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THE PARASITIC PROTOZOA FOUND IN
CANCEROUS DISEASES.

BY ALICE BODINGTON.

In the British Medical Journal for Feb. 26th, 1893, the "steady increase of cancer" is spoken of as a subject requiring serious attention, and as far back as 1887-8, the Council of the Association drew the attention of the Registrar-General to the "steady increase in the deaths from cancer," out of proportion to the deaths from all causes, and showed *that similar conditions exist in most civilized countries*. The "increasing mortality from this terrible disease, not merely kills nearly twenty thousand persons in England and Wales alone" [the southern part of one small island !] but kills the vast majority of them by slow and cruel torture continued during a long series of months, sometimes of years." Cancer, like insanity, seems specially to find in the highest conditions of civilization a hot bed in which it flourishes and spreads; and any clue which can guide civilized man to the secret of grappling successfully with this hitherto unconquerable foe, will be one of the greatest boons which science can confer upon mankind. To know where the enemy lurks, and in what form, is, in the case of parasitic diseases, not only half but sometimes all the battle; as the almost complete immunity from cholera of England has shown.

An army of keen observers has endeavoured for many years past to discover, if possible, the exciting cause of cancer, but till lately the prospect of discovering the foe appeared hopeless. The theory which seemed most firmly established, most consonant with scientific theory, was at the same time a singularly hopeless one. It was assumed that at the decline of life, or under conditions of lowered vitality in the whole or part of the body, certain embryonic structures—especially of the kind known as "survivals"—took on an abnormal growth, and rioted in the production of epithelial cells of a low type which

flourished at the expense of the healthy structures round them. Now any disease arising from degeneration or overgrowth of embryonic survivals, [such as the remains of the Wolffian duct in the female] sets at defiance all human precautions; the embryonic tissue is hidden, and no one can tell either when or why it begins to go wrong. If cancer owed its rise simply and solely to an overgrowth of embryonic tissue, there was no hope but in an early, a thorough, an unsparing use of the knife; no *stamping out* of the disease could be hoped for or thought of. All attempts to trace the disease to the action of bacteria failed. But during the last few months the patient, cautious, untiring labour of years of a number of distinguished pathologists has enabled them to detect the existence of organisms in cancer, which resemble, in all that is known as yet of their life history, the Sporozoa; and more especially the *Coccidium oviforme*. (Leuckart), of the rabbit.

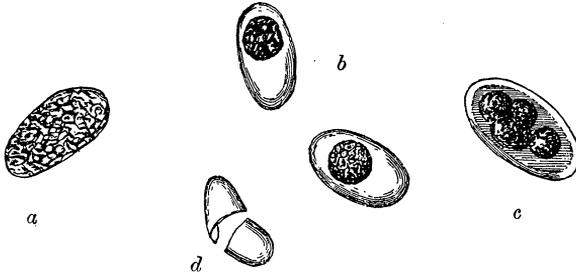


Fig. 1.—*a*, Coccidium showing capsule full of granular protoplasm; *b* shows condensation of the protoplasm into one sphere, after two days' growth external to body; *c*, division of the single sphere into four daughter spherules, after four days' development; *d*, an empty ruptured cyst. (From photographs x about 500.)

The whole life cycle of *Coccidium oviforme* is now known; its discovery has been the work of more than thirty years, so that there is no reason for discouragement if some stages of the life history of the Coccidium found in cancer still elude research.

Dr. Galloway after describing the symptoms of coccidian infection in the rabbit, begins with the life of the protozoon after it leaves the body. "The organism" he says "as it escapes from the alimentary canal consists of a firm translu-

cent cyst oval in shape [see Fig. 1, *a*] enclosing a quantity of very granular protoplasm which fills the whole body. Very

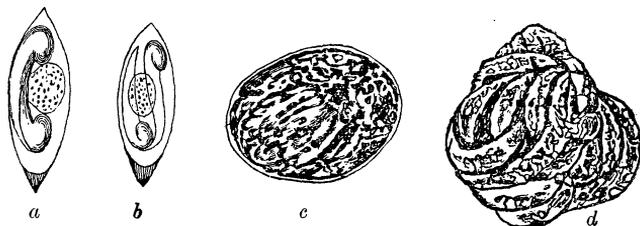


Fig. 2—Stages in Life History of *Coccidium oviforme*. *a, b*. Formation of crescentic spores within the daughter spherules external to the host (after Balbiani); *c, d*, sporulation within the host, division of the spores into numerous crescentic segments. (After photographs by Pfeiffer x 1,000.) From 'Morton Lectures,' by James Galloway, A. M.; M. D. Aberdeen. British Medical Journal. Feb. 4th, 1893.

