THE MORTON LECTURE ON CANCER AND CANCEROUS DISEASES.

Delivered before the Royal College of Surgeons of England.

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[ABSTRACT.]

If cancer was a microparasitic disease, it should be capable of experimental transmission. Mr. Ballance and the lecturer had carried out a series of experiments in which they had inserted portions of freshly removed carcinoma of the breast into the abdominal cavity, the subcutaneous tissue, the muscles, and the anterior chamber of the eye, of various animals. The result was in all cases negative; the portions so inserted underwent coagulation, necrosis, and were either absorbed or became encapsuled.

At the present time there was no authentic case on record in which human carcinoma had been transferred to any of the lower animals. Success, however, had followed in certain cases when the transplantations had been made from one animal to another of the same species. And in this the results followed the laws of grafting rather than those of ordinary infection; they showed that a portion of a growing carcinoma, if so transferred, would grow in a second individual as it would have done in the first; but they did not really show that carcinoma was infective. A graft from one species of animal never formed an integral and permanent part of another of a different species; he referred to Hunter's grafting of human teeth to the combs of cocks, as showing only that the "graft" in certain of these experiments remained aseptic, and, like any aseptic dead substance, it contracted vascular adhesions with the surrounding tissues.

To prove that cancer was infective, it would be necessary either to isolate the infective agent and produce the disease with this, or adopt the less difficult method of using the tissue for purposes of infection after sufficient time had elapsed to ensure that the proper tissue cells were dead. There were two considerations, however, before concluding a negative. It might be that a preparatory inflammation was necessary. It was in this direction that Mr. D'Arcy Power was carrying out excellent work. Or it might be, and it was to this that Mr. Ballance and he inclined, that the phase of the hypothetical infective agent was not such in the tumour as would set up the disease by direct transference.

Although there were such strong clinical reasons for regarding cancer to be an infective disease, it was only lately that methods had been devised of cultivating a contagium vivum. After the rise of bacteriology it was natural to attempt the growth of a specific microphyte from carcinoma. In this country Mr. Ballance and he had made a long series of experiments in this direction, and with a negative result; and he might state that up to the present time no specific microphyte—bacterium, micrococcus, or other—had been cultivated from carcinomatous tumours. This led him to discuss, next, the microzoic theory, which attributed the growth of carcinoma to the action of a specific protozoon. Such a protozoon would induce the new formations, not by its mechanical presence, but, as in the case of bacteria, by the chemical changes incited by it.

An excellent historical summary of the histological appearances held by different observers to indicate the presence of such a body was given by Noegerrath up to the close of 1891. Since then Soudakewitch, in Russia, and L. Pfeiffer, in Germany, had, amongst others, published observations; but if he must select one it would be Dr. Ruffer, who had approached the subject with an intimate knowledge of histology and a commendable spirit of criticism, and the value of whose work had been enhanced by Dr. Galloway's corroboration. He referred to Dr. Ruffer's latest description of the only body in carcinoma that could be claimed with any probability as a protozoon, and then discussed what could

be stated as to its life-history, that is, especially as to its method of reproduction.

In the case of the best known parasitic protozoa in vertebrata and invertebrata there was a distinct life-history, a portion of which was in some cases passed outside the body of the host. And there was highly interesting evidence pointing to the probability that this was so in the case of carcinoma, namely, its endemic character in particular districts. Dr. Haviland's conclusions, drawn from his collection of statistics in England and Wales, were that cancer was most prevalent along the courses of rivers which seasonally flood their banks, and especially where, from the flatness of the country, the floods were retained.

The districts about the Thames, Severn, Mid-Devon and Yorkshire rivers were especially noteworthy. But there were lesser areas where the endemic character was still more highly pronounced. The best of such instances was that described by Mr. Law Webb—a small village in a certain part of Shropshire. In this, in a small group of cottages there were nine houses in which one, two, or more cases of cancer had occurred during the last twenty-five years. A little further off were two houses under one roof, which might be called A. and B. In house A. a man died of cancer of the rectum; the next occupiers were a man and his wife, the former of whom died of cancer of the stomach, the latter of cancer of the rectum. In house B. a woman died with carcinoma of the breast. House A. was then taken by three spinsters, one of whom died of cancer of the uterus, another of cancer of the stomach.

