THE PARASITIC ORIGIN OF CARCINOMA.

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The factor or factors at work in causing this disease, have always been the subject of investigation, and though we are told by numerous wise-heads and old women, that the excessive eating of tomatoes is the chief and only cause, and by eminent observers, that psorozoa, coccidia, and yeast fungi are the guilty ones, the question is still far from settled.

It is the purpose of this paper to briefly review the most important investigations upon the parasitic origin of this disease and also to report the results obtained by the writer from some examinations made by him along this line.

Within the past eight years much interest has been aroused in the study of the occurrence within epithelial cells of psorozoa or coccidia; in some of the lower animals, especially certain fish and rabbits, such bodies have been found, and also in the human subject under certain conditions.

In 1887, Schenerlen* published his observations in which he described a bacillus which he found in mammary cancer. The bacilli were slender rods, from fifteen to two micromillimeters in length, and there were also present oval bodies, greenish in color, which he conceived to be spores. He never found them present in sections of the tumor but in the cancer juice. He succeeded in cultivating the bacilli upon potato, agar-agar, and meat peptone. He injected culture media containing the bacillus into animals and found that nodules were formed at the point of injection, and that the bacilli could be obtained from such nodules.

*Deutsch. Medical Wochenschrift, 1887, No. 48.

Sanarelli and Pfeiffer confirmed his observations so far as demonstrating the presence of these organisms in cancerous material but their inoculations proved failures and they regard the organism as a harmless parasite, in fact, hardly any one, at the present time believes the organisms described by Schenerlen to be the etiological factor in the production of carçinoma.

As long ago as 1858, Gubler reported a case, where, in a man of forty-five, the liver contained tumors, varying in size from a small nut up to an egg, and which when opened, were found to contain fluid, in which were multitudes of the coccidia.

In 1883, Dr. Hadden, before the London Pathological Society, showed portions of the viscera from a case resembling the one just quoted, in which the muscular tissue of the heart, parietal layers of the pleurae and omentum, the liver, kidneys and brain, contained small nodules which were found to be psorospermial cysts.

Several such cases have since then been exhibited before that Society. These psorospermial bodies have also been found to occur in the skin; Darrier, in 1889, found them present in chronic eczema of the nipple, or Paget's disease, and his observations were confirmed in 1890, by Wickham[1] and J. Hutchinson, Jr.[2] These investigators claim that this disease is caused by these organisms, and as it usually ends in cancer of the breast, it is but natural to suspect that they may have something to do with the causation of that disease.

Away back in 1847, Virchow described certain inclusions which he found within the cells of tumors, and it is thought by many that they were the bodies which are now described as psoroza or coccidia, but it was not until 1888-89 that they began to be seriously considered as perhaps bearing some causative relation to cancer. In the latter year Melassez and Albarran published some important observations upon this subject, in which they came

1. Archiv. Exper. Med., Jan. 1890.
2. Trans. Path. Soc., Vol. XLI, page 214.

to the conclusion that carcinoma was caused by psorozoa, and Darrier, Wickham, Wright and Russell came to the same conclusion from their own investigations.

Ruffer and Walker[3], in 1892, published their very important observations upon the etiology of carcinoma and the claims which they made have since received confirmation from Burchardt, Plimmer, Foa, Soudakewitch and Steinhaus.

All of these investigators agree that a peculiar body is almost always present in some of the cells of all of the varieties of carcinoma, generally within the body of the cell, sometimes alone, sometimes multiple, oval or nearly round in shape, from two to ten micromillimeters in diameter, and enclosed by a capsule. They are sometimes described as containing a nucleus, and according to Ruffer, reproduction takes place by division of the nucleus and then of the capsule. Spores have not as yet been demonstrated, although Burchardt[4] has described an appearance which he takes to be a spore; it consisted of a delicate oval capsule, containing a well-defined vesicle, which was filled with small particles, comprising, he thinks, a spore, germ capsule, and germs. The organisms are not very resistant, and Ruffer and Walker claim to have seen them destroyed by attacking leucocytes. According to Royce, the cancer cells in the neighborhood of these bodies do not seem to be more active than elsewhere but the bodies themselves are found in greatest number in the more rapidly growing tumors.

It may be well, just here, to sum up the chief arguments both for and against the parasitic nature of these bodies.

The chief arguments for their parasitic nature are:

1. The body seems to be a foreign substance.
2. It looks like an organized structure.
3. Zoölogists, like Metschnikoff and Balbiani, have decided that it is a parasite.
4. It stains unlike the normal cell products.

3. Jour. Path. and Bacter., Oct., 1892.
4. Virchow's Archiv. Band. 131, page 121, Jan. 2, 1893.

5. Germination has been claimed to have been observed.

Those against its parasitic nature are:

1. It does not resemble in general characteristics the protozoa with which it could best be classed.

2. Spores have not as yet been demonstrated.

3. Cultivation has not been successful.

Galloway[5] thus sums up the various appearances with which the organism has been confounded, and to which those opposed to its parasitic nature refer all the bodies described: Transverse sections through two cells, one of which is invaginated into the other; leucocytes or red blood-corpuscles enclosed in epithelial cells; cell formations, in which the nucleus has divided but not the cell; degenerations of the cancer-cells, particularly if the nucleus is not affected.

