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CONTRIBUTIONS TO THE HISTOGENESIS OF THE
PAPILLARY CYSTOMATA OF THE OVARY.

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*(From the Pathological Laboratory of the Johns Hopkins University
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It is only within the last few years that the ovarian papillomatous cystomata have been recognized as constituting a class of tumors perfectly distinct from the ordinary glandular cystomata; for previous to the year 1877 when Olshausen¹³ first demonstrated this fact the two forms of growths were considered as one, or at most subdivisions of the same class of tumors, and consequently as derived from the same source. This fact must be borne in mind in considering all the early work done upon this subject. Although the ordinary ovarian cystoma had been known for a great length of time as ovarian dropsy, it was not until 1829 that Hodgkin¹ pointed out the existence of papillary growths upon the interior of the cyst. He ascribed their formation to pressure, and it will perhaps be interesting to quote his words describing the process. "I have stated that it is at particular points on the interior surface of the superior cyst that clusters of inferior cysts take their origin. It sometimes happens that the number of cysts forming the clusters is so great in proportion to the space which they occupy that, like trees too thickly planted, they interfere with each other's growth. Their development is more or less limited to an increase of dimension in length. Yet as their free extremities are allowed to diverge, we sometimes find the slender peduncle gradually dilating into a pyriform cyst. At other times the dilatation does not take place till near the extremity of the peduncle, and then produces a cyst more nearly resembling a grape or a currant. At other times no dilatation takes place, probably from the cavities having been wholly obliterated. The pedunculated cysts or the extreme of this variety in the form of filaments are either produced singly, but in the closest approximation from a particular spot of the containing cyst, or they may



be attached to it by a common pedicle from which the proper pedicle of each proceeds. These elongated structures sometimes become highly vascular and in the defect of an internal secretion contribute largely to that which occupies the sac into which they project." We thus see that Hodgkin clearly directed attention to the papillary growths and regarded their origin as identical with that of the secondary cysts.

Following Hodgkin there came a period during which it was thought that all forms of ovarian tumors were derived from the Graafian follicle; and this was the prevailing idea until 1848, when Virchow² showed that the Graafian follicle produced only small cysts, which still contained the ovum, hydrops folliculi, and was incapable of giving rise to the large colloid tumors, for which other modes of origin must be sought. He believed that spaces lined by epithelial cells were constantly appearing in the stroma, from which the cysts were developed, and that they were therefore of connective tissue origin and totally distinct from the cysts developed from the Graafian follicle. More or less similar views as to their origin from connective tissue were advanced by many, among whom were Foerster,³ Rokitansky⁴ and Frerichs.⁵ Once more the Graafian follicle theory was presented in 1864 by Klob⁶ and Wilson Fox,⁷ both of whom considered that all forms of ovarian cysts could be derived from them. Fox described with great accuracy the gross and microscopic appearances of both the glandular and papillary cysts; his ideas of their development were, however, erroneous; for having accurately described the gland-like structures found in the cyst wall, he considered that they were only apparent and were due to depressions formed between villi, which sprang from the wall of the cyst. He explained the production of smaller cysts in the wall of the larger by supposing that the extremities of the villi came into apposition and then became adherent, and thus produced cavities beneath them, which might readily become larger and form small cysts. In several cases he saw structures, which he considered Graafian follicles, sending out diverticula, though in none of his cases was he able to demonstrate the presence of ova in them.

Mayweg,⁸ four years later, attempted to reconcile the conflicting theories. Like Fox,⁷ he supposed that the great majority of ovarian cysts were derived from Graafian follicles, but that a certain proportion had a connective tissue origin, as was believed by Virchow,² Rokitansky⁴ and others. He not only considered the papillary cystoma to be a variety of the ordinary form; but con-

sidered the formation of papillae a constant and necessary occurrence in the formation of the multilocular cystomata. He thought that as the papillae increased in size in a small cyst, they would be subjected to increased pressure by the contained liquid, and that in this way their tips would be forced into contact and, after they had lost their epithelium by attrition, become adherent and thus form secondary cysts by a method very similar to that described by Fox.

In this connection, he gave a most interesting figure (*Fig. 1, A, a*, in Mayweg's article), in which he depicted a small papillary growth arising from the wall of a Graafian follicle, in which the ovum was still present.

During the year before and after Mayweg's⁸ dissertation the papers, which prepared the way for Waldeyer's wonderful article on the subject, were written. In the year 1867, Luecke and Klebs,⁹ after studying several tumors removed by Spiegelberg came to the conclusion that the growths were to be compared to the adenomata and it was impossible for them to be of connective tissue origin. In 1869, Boettcher¹⁰ foreshadowed Waldeyer's¹² work, for in the more solid portions of a cystoma, he found "an abundance of epithelial duct-like structures, which could be seen dilating into small cysts;" these structures he compared to Pflueger's ducts and stated that the cystomata might arise from these structures or from Graafian follicles or from both. He also considered that papillomatous growths were formed by epithelial structures growing down into the stroma, and not by the stroma pushing forward the epithelium.

Up to this time there was considered to be no particular difference between the papillary and glandular tumors; indeed they were usually considered merely as different phases of growth in the same tumor. As to their histogenesis, both forms alike were supposed to be derived from the Graafian follicle or ovarian stroma or both, according to the theory prevailing at the time. Though occasionally the proofs did not appear convincing, and the writers refused to commit themselves to any theory, as Bauchet¹¹ who said, "Some authors suppose they arise from the Graafian follicle; others from the ovarian stroma. It may be so; but there is absolutely no anatomical ground for the supposition." To Waldeyer¹² is due the honor of having settled the question as to the histogenesis of the ovarian cystomata and of placing the entire subject upon a sound basis. For in his epoch-making work, "Eirstock

und Ei," he gave a perfectly clear description of the anatomy and development of the ovary and thus laid the foundations for scientific study of its pathology; and in his work on the epithelial ovarian tumors he clearly demonstrated that the cystomata were derived from Pflueger's ducts, which were either remnants from foetal life or newly formed in the adult. According as the cystomata contained papillary ingrowths or not, he divided them into two classes:

1. *Cystoma proliferum glandulare*. 2. *Cystoma proliferum papillare*. He did not, however, consider that there was any generic difference between the two classes of growths; the difference depending entirely upon the relative rapidity of growth of the component parts of the tumor. If the epithelium took the more active part in the growth, an adenomatous tissue resulted and a glandular cystoma was produced; if, on the other hand, the connective tissue was the actively growing part, it pushed forward the epithelium and produced papillary ingrowths from the cyst wall and gave rise to a papillary cystoma.

