

GIBBES (H) *with the Author's Compliments*
SOME OBSERVATIONS *abl*

ON

THE ORIGIN OF OVARIAN CYSTS.

BY

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presented by the author -

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SOME OBSERVATIONS ON THE ORIGIN OF OVARIAN CYSTS.

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THE facts recorded in this paper have been derived from a series of investigations in fifteen cases of ovarian cysts removed during life from human subjects and from two cases where similar changes were found in the ovaries of the cat and rabbit.

The human cases consisted of some where the symptoms had induced the surgeon to remove the ovary although it was not excessively enlarged and of others where one ovary was transformed into an enormous sac, while the other was only four or five times the natural size and could therefore be utilized for the purpose of studying the changes which produced this abnormal condition.

I shall not touch in this paper on the clinical side of the question. I wish to point out some of the different causes which may produce cystic disease of the ovaries. The pathological changes found in these ovaries are of three kinds.

(1) An overgrowth of pre-existing tissue, which overgrowth is of such a character that it formed cysts from its mode of growth.

(2) A degeneration which by its breaking down forms cysts.

(3) Simple distension of Graafian follicles.

In the first form the walls of the cysts are composed of polyhedral cells, each with a nucleus. The cells

have a granular appearance caused by the presence of a fine network which is continuous with a similar network in the nucleus. The nucleus has a distinct membrane. The number of cells forming the wall varies and consequently its thickness, and their blood supply is very large, capillary vessels passing vertically between them at frequent intervals. They are surrounded on the outside by a layer of tissue resembling the stroma of the ovary, and processes from this layer pass in for a short distance here and there. On the inner surface there is a narrow band of fibrous tissue, while in the cavity is the remains of the coagulated fluid which has a decided yellow tinge, but no structure, beyond fibrin and a few leucocytes.

The first case of this kind that I examined was where an enormously enlarged ovary had been removed; and on examining it I found, lying in a small concavity but not attached, an oval cyst measuring half an inch in its longest diameter. On making sections of the wall, I found that it consisted of cells, etc., as described above. The next case was sent me by Dr. Ernest Copeland, of Milwaukee. He says, "The left ovary was nearly three times as large as the right and appeared quite vascular." On making a section a round body shelled out quite easily. In the right ovary there is a round body about three-quarters of an inch in diameter, growing in the substance of the ovary and forming a part of it. Sections of these show exactly the same appearances as described above. Another case is almost identical.

I also found this change in the ovaries of cat and rabbit, and here I could study it in the earliest stages. In the ovary of a cat I found the normal stroma largely replaced by a growth of these large cells. They were variously arranged, but in many places they formed circular or oval masses with a small central hollow in

which was a homogeneous material, resembling in appearance colloid matter, but differing in its chemical reaction. Colloid matter as also the liquor folliculi in the Graafian follicles, gives a distinctly alkaline reaction. This appeared to be neutral or slightly acid. In other parts these cells were arranged in rows extending nearly to the periphery of the organ, and in the rabbit's ovary the arrangement was the same except that only a very small portion of normal stroma at the extreme periphery was left. This new tissue in some parts surrounded a few large Graafian follicles, but the majority of the smaller ones had disappeared. This was notably the case in the rabbit's ovary, where only a very few remained at the extreme edge of the section.

From what I have said, it will be seen that in these ovaries the change is produced by an overgrowth of large cells, and the question to decide is what these cells are. Every histologist is familiar with the groups of cells described first, I think, by Kolliker, and considered by him to be of connective tissue origin, which are found both in the normal testis and ovary. Henle, Leydig, Waldeyer and Mihalkovics have also described them as connective tissue cells. Klein, on the other hand, considers them to be epithelial cells derived from the epithelial columns of the Wolffian body, and in the ovary Balfour has traced them from the Wolffian body. There is little doubt that the earlier observers were wrong and that they are of epithelial origin. After a very careful study of these cells in the normal ovary, I am convinced that the large cells I have described in the diseased ovaries are identical with them. What their normal function is cannot be made out; and it would seem as if they were embryonic remains not used in the development of the organ, and one is naturally surprised to find them overlooked by Cohnheim

in his theory of the development of neoplastic growths from embryonic remains. On examining the organs of various animals it will be seen that their number is very much larger in the testes and ovaries of some than in others. They are very abundant in the dog and the cat, while, as Leydig stated, they form the major part of the testis in the boar. Whatever these cells may be, I wish to point out that in these cysts of the ovary the wall is formed of them, and, as in the normal condition they have a large and separate blood supply, so in the abnormal growth they are abundantly supplied with blood-vessels. They are absolutely distinct from corpora lutea as I have many sections where a large corpus luteum is completely surrounded by them and the difference is very marked. There is also a difference in their reaction to staining agents. I have noticed marked vacuolation in many of these cells, a feature which has been attributed to the cells of malignant disease.