soon after expulsion, and often while within the host, the protoplasmic contents contract [Fig. 1, *b*] and form a sphere lying free within the cell wall. Under suitable circumstances, this ball of protoplasm sends out projections and at length divides into four distinct smaller spherules [Fig. 1, *c*.] These four spherules are "transformed¹ into four spores provided with a very resistant external covering. Each spore encloses two falciform and very delicate embryos, [Fig. 2.] which give birth to new parasites, and thus engender the terrible disease when swallowed in polluted food. The sporiferous coccidia penetrate into the digestive canal of rabbits, and the envelope of the spore protects the falciform embryos against the action of the gastric juice. So strong is the protecting capsule that the spores can live for at least six months outside the body [Galloway]. The epithelial cells of the small intestine and of the biliary ducts are the seat of the internal activity of the parasite, on reaching which a "new cycle of intense activity is observed. The falciform young take on a rounded shape, and probably acquire the power of locomotion. Most of the naked amœboid forms of the organism divide into small crescentic

¹ Carcinomata and Coccidia, Elias Metschnikoff, M. D. Chef de Service, Institut Pasteur. Revue Générale des Sciences Pures et Appliquées. Brit. Medical Journal. Dec. 10th, 1892.

sporules, which, in their turn, also become free, and myriads of young sporozoa are soon formed. These possess the "power of insinuating themselves into the protoplasm of epithelial cells, where they grow and become transformed into oval parasites resembling the adult form" [Metschnikoff]. In course of time, the epithelial cell wall is ruptured and the parasite escapes, without necessarily causing the destruction of the host cell; it passes through the alimentary canal, gains access to the atmosphere, and thus attains the conditions necessary to recommencing its cycle of development. Having been shown the life history of the coccidian parasite of the rabbit,² we shall be better prepared to recognize the [apparently] kindred disease in man and some of the higher vertebrates. "Taking cancer of the breast as an example," says Dr. Galloway, "if careful microscopic examination is made, there will be found lying, most commonly within the cell body, rounded or oval structures varying in most cases from $2\ \mu$ to $10\ \mu$ in diameter, having, when large, a very distinct capsule, and containing a smaller body of variable shape. From the capsule there may be seen passing towards the centre numerous fine radial striations, . . . and processes of a somewhat different character may also be seen passing from the nucleus towards the periphery; they are not so regular and appear to be prolongations of the nucleus.

"These bodies occur sometimes singly, sometimes in twos and threes, and occasionally to the number of nine or ten—and even twenty,³ of small size—in a single cell. In a successful preparation each of the small ones will be seen to contain the usual nuclear substance (see Figs. 3 and 4). Similar structures of smaller size may be observed lying *inside the nucleus* of the epithelial cells. In this case the capsule, so very characteristic of the intracellular bodies, is very slight, and indeed, appears to be absent in most cases. "The intra-nuclear bodies also occur either singly or in small groups." Occasionally the

² See also Fig. XVII, Sporozoa; *Gregarinidae* article Protozoa, Encyclopedia Britannica, pp. 852-3.

³ "I have seen over 20 parasites in the same nucleus."—M. Armand Ruffer, M. D., *B. Medical Journal*, Nov. 5, 1892.

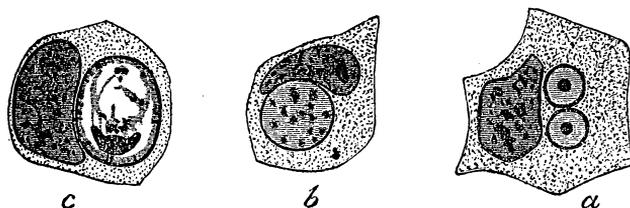


FIG. 3.

Cells from different cancers of the breast, showing various forms of parasites in the cell protoplasm $\times 1,200$.