This was the state of affairs until 1877, when Olshausen¹³ showed that the papillary cystoma differed both anatomically and clinically from the glandular form and should therefore be considered as constituting a class of growths totally independent from them. He came to this conclusion by considering the following facts: "Anatomically these tumors differ from the cystomata in that they are usually only of moderate size and never attain the huge proportions which are frequently observed in the glandular cystomata. They contain in their interior numerous papillary, cauliflower-like tumors, which often entirely fill the lumen of the smaller cysts and break through their walls, and not infrequently through the walls of the principal cyst. After breaking through the cyst wall, they usually spread to the neighboring organs and grow particularly upon the peritoneum. The interior of the cysts is usually lined by ciliated epithelium. The number of cysts making up the tumor is quite limited.

The growths are usually bilateral and in three-fourths of the cases develop extra-peritoneally, usually between the folds of the broad ligament; and lastly the fluid contents are characterized by a lack of colloid constituents. Clinically, these tumors grow far more slowly and soon give rise to pressure symptoms, owing to the fact that they are developed *extra saccum peritonei*. They are frequently accompanied by ascites, which is often of consider-

able amount and recurs rapidly after tapping. And lastly they form metastases, or, more properly speaking, grow by dissemination of the papillomata over the peritoneum and invade the other organs."

From the fact that they grew within the folds of the broad ligament and were lined by ciliated epithelium, Olshausen concluded that their development was in some way connected with the parovarium, which was known to contain ciliated epithelium and which in some cases penetrate the hilum of the ovary as the so called medullary cords (Markstraenge) of Koelliker.¹⁴ This view appeared quite plausible and soon gained general acceptance, and, in spite of the fact that it has since been repudiated by its originator, is still held by many writers on the subject.

Olshausen's work was soon followed by an article by Fischel,¹⁵ who accepted Koelliker's¹⁴ theory of the development of the ovary (that is, that only the ova are developed from the germ epithelium, and that the membrana granulosa is derived from strings of cells, of Wolffian body origin, which penetrate the hilum of the ovary), and stated "that we must consider the ciliated ovarian cystomata to be derived from parovarial elements, particularly from the granulosa cells and not from the parovarium or organ of Rosenmueller as such." He adduced no evidence to prove this point, and from the description of his specimen it is not at all clear that he had to do with an ovarian tumor at all, but rather with a papillary cyst developing in the broad ligament; for he stated that on the upper part of the cyst the flattened out ovary was found, and that the tumor developed from the hilum. And according to his description it might have arisen just as well from the parovarium. The only point that he brought forward to prove the truth of Koelliker's hypothesis was that here and there in his specimens he found ova around which he could find no trace of a membrana granulosa, and considered that they lacked a membrana granulosa because the ingrowths from the Wolffian body had not reached up to them. Coblenz,¹⁶ the same year, described two cases of papillary cysts of the ovary; one of which was the size of a goose egg and was covered with papillary growths; it contained small cysts, from whose walls papillary projections arose. On section, he found the ovary traversed in all directions by bands of epithelial cells, arranged more or less radially to the hilum and resembling Pflueger's ducts in appearance. Some of these structures communicated directly with the surface of the ovary but never contained ova. These bands of cells could be

seen dilating into small cysts, which were lined by ciliated epithelium and contained papillary ingrowths.

A similar condition was noted in a small superficial papilloma of the ovary in another case. These structures he thought were of Wolffian body origin and corresponded to Koelliker's "Markstraenge." From his elaborate study of the subject, he concluded "that the lining of Pflueger's ducts, as well as Koelliker's "Markstraenge," is capable of functioning as a real mucous membrane, since they are both descendants of such structures; and that the starting point of the glandular cystomata is from Pflueger's ducts and that of the papillary ciliated cystomata from Koelliker's "Markstraenge," at a time before they are differentiated, the one into ova and the other into granulosa cells.

The work of Fischel¹⁵ was confirmed by Stryczek¹⁷ in every particular, and he stated that growths developed from parovarial elements were far more frequent than was usually supposed.

The theory of development from remains of the Wolffian body has appeared fascinating to English and American writers on the subject, and even now, when most others have forsaken the theory, they still cling to it.

Thus, Doran¹⁸ still accepts the theory in its widest possible sense. For he regarded even very small papillary cysts in the zona parenchymatosa of the ovary and far removed from the hilum (the seat of the remains of the Wolffian body), as of Wolffian body and origin, and stated that "they must have originated from Wolffian elements in the stroma of the parenchyma of the ovary." And in speaking of a case of papillary broad ligament cyst, he said "the absence of any trace of ovary in this specimen of Mr. Thornton is strong evidence in favor of the supposition that the cyst arose in the hilus of the ovary and forced its way into the broad ligament, and on the other hand absorbed or destroyed the tissue of the parenchyma of the ovary." In his work,¹⁹ "Tumors of the ovary, fallopian tubes and broad ligaments," he recorded a most interesting case, which he observed in the ovary of a seven months' foetus. It contained several small cysts 1-16 to 1-12 of an inch in diameter, which were lined by ciliated epithelium and filled by papillary growths; and in spite of the fact that the ovary contained no ova, while the other ovary contained them in large quantities, he concluded that they were also derived from Wolffian body elements.