The coccidium of the rabbit offered one of the best known illustrations of the process in which a certain phase was passed outside the host, and this had been fully referred to by Dr. Galloway in the Morton Lecture of last year. In other cases the entire series of phases were passed through within the host. The parasite which J. Steinhaus had named *karyophagus salamandræ* was an illustration. This passed its life entirely within the cells of the intestinal epithelium of the salamander, and though in certain phases its nature might admit of doubt, the proof of its being parasitic was obvious in the formation of sickle-shaped spores. This led him to point out that this pathognomonic sign of a parasitic element, though it had been alleged to occur in cancer, was not yet forthcoming. The so-called sickle-shaped bodies described and figured by Soudakewitch and others had been discountenanced by Metchnikoff; they had not the regularity of true sickles, and in their forms and staining reactions they were represented by chromatic degenerations of cell nuclei. He referred to an instructive series of forms similar to such, which were figured by Demarbaix¹ in the small lymphoid cells of the bone marrow of the rat examined several hours after death, and one might see the same in dying leucocytes in inflammatory foci; the nuclear chromatin became ring-shaped, or parted into sickles or less regularly shapen elements, and finally became fragmented into lesser portions and distributed through the cell; in polynucleated cells the different nuclei, or parts of the nucleus, might undergo like cadaveric alterations.

In cancer cells such false sickles might arise from changes occurring in included leucocytes, or the smaller lymphocytes, or possibly in portions of the cell nucleus divided off from the rest, or in the residues of chromatin resulting from irregular mitosis.

As to the method of multiplication of the alleged parasite in carcinoma, this had been described by Dr. Ruffer as occurring only by binary division; or, as a modified process, the nucleus might divide into parts which would become arranged peripherally, after which the protoplasm and capsule followed suit in the subdivision.

In a recent number of the *Journal of Pathology and Bacteriology*, Dr. Cattle, of Nottingham, had figured what might be a spore cyst within a cancer cell. So important did this observation seem that he (the lecturer) wrote to Dr. Cattle, who kindly forwarded the specimen in question; but, after careful study, he had formed a definite opinion that this body was only a cell invagination, in which the cell protoplasm of the included cell was highly vacuolated and the cell membrane well marked; there were in other parts of the section epithelial cells, of which the protoplasm presented precisely

¹ *La Cellule*, Tome v.

similar appearances. At present there was no unimpeachable observation to the effect that a spore cyst was produced in carcinoma. He had limited his remarks to carcinoma of the breast, because in squamous-celled carcinomata the complications arising from horny change were introduced, and certain appearances, due to this, had been taken by L. Pfeiffer and others as parasitic: the cell body became homogeneous, and the nucleus ceased to stain; in other cases invaginations of keratinising prickly cells were encountered, and these, too, had been mistaken for parasites; J. Steinhaus had particularly drawn attention to such semblances.

In these carcinomata, also, exposed, as they were, to the causes of common inflammation, collections of leucocytes had been taken for spore cysts holding nucleated spores, some such might be sections of vessels, but others lay in the epithelium; their nature, however, was obvious, from the fact that leucocytes could be seen in various numbers between the cells, and precisely similar collections had been described and figured by Mr. D'Arcy Power in the epithelium of the rabbit's vagina after the repeated application of linimentum iodi: a collection of polynucleated leucocytes so closely packed that the outlines of the individual cells were not recognisable was at first sight, nevertheless, a striking object.

As to the particular body figured by Nils Sjöbring, Soudakewitch and Ruffer, it ran perilously close, as usually displayed by the triple stain, to certain results of hyaline degeneration; yet when similar bodies, provided with exquisitely-arranged peripheral bars or granules, were encountered, one's trust revived, for the only thing to which these were comparable were certain forms of such a protozoon as the *coccidium oviforme* of the rabbit's liver.