Observers have described bodies which were undoubtedly some of the appearances described: Korotneff, Jackson Clark, Wickham, Russell and others have, no doubt, mistaken such appearances for parasites, but that there is a body present in cancer which is parasitic in nature, the majority of investigators firmly believe. Foa, at the International Medical Congress, held in Rome in 1894, read a paper in which he described the bodies which he thinks are the cause of cancer. They are endoprotoplasmatic bodies having a nucleus and enclosed by a capsule with a double outline, composed of protoplasm. In size they vary from a small to a large nucleus. When the body is large the protoplasm is festooned upon the surface, being cockade shaped or regularly segmented, looking like a rosette. They increase by the central body or nucleus dividing into a number of smaller bodies, which fill the cyst like cells. He thinks these bodies are spores. Owing to the number of them in a single cell they could hardly be mistaken for degenerated nuclei. He believes these organisms, which are the same as those described

5. Schenck's Bacteriology, page 292.

by Ruffer, Plimmer, Soudakewitch and Walker, are the cause of cancer.

Plimmer and Ruffer have shown that these bodies are present in fresh cancer cells, so that they cannot be produced by changes occurring in the cells during the process of hardening. Plimmer found them present in every case of cancer which he examined (four hundred consecutive cases) and never found them in any other variety of tumor.

Shattuck,[6] in the Morton Lecture, said that the only bodies so far described which seemed to him to be at all suggestive of parasites, were those of Ruffer, Plimmer and Foa, and described his method of cultivating on sand, growths from the margins of a mammary cancer; in five out of six cultivations he obtained actively moving amoebae, in some of which a process of encapsulation and sporulation was going on.

D'Arcy Powers placed in the irritated mucous membrane of a rat a piece of cancer, and succeded in obtaining from the cells so affected, bodies which were identical with those described by Ruffer, Plimmer and Foa.

Cornil does not agree with their conclusions, but holds that the bodies believed by them to be parasites were nuclei which had been disintegrated, and Adler, in an article in the American Journal of Medical Sciences for January, 1894, states that in examinations of more than sixty cancers, taken from various parts of the body, he did not find in one of them anything but which could be easily explained away, without falling back upon the parasitic theory, but the claim made by Ruffer, that the parasite described by himself and the other investigators named, gives distinct staining reactions differing entirely from those given by carcinomatous nuclei is true, and goes far to prove the correctness of their theory.

My own work on this subject is very limited, and done merely to see if I could find the appearances described. I have examined several sections prepared in the manner

6. British Medical Journal, May 19, 1894.

recommended by Ruffer, Plimmer and Soudakewitch, from two carcinoma of the breast, and in all of them detected bodies which answer to those described by the observers mentioned.

The method which gave the most satisfactory results in my work was as follows: The section was stained for ten minutes in a saturated fuchsin solution, made by dissolving in two per cent. carbolic acid water, then washed in water and alcohol, and stained for five minutes in methyl blue. The section so stained show the parasites a dark red color while the remainder of the tissue is blue. In the method used by Soudakewitch the sections are stained by hematoxylin, which gives these bodies a different blue color from the rest of the tissue. The bodies which I have been able to demonstrate by these methods are the same, as I stated, as those described by Ruffer, Plimmer and Foa, and in my sections I noticed the following varieties:

1. A large, rosette shaped body, enclosed within a well-defined capsule, and occupying nearly the whole of the cell, pushing the nucleus to one side.

2. Smaller bodies, oval in shape, lying within the epithelial cells.

3. Large bodies, round or irregular in shape, enclosed within a capsule, lying within the cancer-cells.

4. Large, oval bodies, enclosed in a capsule, pushing the nucleus to one side.

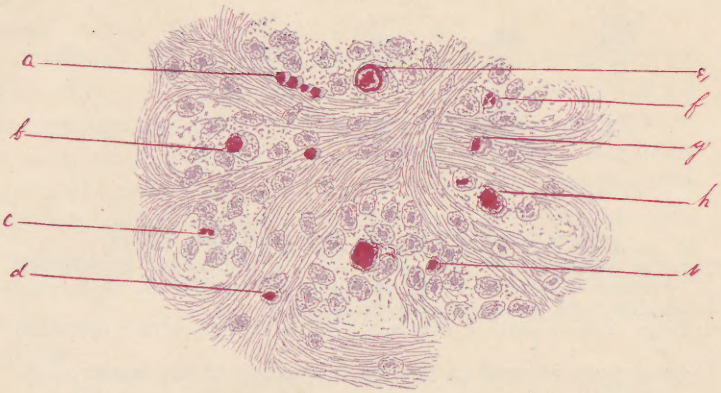
5. Groups of two or three small coccidia enclosed in a common capsule round in shape, and situated within the cancer-cells.