The latest American writer on the subject is Howell,²⁰ in Mann's System of Gynæcology (1889), who accepted the same views as Doran, and stated "that other views as to their development are far from satisfactory."

We will now turn from these theories, which at present are considered by most original workers on the subject to be unfounded, and consider those which offer simpler and more rational explanations of the development of these growths.

We will first consider the theories which suppose the germinal epithelium of the ovary to be the source of origin for the papillomatous growths. The first important theory advanced in this direction was that of Marchand,²¹ in 1878, who, in an able work on the subject, was able to substantiate Olshausen's statement as to the distinction between the glandular and papillary cystomata, and stated that the presence or absence of cilia in the growths made no difference in this regard. He also stated that they were developed from several points of origin, basing the statement upon a case of Olshausen's, in which the lateral half of an ovary, enlarged to the size of a walnut, was studded with small cysts, varying from a pin's point to a cherry in size, and which were lined by ciliated epithelium and were filled by papillary growths. He repudiated the theory that they were developed from the Wolffian body, and directed attention to the near relationship existing between the epithelium of the tube and that covering the surface of the ovary, and pointed out that at an early period of foetal life they are one and the same surface, and in the adult are only separated from one another by a small band of tissue at the fimbria ovarica. His theory was that in some cases the dividing line between the two forms of epithelium, instead of remaining at the end of the fimbria ovarica, might extend over the lateral portion of the ovary, and thus cover it with ciliated epithelium, from which ciliated processes analogous to Pflueger's ducts might extend into the stroma and possibly in some cases form Graafian follicles lined by ciliated epithelium, from which ciliated cysts might readily arise. Owing to the near relationship of such structures to the epithelium of the tube with its peculiar arborescent structure, it was not difficult to conceive that these cysts should have a tendency to form papillary ingrowths.

The same year, a most interesting observation of De Sinety and Malassez²² placed the entire subject in a new light. For, on microscopic sections of what appeared to be an ordinary small

cystic ovary, with dilated follicles in both its superficial and deeper portions, they were surprised to discover that the cysts were not dilated follicles at all, but were lined by a single layer of columnar epithelium, which at times was ciliated. Epithelial tubes running through the ovary in various directions were also seen. These structures were lined by columnar epithelium, which was also ciliated; and some of them were seen to open directly upon the surface of the ovary, and their epithelial lining to be continuous with the germinal epithelium of the ovary; while others were seen to communicate with smaller cysts, which were evidently formed by dilation of the above mentioned epithelial tubes. They observed this condition in two cases, and considered the structures to be analogous to Pflueger's ducts, and to have been formed in adult life. These structures they naturally considered to be the source of the papillary ciliated growths, and they certainly offered a more rational explanation of their production than the Wolffian body theory. They believed that the frequent occurrence of these cysts near the hilum was due to the increased vascularity of that part of the ovary: "note also that the most frequent seat for vegetations is in the neighborhood of the pedicle, as if the more vascular portions of the ovary were more propitious for pathological development."

The observations of De Sinety and Malassez were soon confirmed, for the next year Fleischlen²³ published similar cases. Both of his observations were made in cases of papillary cystomata, and in each he found epithelial tubes, lined by columnar and ciliated epithelium, penetrating in all directions the intact portions of the ovary, which presented an appearance similar to that of the Pflueger's ducts, as described by Waldeyer¹² in the foetal ovary. These structures could be seen dilating into cysts, lined by columnar and ciliated epithelium, which sometimes contained papillary growths; and occasionally a direct communication between these structures and the superficial epithelium of the ovary could be demonstrated. The following year he was able to demonstrate a similar condition in another papillary cystoma, in which the surface of the intact portion of the ovary was covered by ciliated epithelium, between which and the epithelial tubes and the small cysts a distinct connection could be traced. This was certainly conclusive proof, and no one could possibly object to his conclusions:²⁴ "that the papillary cystomata arise from the ovary and not from the parovarium, and that they take their origin from

tubes lined by columnar and ciliated epithelium, which originated from the germinal epithelium."

Indeed the observations of De Sinety and Malassez and Fleischlen were so convincing, that Olshausen,²⁵ in the second edition of his work "Die Krankheiten der Ovarien," in 1886, totally repudiated his original idea as to their development from the Wolffian body, and stated that he could take no exception to Fleischlen's statements.

The latest work in this connection was by Frommel²⁶ (1890), who described a case of superficial papilloma of the ovary, which was clearly derived from the germinal epithelium. He also thought that the usual form of papillary cystoma might develop from the germ epithelium or from the granulosa cells of the Graafian follicle. He arrived at the latter conclusion purely by a logical process and had no preparations upon which to base his statements. He argued thus: "We know by Waldeyer's researches that the granulosa cells of the Graafian follicle are derived from the germinal epithelium; we also know from Fleischlen's observations that, under certain circumstances, the germinal epithelium may become ciliated, and investigations upon certain of the lower animals have shown that in some species both the germinal epithelium and the granulosa cells are ciliated; such being the case, why cannot the granulosa cells in man become ciliated under certain circumstances of which we are as yet ignorant? And if so, why may not papillary cystomata sometimes arise from the Graafian follicle?"

According to him, the superficial papilloma is more liable to be developed when a few broad ingrowths of germinal epithelium occur at some distance apart from each other; while, if a number of ingrowths take place from a comparatively small area, the papillary cystoma is more apt to be formed.

The germinal epithelium theory received a qualified support from Steffeck,²⁷ who thought that it might play a part in the development in some cases.

Somewhat allied to the views just mentioned, is the theory of Nagel,²⁸ who pointed out the fact that the germinal epithelium is frequently preserved under peritoneal adhesions about the ovary, and that the irritation caused by the inflammatory changes might lead to a proliferation of the germinal epithelium, with the formation of pseudo-Pflueger's ducts and the development from them of all forms of ovarian tumors. The proof adduced in support of these observations is not at all convincing.