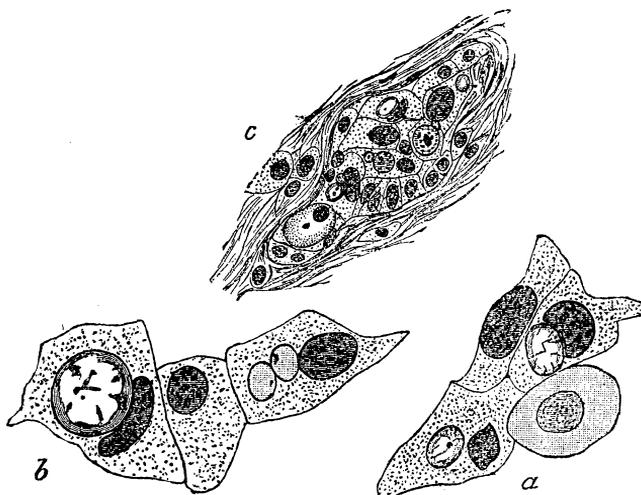


FIG. 4.

a and *b*, Groups of cells containing intracellular parasites \times about 1,000; *c* cancer alveolus from edge of rapidly growing carcinoma of breast, showing numerous parasites \times about 400.

bodies may be seen partly within and partly without the nucleus in the act of passing through the latter into the cell protoplasm. In certain cases the nucleus seems to become filled up with numerous small parasites which escape into the cell protoplasm after having burst through the nucleus.⁴ The

⁴ See "Preliminary Note on some Parasitic Protozoa found in Cancerous Diseases." By M. Armand Ruffer, M. D. and J. Herbert Walker, M. A. *B. Medical Journal*, July 16, 1892.

Also, "Recent Researches on Protozoa and Disease." By M. Armand Ruffer, M. D. *B. Medical Journal*, Oct. 14, 1893.

nucleus of the cancer cell when it bursts through over-distension with parasites, perishes, but when only one or two parasites escape, it usually heals up perfectly.

For the further life history of protozoa of cancer, we may follow Mr. Jackson Clarke.⁵ In describing his examination of a myeloid sarcoma, he says: "In the most interesting portion of the neoplasm, its advancing border, the entire peripheral zone of the section could be examined from end to end without anything but amœboid psorosperms and remains of infiltrated connective tissues coming into view. In the centre of the field [Fig. 5] is a psorosperm in the plasmodium stage, in which spore-formation is commencing. Below is part of a giant cell containing one encapsuled and two amœboid psorosperms; numerous free amœboid parasites, and to the left is part of a large plasmodium, within which are nuclei and fibres undergoing digestion.

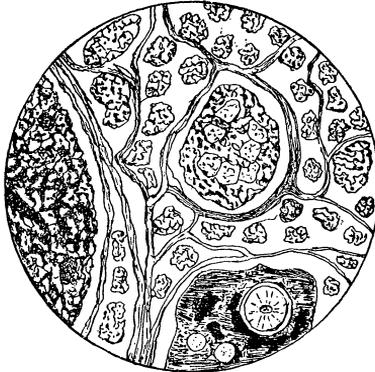


FIG. 5.

In this sarcoma, as in all the cancers, I have examined recently, there is, in the advancing zone, an army of amœboid psorosperms invading and digesting the tissues beyond, and *determining new growth in the special tissue with which the parasites have established a symbiosis*. For it appears that the curious inter-dependence of two organisms, known as symbiosis, has

⁵ Sarcomá Caused by Psorosperms. By J. Jackson Clarke, M. B., F.R.C.S. *B. Medical Journal*, Dec. 24, 1892, and Jan. 21, 1893.

been established between the malignant parasite of cancer and certain epithelial and mesoblastic tissues. *These tissues are excited to enormous overgrowth by the presence of the parasites, whilst the tissues with which they have not established a symbiosis are invaded, devoured and destroyed.* Mr. Jackson Clarke thus describes the process: "The amœboid parasites make their way between the epithelial cells and pass in vast numbers into the connective tissue spaces beyond the epithelial part of the growth. In their passage they cause the rows of epithelial cells to separate, and thus bring about a multiplication of the points of epithelial ingrowth and detachments of small groups of epithelial cells. A considerable amount of inflammation is caused by the invasion of the vascular tissues by the amœbæ, with the same result as that seen in inflammatory papillomata; an extension of epithelial growth, and a formation of new blood-vessels. Most of the amœbæ disappear, but a small proportion enter epithelial cells, where, even in the non-nucleated stage, they could be detected," and the evil cycle is carried on.