One test, certainly, the body stood well, and that was the test of constancy. It was present in all carcinomata; and no precisely similar body had been produced in epithelium by common irritation, though Mr. D'Arcy Power had produced not a few other forms alleged in certain quarters to be parasitic.

Dr. Richard Hebb had figured the particular body in question in a case of what he designated peritoneal fibrosis, but he (the lecturer) thought that most who read the report—in the Pathological Society's *Transactions*—would come to the conclusion that this case was really one of malignant disease and confirmed rather than threw doubt on the contention put forward.

As still related to Koch's first postulate, he next drew attention to certain chemical questions.

Three years ago, for certain chemical reasons, Mr. Ballance and he had been led to test the effect of aqueous or 50 per cent. glycerine extract of minced carcinoma and sarcoma, to which thymol or a small proportion of carbolic acid had been added for preservative purposes. The extracts were filtered and kept in sterilised test tubes in a refrigerator. Such extracts had no local or general effect upon rabbits when used subcutaneously.

Two cases he might notice, in passing, out of several that were treated by the subcutaneous injection of 20 minims daily, as showing that no local reaction occurred, such as happened in tuberculous lesions from the injection of tuberculin, and that no curative or preventive property could be assigned to such extracts. One concerned a lady under the care of Sir William MacCormac, who had been subjected to four operations for scirrhus in six months. A few weeks after the fourth operation the injections were used—forty in all. Recurrence took place during the course, and death ultimately from intrathoracic disease. The other case was one of recurrent sarcoma. Treatment was adopted a few days after a second operation. Recurrence took place, however, as in the other instance, whilst treatment was proceeding.

Speaking generally, the pathogenic action of bacteria arose from the specific albumoses and alkaloids which they elaborated. Could any such substances be extracted from carcinoma? If an aqueous extract of minced carcinoma were boiled and filtered, the filtrate would give evidence of containing proteid, but this was due to the presence of acid or alkali albumen, according to the reaction of the tumour, which was uncoagulated by boiling. If the fluid were first acidulated with acetic acid, or, better still, boiled with an equal bulk of

10 per cent. trichloroacetic acid, all the common proteids were precipitated; the filtrate was quite clear, and the test with dilute cupric sulphate solution, or with concentrated hydric nitrate, gave no trace of precipitate, proving the complete absence of albumose. As to alkaloids he could say, from the results obtained by Mr. Edmund White, that these were equally absent.

Albumose, however, might possibly be obtained from carcinoma under two circumstances, though in neither would it be of a specific or pathogenic kind. If putrefaction was allowed to ensue, such a substance might be found. Many years ago Mr. John Marshall had made the observation that the reaction of a scirrhus of the breast was acid. He (the lecturer) had often found this in the tumours of which the unfailing kindness of Mr. Edgar Willett had supplied so many; and he had found the same in sarcomata. But this acid reaction arose only a certain number of hours after removal. As Mr. D'Arcy Power had shown, the reaction of a scirrhus immediately after its excision was alkaline or neutral. In fact all, or nearly all, tissues became acid after death; this fact was well known in the case of muscle; and from the latter albumose was derivable owing to the action of the pepsin, of which a certain amount was in the general circulation; and so it might happen in carcinoma were the examination long delayed. There was another chemical question of much interest. The capsule of encysted protozoa consisted of cellulose, or of what was, in other cases, assumed to be chitin. Was either such demonstrable in carcinoma? These substances were not present in the tissues of vertebrates. Professor Halliburton kindly undertook to test this possibility, and the investigation was most carefully carried out in the physiological laboratory of King's College by Dr. Gregor Brodie. At first the results were encouraging, but as Dr. Brodie perfected his method they became less so, and ended in a complete negative. The principle of the method was as follows: The tumours were minced and boiled in 20 per cent. caustic soda, and filtered hot through asbestos. A small residue of fats in excess was left upon the filter, and in this residue there would have been any cellulose or chitin, which were insoluble in boiling caustic soda or potash. The residue, after being washed with boiling caustic potash solution, then boiling distilled water, and then with weak hydric sulphate to neutralise the alkali, etc., was treated with concentrated hydric sulphate. Cellulose was soluble in hydric sulphate, chitin insoluble in this, but soluble in hydric chloride. The acid drawn through the asbestos by means of a pump was diluted and boiled. Had cellulose been present it would thus have been converted into dextrose or grape sugar, and the presence of this would be easily recognisable by means of Fehling's solution. No such reducing substance was formed. The asbestos was next treated with concentrated hydrochloric acid. The filtrate was quite clear, and gave no precipitate on dilution, as it would have done had chitin been in solution; nor was a reducing substance obtained by boiling the hydrochloric acid after dilution.