In this connection we might also refer to the case of superficial papilloma of the ovary, reported by Gusserow and Eberth,²² whose development they stated was dependent upon inflammatory changes and probably upon an oöphoritis. But in view of what has been said above, such a theory is absolutely without foundation.

Having considered all other possible sources of development, we will now consider those theories which take the Graafian follicle as the point of development for these growths. As I pointed out in the first part of the article, this was one of the earliest theories concerning the origin of all forms of ovarian tumors, and one which always received more or less support, except for a short time after the appearance of the work of Waldeyer and Olshausen, when it was almost completely lost sight of. In this connection it is only necessary to recall the fact that Fox,⁷ Klob,⁶ Mayweg,⁸ Spiegelberg³⁰ and Boettcher¹⁰ accepted the Graafian follicle as the origin of most, if not all, cysts of the ovary; and that Mayweg and Fox considered the formation of papillary processes from the wall of the follicle to be the first step toward the formation of multilocular cystomata. The idea that ciliated papillary cysts might be derived from ciliated Graafian follicles was advanced by Marchand²¹ and Frommel,²⁶ from purely theoretical considerations; but they had no specimens to prove that the Graafian follicle in man could ever become ciliated, and much less give rise to papillary growths.

Another recent believer in the Graafian follicle origin of the papillomata, was Koeberle;³¹ but, like Marchand and Frommel, he possessed no accurate observations upon which to base his statements.

The most recent work on the subject has tended, however, to bear out the theoretical deductions of Marchand and Frommel, as will be seen from the consideration of the recent work of Von Velits and Steffeck.

Von Velits,³² in 1889, wrote a most interesting article on the histology and genesis of the ciliated papillary cystomata, basing his work upon the consideration of nine cases. In two cases, in relatively intact portions of the ovary, he found small cysts, apparently dilated follicles, which were lined by a single layer of cylindrical epithelium, which in some cases was ciliated; and in one instance he was fortunate enough to find an ovum in one of them, which abundantly proved that the theories of Marchand²⁰ and Frommel²⁶ were correct, and that it was possible for the human Graafian follicle to become ciliated.

As none of these small cysts communicated with the germinal epithelium, he considered them all Graafian follicles, and stated that it was from them that the papillomata were developed. In none of them, however, was he able to demonstrate papillary growths, and consequently absolute proof of the correctness of his assertions was still lacking. He, however, considered the presence of psammoma bodies to be absolutely pathognomonic of ciliated papillary cystomata, and, as he found them in the neighborhood of the ciliated Graafian follicles, he considered his position positively proved.

The very latest work published on the subject of the ovarian tumors was by Steffeck,²⁷ 1890, who once more reverted to the old view that the glandular cystomata might arise from the Graafian follicle. He came to this conclusion on finding Graafian follicles, which still contained ova, undergoing proliferative changes and sending out offshoots into the surrounding tissue, from which daughter cysts were developed. He sustained his position by drawings, which, if correct, prove his point. He did not consider the follicle the only source of origin, but stated that they might be developed equally as well from Pflueger's ducts; and that if either of these structures became ciliated, they might give rise to the ciliated papillary cystoma. He stated the case as follows: "Primarily, neither the germinal epithelium nor follicular epithelium is ciliated; but at any time either epithelium may be converted into high cylindrical epithelium. If, now, under certain circumstances, an 'irritation' be given, which will cause cylindrical epithelium to become ciliated, nothing could be more natural than for this 'irritation' to affect the cylindrical follicular epithelium, as well as the cylindrical germinal epithelium; and consequently both forms of epithelium could take part in the production of the ciliated papillary cystomata."

In the preceding pages I have endeavored to trace the history of the several theories advanced in connection with the development of these growths; and from their variety, it will readily be seen that a definite conclusion has not yet been reached. Indeed, the number of theories advanced has been limited only by the number of structures entering into the composition of the ovary. Thus, before the time of Waldeyer, we had the connective tissue and Graafian follicle theories; and after the work of Pflueger and Waldeyer added the Pflueger's ducts and germinal epithelium to the component parts of the ovary, the limits of possibility

were extended, and we had these structures utilized as sources of origin. When to this we add Noeggerath's³³ theory of the development of the cystomata from the blood-vessels, we see that every tissue entering into the formation of the ovary has been laid hold upon and made the basis of one or more theories. As if these were not theories enough, others have sought in the parovarium or Wolffian body the possible source of these growths.

I now desire to record several interesting cases, which I hope will throw more light upon the subject of the histogenesis of the papillary ovarian cystomata and enable me to show that several of the theories, instead of contradicting one another, are based upon accurate observations and are entitled to consideration.

CASE I.—“*Adherent tubes and ovaries,*” *peri-salpingo-oöphoritis, small papillary cyst in mesosalpinx, and ciliated structures of tubal origin in the ovarian stroma.*

Mrs. V., March 26, 1890, both tubes and ovaries removed by Dr. Kelly for chronic salpingo-oöphoritis; recovery. The structures removed presented the usual appearance in such cases; both tubes and ovaries being covered by thin adhesions and more or less bound together. The ovaries presented numerous dropsical follicles and the tubes a moderate degree of catarrhal salpingitis. The left tube and ovary were adherent, particularly at their lateral ends, where the fimbriated extremity of the tube was densely adherent to the ovary. Just at this point, apparently on the surface of the ovary, was a small cyst 5 mm. in diameter, with clear contents; which was apparently a dilated follicle.

On cutting sections through this cyst and the adjoining portions of the tube and ovary, one obtained the appearance represented in *Fig. 1*. It was then seen that the cyst did not arise from the ovary at all, but was situated in the mesosalpinx, surrounded by a thin layer of non-striated longitudinal muscular fibres. From the inner wall of the cyst arose several small papillary projections, three of which are represented in the drawing. All of them possessed a framework composed of spindle-shaped connective tissue cells, are well supplied with blood-vessels, and are covered with a single layer of high columnar ciliated epithelium, with large oval nuclei. In the lower portion of the figure is seen ovarian tissue, which contains primitive Graafian follicles (*Fig. 1, a*).