Doran in his work on "Tumors of the Ovary" (p. 102) describes a case, where he says "the microscopical appearances proved to be rather puzzling." I think the tumor in this case was one of these I have described.

In the *New York Medical Journal*, September 28, 1889, Dr. M. A. D. Jones describes a disease of the ovary which is called endothelioma. Fig. 3 of this paper is an exact representation of the naked-eye appearances I have described, and Fig. 9 shows the microscopical appearances under a magnification of six hundred diameters. It seems evident that the writer has been dealing with similar cases to those I have described, although I cannot agree with the deductions made.

From what I have said, it will be seen that these cells, which occur normally in the ovary, have, under

certain conditions, the power of germinating and permeating the organs, and in doing so, destroying the parenchyma of that organ, and their mode of growth is such as to produce a cystic change. There is nothing, however, to show that this new growth has any resemblance in structure or progress to carcinoma. The cells newly formed are identical with the originals, their arrangement is the same, there is no stroma further than that which is continuous with the stroma of the ovary, and they differ *in toto* from every case of carcinoma of the ovary I have ever seen.

The morbid change in the next class was one having a totally different character. It consisted of a degeneration of a peculiar kind. This occurs in different parts of the organ, and varies very much in amount. The earliest change appears as very small sinuous bands of homogeneous material amongst the spindle cells of the stroma, which have disappeared and are replaced by this substance. It also occurs in the walls of the arteries, in the adventitia, which becomes very much thickened and appears to be transformed into this homogeneous material; the muscle coat is not involved, although some of this material may be found between the muscle cells. The change in the adventitia is, however, very marked. This degeneration of the arteries is not universal, but affects a few vessels here and there. As the degeneration increases, it extends to some distance round the arteries. At the same time numerous isolated masses are seen throughout the organ, these vary in size and shape, some being sufficiently large to be visible to the naked eye. The change in all is, however, the same, a transformation of the normal tissue into a homogeneous hyaline material. This has generally a wavy outline, and in those masses visible to the naked eye it seems to have a stellate arrangement. It appears to

be entirely without structure, but branched cells are seen in it. Although there are large masses of this substance in places they are not solid, but appear to be made up of wavy rods, and between these in some parts are the branched cells. It may be uniform throughout, or in the larger masses the centre may be broken down forming a cavity. This degeneration has been variously described, but has generally been considered to be colloid. This it is not, at any rate, in its early formation, it does not give anything approaching to colloid reaction in sections of the organ. I have made a large number of experiments in this, and although I can show the colloid reaction in the wall of a small artery of the spleen where true colloid degeneration is going on, I can get no such reaction in an artery in the ovary, although when stained with log-wood they appear to be exactly alike. Whatever the degeneration may be its effect is to destroy portions of the ovary by changing them into this hyaline material, the centre of which is prone to break down and thus form a cyst. I have in one case seen a corpus luteum undergoing this change. I have examined several ovaries which have been removed as their fellows had undergone enormous cystic degeneration, and although it was impossible to trace this hyaline degeneration in the large one, it may be inferred from the changes found in the smaller that the degeneration was produced in the same manner in each.

In the third class, the cyst appears to be formed by dilatation of the Graafian follicles. In some of these cases where the ovary examined contained cysts two inches in diameter, and the other ovary had formed an immense sac, the wall was composed of normal ovarian stroma slightly condensed, but showing plainly the spindle cells. In others presenting similar appearances to the naked eye, a section under the microscope showed

a layer of rounded cells, varying in size, and somewhat resembling the normal cells of the Graafian follicles. I have sometimes found in connection with these cysts hyaline degeneration in some parts of the ovary, but not often. The appearances showed plainly that this degeneration had not, in these instances, caused the cystic formation. Microscopical examination of the cyst wall in the large sacs revealed nothing as to their causation.

The above observations may be of interest as showing some morbid conditions which can result in the formation of cysts. The peculiar formation first described from the epithelial cells is not of common occurrence, but is of great interest to the pathologist, and the problem is why these cells, when they have started into growth, should produce the forms they do. To understand this, their origin will have to be determined. It seems hardly credible that more than one-half of a boar's testes should be formed of tissue which was left over after the development of the organ. Ziegler describes a hyaline degeneration of the walls of blood-vessels which he calls a myxo-sarcoma, but so many different forms are described under this head, it is plain they are not all of similar origin. That there is nothing cancerous or malignant in this degeneration of the ovaries is plainly shown by the after-histories of all the cases from which they were removed.

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