the commoner cases of limited dissemination. The subject of lymphatic anatomy was a very important one, and he believed there were considerable discoveries to be made by the anatomist who devoted himself to it. He had looked out a volume of anatomy of 1,200 pages, and the amount devoted to lymphatic anatomy—20 pages—hardly showed its relative importance. He thanked them for their kind reception. It had been a great privilege to address the Section.