He next proceeded to consider the second postulate of Koch, namely, the cultivation of a micro-organism alleged to be in the tissues, outside the body. It was with this that Mr. Ballance and he had been for some time occupied. They had used test tubes of milk, with 5 per cent. glycerine, dilute broth and other fluid media; into these, portions of the growing edge of carcinomata of the breast had been placed, and examined by means of sections at different dates. They had, however, given up such methods as not sufficiently natural, or like the conditions a parasite would meet with in its natural history outside the body.

They had found that psorospermial material from the rabbit's liver placed in broth or even in sterilised rabbit serum underwent practically no further change; the conditions were not sufficiently natural. He then described and showed the method they had now adopted of using sterilised sand in Petri capsules or deeper ones, kept between double dishes, and the whole beneath a shade, on a sheet of glass. Specially distilled water was used, and this was boiled four hours in a sterilised flask before use. Into such capsules pieces of the growing edge of mammary carcinomata were placed. And now he came to a result which, if confirmed, would fully repay for the negative character of the rest.

In no fewer than six capsules, five of which were infected from different tumours, they had obtained actively moving amœbæ. Some of the earlier of these experiments were not conducted with all the precautions desirable, and they hoped in a few weeks to satisfy themselves on this question, as they had a new series of such experiments almost mature for examination, together with many check experiments made with the muscle, pancreas, spleen, mamma, etc., of the human subject, as well as of dogs. In check experiments made with sterilised sand and distilled water, or tap water, to which a small quantity of broth or blood plasma had been added, they had obtained no similar results.

There was one body that for a while diverted attention. This was a flattened circular or oval structure, radially striated in its periphery, and corresponding in size with the element met with in carcinoma. It occurred in all the samples of silver sand examined, as well as in sea sand, and its general look suggested a skeletal nature. It was unaffected by baking; on the addition of hydrochloric acid it rapidly parted into radial segments, and then utterly vanished. Professor Dallinger had not been as yet able to name it, but it was probably a segment of some foraminiferous protozoon. Were the amœbæ leucocytes? Professor Sherrington had made the interesting observation that in the blood drawn from the dog and prevented from coagulating by the intravenous injection during life of oxalate of potassium the white corpuscles will exhibit movement for as long as three weeks; in the frog, observation had also shown that the leucocytes will remain alive six weeks after the blood is drawn. That the bodies in question, however, were not surviving leucocytes was proved by their living in water, the action of which was lethal in the case of the mammalian corpuscle; and it was evident, from the great numbers found in the larger capsules, that a process of multiplication was concerned. But what completely disproved this possibility was that there were other phases met with in the sand of the capsules: encapsulation and sporulation.

One of the tumours used was a sarcoma. And, should the results be true, it was not a little curious that the same microzoon occurred in carcinoma and sarcoma. In sarcoma Dr. Ruffer had not yet described such a body as that present in carcinoma.

He concluded, however, with an analogy. One of the most remarkable modern discoveries in connection with vegetable galls was Professor Adler's, that what were once taken to be two distinct gall-making insects are but different phases or alternating generations of a single one; and there were many such instances. And the interesting point was that the galls produced by the same insect in its alternating phases were markedly different. One of the commonest kinds was one of the best illustrations. The common spangle on the under side of the oak leaf was the produce of one phase of a gall-making insect, the currant gall on the male flower was the produce of the other phase of the same.