The ovary and mesosalpinx were densely adherent for the greater part; but in a part of their extent, where they were not adherent, a double line of epithelium was seen, which varied from flat to columnar in shape, and represented the original germinal epithelium and the peritoneal surface of the mesosalpinx (*Fig. 1, b*). At the lower left hand corner of the drawing (*Fig. 1, c*), is seen a portion of the fimbriated extremity of the tube, which is densely adherent to the ovary and covered by high columnar ciliated epithelium. The most interesting feature of the specimen and the one to which I desire to direct particular attention, is the occurrence of larger or smaller spaces, lined by high columnar ciliated epithelium and imbedded in the stroma of the ovary just adjacent to the fimbriated extremity (*Fig. 1, d*). These structures are quite numerous and vary considerably in size, from very small circular structures to larger structures with an irregular outline. They are all lined by high columnar ciliated epithelium, similar to that seen on the fimbriated end of the tube, and apparently represent sections made through epithelial ducts in various directions. Their origin was not, at first sight, apparent; but on cutting serial sections it could be seen that several of them were directly continuous with the epithelium covering the adherent fimbriated extremity of the tube, from which they were clearly outgrowths.

As represented in the drawing (*Fig. 1, d*), they were not confined to the stroma of the ovary, but were also found between the muscular layers of the mesosalpinx. Whether the small cyst above referred to was derived from such a structure I am unable to state absolutely; for I have seen similar cysts in the mesosalpinx in cases in which there was no suspicion of such epithelial growths as those mentioned. This point, however, is a matter of indifference; for whatever may be the origin of the cyst in the mesosalpinx, there can be no doubt as to the presence of these epithelial structures in the ovary and their origin from the tubal epithelium. This observation, as far as I am able to discover, is unique, and tends in a limited way to substantiate Marchand's²¹ theory of the origin of papillary cysts from ingrowths of ciliated epithelium, which were derived from that of the tube by Nature's failure to establish at the end of the fimbria ovarica the usual division line between the non-ciliated germinal epithelium and the ciliated epithelium of the tube.

The difference between Marchand's theory and my observation is, that in his case, the presence of ciliated epithelium on the ovary was a congenital defect; while in my case it occurred in adult life and probably was the result of disease.

I will refrain from any theoretical attempts to explain the cause of this proliferation of the tubal epithelium, and will be content with the mere statement of the fact.

In this case we have structures lined by columnar ciliated epithelium, of tubal origin in the stroma of the ovary; and we might readily conceive that in some instances papillary ciliated cysts might develop from them. This mode of origin is closely related to that supposed by Marchand and clearly indicates that his theory is not beyond the limits of possibility.

CASE II.—*Superficial Papilloma of the Ovary; Hydrosalpinx, with peculiar cystic formation in the tube, small corpus luteum cyst and adhesions about tube and ovary.*

Mrs. H., laparotomy by Dr. Kelly, October 15, 1890. Both ovaries and tubes removed; recovery. Description of specimens: Right side—Tube measures 6 cm. in length, 0.3 at narrowest part and 0.9 cm. at thickest part, fimbriated extremity free; the tube appears normal. Ovary measures 4, 3, 1½ cm. in its several diameters; is covered by thin adhesions, with many cicatrices on its surface. On section, one sees at its median extremity, near its upper border, a corpus luteum cyst 1 cm. in diameter and adjoining it a dilated follicle. On the superior surface of the tube are numerous small clear cysts, ½ to 2 mm. in diameter, and below the tube the enlarged parovarium. Left side—The tube was represented by a hydrosalpinx, which was ruptured during the operation. Its fimbriated end was closed and its uterine end firmly adherent to the ovary.

Left ovary measures 4, 2, 1.5 cm. in its various diameters; and its surface covered with numerous adhesions and cicatrices. At its lateral end and adherent to the end of the tube is a mass of small cysts 1.5 cm. in diameter, apparently a beginning cystoma. On the superior surface of the ovary, about its middle, is a papillary mushroom-like mass, triangular in shape, and 1 cm. in diameter and 3 mm. thick, which arises from the ovary by a pedicle about 2 mm. long and the same in diameter. The surface of the mass is marked by numerous fine lines, indicating depressions into its interior.

Sections through the apparently cystic formation at the end of the ovary show that it consists of a twisted mass of epithelial structures, which is connected with the lumen of the tube. The tube and ovary were adherent, and between them and lining the interior of some of the adhesions is well-preserved germinal epithelium. Remains of the Wolffian body were seen in the mesosalpinx.

The point of interest for us in this very interesting specimen, is the superficial papilloma of the ovary, which, as far as I can learn, is the ninth case on record^{16, 21, 26, 29, 34, 35, 36}. Sections through the papillomatous mass and the subjacent portions of the ovary (*Fig. 2*) reveal most interesting conditions. The growth had a distinctly mushroom-like shape and was composed principally of spindle-shaped cells, exactly similar to those found in the ovary, with which they were continuous through the pedicle; its blood supply was very scanty. Its most interesting feature was that it was penetrated in all directions by epithelial structures, varying in shape from simple cylindrical canals to broad, flat depressions, some of which extended through almost its entire thickness, and all of which were lined by a single layer of ciliated cylindrical epithelium (*Fig. 2, a*). All these epithelial structures could readily be traced to the surface of the growth, where the broad, flat depressions were seen to correspond to the lines mentioned in the macroscopic description. The ciliated epithelium lining them extended up to the surface of the papilloma, from which the epithelium unfortunately had been rubbed off, but which I suppose was similar to and continuous with the epithelial lining of these structures.

The pedicle presented the same structure as the growth itself, and was perforated by numerous epithelial structures, lined by ciliated epithelium. It also contained a typical psammoma body (*Fig. 2, b*). The subjacent ovarian tissue contained no ova, but was perforated in several places by epithelial structures similar to those found in the papillomatous mass (*Fig. 2, c*). It also contained psammoma bodies (*Fig. 2, d*).