Messrs Ruffer and Walker, the first pathologists who demonstrated the existence of the cancer parasite in England, state that they found a mixture of Foll's solution, with 1 per cent. of osmic acid, gave the most satisfactory results as a hardening reagent,⁶ especially in demonstrating the intranuclear parasites. Biondi's mixture as a coloring agent brings out the organisms with all the clearness that can be desired. The "coccidia, stained a light blue, enclose a dark brown nucleus, the cancerous cell is stained a dirty yellow white, while its nucleus takes a green tint" [Metschnikoff].

Metschnikoff is of opinion that the coccidiosis of the rabbit is a miasmatic disease of the most typical kind, and that carcinomata also approximate to the category of miasmatic affections. "Although less pronounced than malaria or goitre," he observes, "the endemic character of cancer is a fact that has often struck observers. The frequency of these malignant tumors is far from being the same in all countries. By the side

⁶ Second Note on Parasitic Protozoa in Cancerous Tumors. *B. Medical Journal*, Nov. 5, 1892.

of regions of the globe which are exempt, or very nearly so, from this disease [Faröe Islands] there are others where carcinomata are very common." According to Cohnheim's theory of a simple overgrowth of embryonic survival tissues, the average of victims to cancer should be the same in every part of the world, and liability to its ravages should be common to all the Metazoa. Metschnikoff points out another feature which cancers have in common with coccidian diseases—the exaggerated proliferation of the epithelial cells in the affected organs. How close the resemblance is, the following figures show.

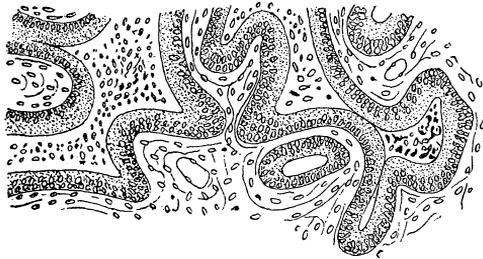


FIG. 6.

Adeno-Carcinoma of the Rectum in Man.

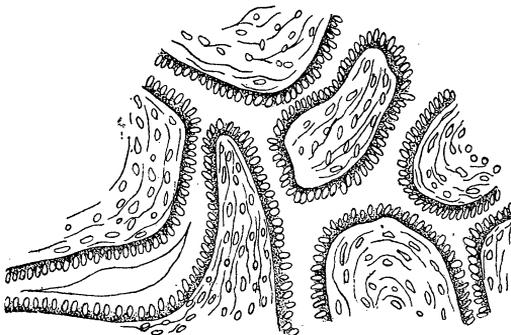


FIG. 7.

Hyperplasia of the biliary ducts of the rabbit under the influence of coccidia.

As yet, the study of parasitism in cancerous diseases is only beginning. The coccidia of the rabbit have been known for

half a century, but it is only quite recently that an important stage in their life-history has been made out. There are differences of opinion between observers; Mr. Jackson Clarke's amoeba-like organisms do not exactly correspond with the various forms of parasites described by some other pathologists. It is thought possible that the whole life-cycle of the protozoön may be passed within its human host; in any case, its exogenous history is not known, and this stage is the one which it would be the most useful to discover, since we are, at present, in utter darkness as to the mode in which the contagion is conveyed to the host. Cancer is pronounced to be a disease in which heredity plays an important part. Does it do so in the same way that hereditary predisposition acts in tuberculous diseases; not by a direct transmission of the tubercle bacillus, but by some mysterious lowering of the vital powers of resistance? It is hardly possible to imagine that microsporidia, hereafter to develop into the protozoön of cancer, can remain dormant for 50, 60, 70, 80 years.

The disease [so far as can be ascertained from experiments upon animals, themselves liable to cancer] is not directly transferable from one host to another. There remains, therefore, as a highly probable hypothesis that the exogenous form of the protozoön of cancer, like the flagellate monad of malaria and the coccidia of the rabbit, must be sought in contaminated soil or water. It is because this most important stage of the life history of the protozoön of cancer is unknown, that I have ventured to present a summary of some of the papers which have been appearing for some months in the *British Medical Journal* to the readers of the AMERICAN NATURALIST; hoping that workers skilled in researches among the Protozoa may take up the subject, and may come to the aid of the brilliant band of pathologists who have thrown so much light on a most difficult problem.