6. Small round bodies, generally two in number, enclosed in a common capsule, which is well-defined, and stained at its outer border.

7. Small round bodies, deeply stained, which lie in the intercellular spaces, outside of the epithelial cells, and which are probably blood-corpuscles.

I have made drawings from two sections of these tumors, just as they appeared beneath the microscope, and

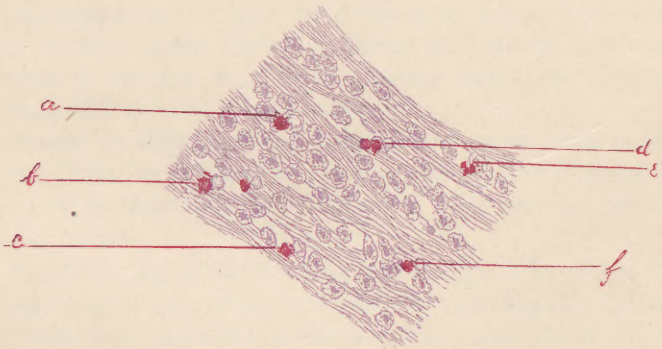
Fig. I.



Scirrhous Cancer of the Breast, (X 450.)

a. Fuchsin stained bodies, without epithelial cells.
b. d. i. Fuchsin stained body with the epithelial cells, capsulated.
c. Small stained organisms within the epithelial cell.
e. Rosette-shaped body, within large cell, enclosed in a capsule.
f. Group of three small bodies within epithelial cell.
g. Deeply stained organism, pushing nucleus to one side of cell.
h. j. Large fuchsin stained bodies, enclosed within a hyaline capsule within epithelial cells.

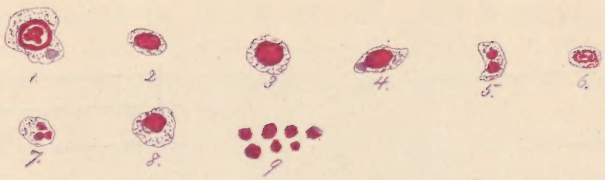
Fig. II.



Scirrhous Cancer of the Breast, (X 450.)

a. Fuchsin stained body within cancer cell.
b. d. f. Small bodies without the cells, of doubtful nature.
c. Fuchsin stained body, enclosed in capsule, in cell.
e. Groupe of three psorospermae within epithelial cell.

Fig. III.



Various Forms of Parasitic Bodies found in Cancer.

1. Large rosette-shaped body, enclosed in a well-defined capsule, and pushing the nucleus of the epithelial cell to one side.
2. Smaller body, lying within epithelial cell.
3. Large body, contained within a hyaline capsule, within epithelial cell.
4. Large body, engaged in pushing the nucleus of the cancer cell to one side.
5. Two small bodies, psorospermae or coccidia within epithelial cell.
6. Two small bodies enclosed in a well-defined capsule, within cancer cell.
7. Group of three coccidia within epithelial cell.
8. Large stained body, within cell.
9. Small stained bodies which lie without the cancer cells, free in the fibrous portion of the tumor. Their nature has not yet been determined, probably blood corpuscles.

All the above are stained with fuchsin.

also a drawing showing the different forms which I noticed, which may be of interest to you.

The difference in appearance of these organisms is due, probably, to changes in their life history and though I cannot say that I am convinced that they are the cause of cancer, their constant presence, their staining reactions, general appearance, differing so markedly from the cancer-cell nuclei, and the fact that they have been proven to have caused proliferative changes in the tissues of some of the lower animals, leads me to suspect that these psorozoa or coccidia have something to do with its causation.

Dr. Ruffer has recently claimed to have seen movements in these organisms and hopes to be able soon to photograph them. He says that if daily examinations be made of a recently removed cancer, one could follow all the stages of degeneration of these parasites, and also certain phases of their life history.

This paper would be incomplete were I to omit in closing, mention of the recent researches of Neumayer, Raum, Sanfelice, Roncali and Rabinowitch, upon the causation of tumors by the yeast-plant.

Neumayer found that the yeast-cells were very resistant to the human digestive juices and Raum produced death in rabbits with intravascular injections of pure cultures of various yeast-plants.

Busse, in 1894, isolated a species of yeast from a sarcoma from the tibia of a woman, and produced death in rabbits by injecting pure cultures, although no tumors were found.

Sanfelice has produced neoplasms, especially in guinea-pigs, by injections of pure cultures of a pathogenic variety of yeast and he calls attention to the resemblance of the yeast-cells to the cancer parasites thus far described.

Roncali has published a paper in which he describes certain bodies in cancer-cells which he insists are yeast-like in character.

Lydia Rabinowitch, under the direction of Koch, made

inoculation experiments with fifty different varieties of yeast organisms, out of which she found only seven which were pathogenic, the yeast-cells being found abundantly in all of the organs of the infected animals, but in none of them was there produced any chronic illness or neoplasms.

Such, then, is the condition of the question of the parasitic origin of carcinoma at the present time.