The germinal epithelium was absent from the greater part of the surface of the ovary and was only preserved in one or two protected portions (*Fig. 2, e*), when it was found to be represented by a single layer of tolerably high, columnar, ciliated epithelial cells, which were of the same appearance as those lining the epithelial structures in the papillomatous mass and the ovary. This condition of the germinal epithelium present, indicated that the

entire epithelial covering of the ovary had been of the same character, and made it most probable that the surface of the papilloma had also been covered by ciliated epithelium.

The ciliated condition of the germinal epithelium is most interesting, and is similar to that reported by Flaischlen in another case. It also proves conclusively that under some circumstances the germinal epithelium may become ciliated, without supposing any connection to exist between it and the epithelium of the tube, as Marchand did. The appearance of the growth and the ciliated condition of the epithelium is conclusive proof that it was in some way formed by ingrowths of the germinal epithelium into the stroma of the ovary; and most probably, as described by Frommel²⁶ in a similar case, by broad, flat processes of epithelial cells extending down into the stroma of the ovary and almost cutting out a portion of it, which, as it grew, was raised above the surface of the germinal epithelium and thus made to appear as a superficial growth. Moreover, the presence of spaces lined by ciliated epithelium in the stroma of the ovary is analogous to those described by De Sinety and Malassez,²² and Flaischlen,²⁴ and it is most probable that papillary growths would have sprung from their walls as they increased in size, and thus have given rise to a papillary cystoma.

This observation cannot be considered ambiguous in any sense, and the only possible conclusion which can be drawn from it is, that under certain circumstances the germinal epithelium may become ciliated and give rise to papillary growths, of both varieties, as stated by De Sinety and Malassez,²² Flaischlen,²⁴ and Frommel.²⁶

This is certainly a rational explanation for many cases, and it is more than probable that the epithelial structures described by Coblentz¹⁶ in several of his cases, were derived from the germinal epithelium instead of the Wolffian body.

CASE III.—*Beginning Papilloma of the Ovary; acute purulent salpingitis.*

K. K., aged 27 years; laparotomy, November 1, 1890, by Dr. Kelly; recovery. Ovaries and tubes of both sides removed. Description of specimens: Left side—Tube measures 10 cm. in length, 0.5 at uterine and 1.5 cm. at fimbriated end; fimbriated extremity free. The tube is filled with bloody pus, and its outer

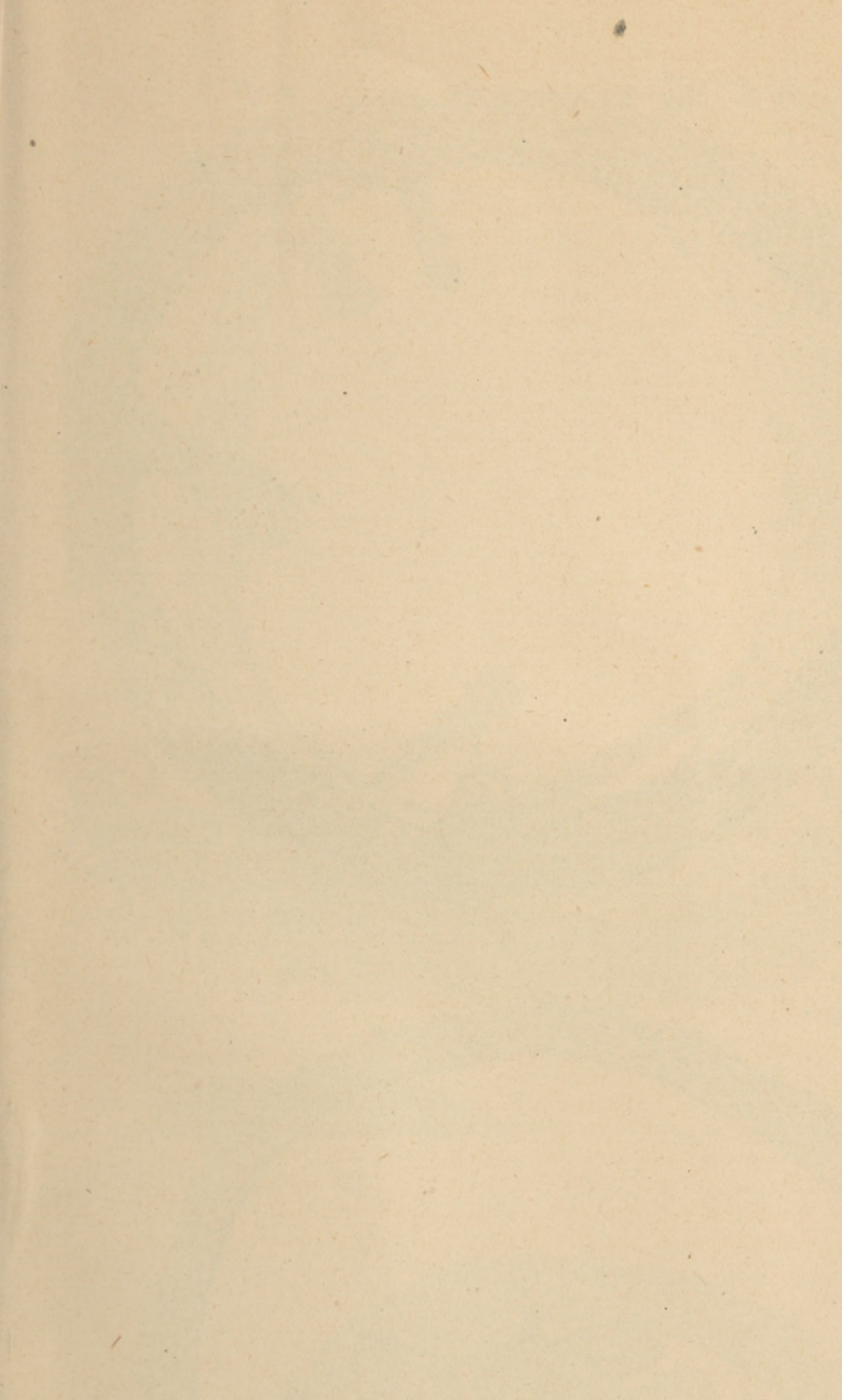


Fig. I.