So it might be in carcinoma and sarcoma.

THE MAMMALIAN HAND.—At the meeting of the Zoological Society of London, held recently, Professor Karl von Bardeleben, of Jena, read a paper on "Bones and Muscles of the Mammalian Hand and Foot," in which he explained his views on the rudiments of the sixth and seventh digits or rays. These rudiments, as he showed, are situated both on the inner and the outer borders of the hand and foot; they are present in nearly all the orders of mammals, especially in the lower forms, and are always provided with special muscles.

ROYAL SOCIETY OF EDINBURGH.—At the meeting of this Society on May 7th Dr. Robert Munro, at the request of the Council, read a communication on the Rise and Progress of Anthropology. He held that the coalescence of the power of deciphering unwritten records, with the almost coincident teaching of Darwin, first enabled the antiquary to look beyond the horizon of mere historic vision, and to gather the materials for a science of anthropology. Dr. Munro held that the chief materials in attaining this science were (1) ethnology, (2) language, (3) the structure of man, (4) fossil man, (5) the handicraft products of man, (6) the bearing of geology on the prehistoric remains of man.

AN ADDRESS

ON

THE ETHICS AND PROSPECTS OF THE PROFESSION IN NEW SOUTH WALES.

Being the Presidential Address delivered before the Sydney and New South Wales Branch of the British Medical Association, March 2nd, 1894.

By RALPH WORRALL, M.D., M.C.B.

GENTLEMEN,—First let me again express my grateful acknowledgment of the high compliment paid me in electing me to be President of the Sydney and New South Wales Branch of the British Medical Association for the year which has just closed. No one can be more conscious than myself of my many shortcomings in filling this high position; but I am solaced by the thought that failure, more or less, is the common lot of humanity, and that I have striven, as far as in me lay, to uphold the dignity of the office and the interests of the profession. I thank you for the indulgence and courtesy which you have always extended to me, and I would express my special indebtedness to my brother officers in the Council and to our Assistant Secretary, Mr. Green, for the valuable help so often given.

THE PAST AND FUTURE OF THE BRANCH.

The past year has been one of unexampled prosperity for our Branch. Nineteen new members have joined, making our total strength 192. We have a credit balance of £331 5s. 2d., and this after paying £32 14s., in accordance with a vote of the Branch, to Dr. Martin to aid his experiments in snake poison. We have to deplore the loss of two valuable members, Dr. Geo. Bennet and Dr. W. Spencer.

There have been 12 Council meetings, and 10 general meetings, at which 23 papers were read and 12 exhibits shown. The whole of these contributions were made by 20 members; that is, out of a total of 192 members, many of whom have great opportunities for scientific and clinical researches, only 20 took the trouble to lay before their brethren any result of their observations and experience. This is surely an undesirable state of things. Those who have opportunities should make use of them in the interests of science and humanity; in omitting to do so they neglect a powerful means of self-culture, for the preparation of a paper entails much healthy exercise of the judgment and reasoning faculties in addition to materially adding to an accurate knowledge of the subject treated. I trust that in the ensuing session members will rouse themselves, and that we shall have such a plethora of papers that the Council will be called upon to make a selection of the most valuable for presentation at our meetings.

The average attendance at our general meetings has been greater than in any previous session, yet we have to regret that many of the senior members are conspicuous by their absence. These gentlemen owe everything to the profession. Surely it should not be too much to expect that in return they would make the small sacrifice involved in attending once a month and endeavouring as far as they could to aid the success of these meetings, which help so greatly to bind together the profession and add to its sense of knowledge. In Liverpool, throughout the session, meetings were held fortnightly, and notwithstanding this tax on their time, the leading medical men were characterised by the punctuality and constancy of their attendance. They recognised that the man who lives self-centred, with no regard for the commonweal and no object but his own narrow personal interests, misses much unalloyed pleasure and cuts himself off from valuable sources of instruction and self improvement.

The discussions have not shown as much advancement as the increased attendances would warrant us expecting. Some members are too proud—because they do not speak as well as others they refrain altogether—others are too diffident. Both