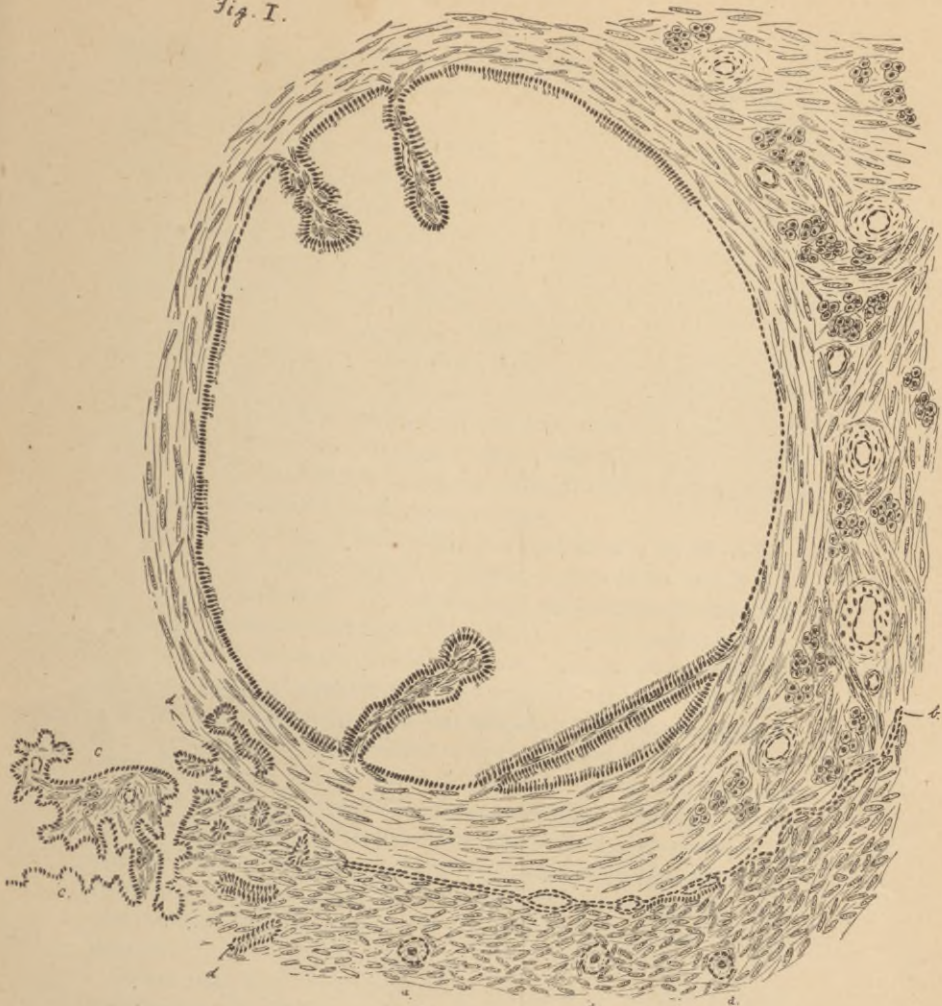


Fig. III.

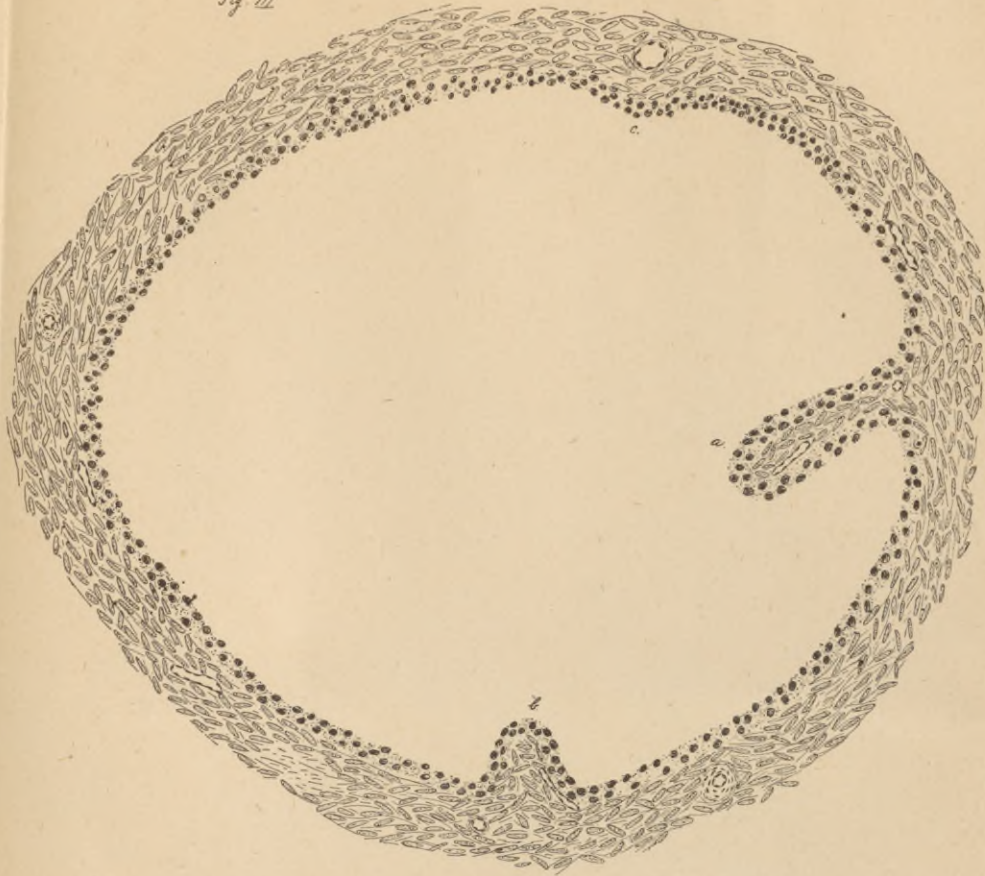


Fig. II.

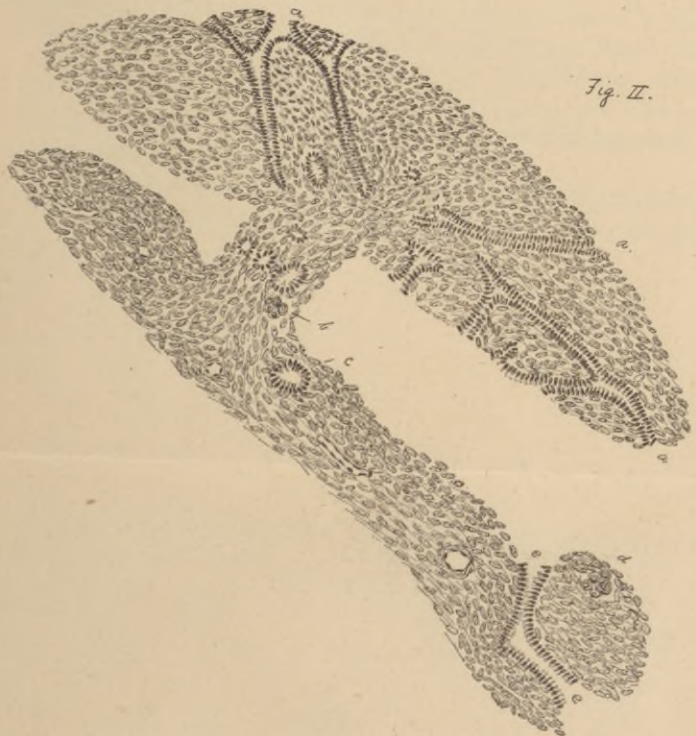


Fig. IV.



half is of a dark red color, owing to the intense congestion. The mesosalpinx is apparently normal. The ovary is very flattened out and measures 5, 3 and $\frac{1}{2}$ cm. in its various diameters; on its surface are numerous thin adhesions, and on section it is soft and presents numerous follicles with haemorrhagic walls. Microscopic sections of the tube show that it is intensely inflamed, with its vessels engorged and its lumen filled with pus. Its outer half is so intensely congested that the folds of the mucous membrane are almost entirely filled with blood. On its peritoneal surface is seen a fresh fibrinous exudate. Cultures from the pus demonstrate the presence of numerous colonies of the staphylococcus aureus. Sections of the left ovary show numerous ripe and dilated follicles, with hæmorrhage into them and also into the stroma. Right side—The tube measures 6 cm. in length, 0.4 at uterine and 1.5 cm. at the fimbriated extremity; the fimbriated extremity is occluded and somewhat adherent to ovary.

The ovary is small, measuring 3, 2 and $1\frac{1}{2}$ cm. in its various diameters; its surface presents numerous cicatrices and is covered by thin adhesions. A longitudinal section through the ovary shows the portion about the hilum filled with large thick-walled vessels; while the zona parenchymatosa contains many dropsical follicles, many of which have very irregular outlines. The most interesting condition for us in this specimen is a Graafian follicle, which presents marked evidence of beginning papillary formation. This is a dilated follicle about 4 mm. in diameter, and situated near the superior surface of the ovary, and filled with clear liquid.

On section (*Fig. 3*), it presented the typical appearance of a dilated follicle, having a typical membrana granulosa, which was composed of several layers of cuboidal epithelial cells, with large clear nuclei and surrounded by the spindle cells of the ovarian stroma.

From one point of its inner wall a club-shaped process about 1 mm. long projected into its interior (*Fig. 3, a*). This process was covered by the many layered membrana granulosa cells, and its framework composed of spindle cells and blood vessels, which were continuous with those of the surrounding stroma. A short distance from this, a similar but smaller process was also noted (*Fig. 3, b*), and at a third point, a slight elevation indicated the beginning of a similar process (*Fig. 3, c*).

All of these structures were covered by several layers of epithelial cells, similar to and continuous with those lining the rest of

the follicle, and their framework was composed of the spindle-shaped stroma cells, containing vessels. These projections were evidently produced by ingrowths of the ovarian stroma toward the interior of the follicle, which simply pushed before them the membrana granulosa, which still covered them.

I consider that this specimen represents the very earliest stage in the development of the ovarian papillomata and clearly demonstrates that they may be developed from the Graafian follicle.

In spite of the fact that I was unable to demonstrate an ovum within the follicle, I believe that there can be no question as to its identity. For it is only necessary to look at the epithelium lining it to recognize in it the typical membrana granulosa; and a comparison of this follicle with others which still contain ova places the question beyond all doubt.

The specimen just described does not, however, place the histogenesis of the papillomata beyond all doubt; for it would be impossible to state *a priori* that these simple outgrowths could give rise to the complicated forms of the developed growth. But my next observation will demonstrate that this is the case and will thoroughly establish this mode of origin for the papillomata.

CASE IV.—*Peri-salpingo-öophoritis, hydrosalpinx and Beginning Papilloma of the Ovary.*

E. R., both tubes and ovaries removed by Dr. Kelly, October 2, 1890. Description of specimens: Right side—The tube and ovary are represented by a ragged mass of tissue, in which it is impossible to distinguish the component parts. Left side—The tube is converted into a hydrosalpinx, which measures 10 cm. in length, 0.5 at the thinnest, and 2.5 cm. at the thickest part. It is wound around the ovary and filled with clear, transparent liquid. The fimbriated end is occluded and its site indicated by a stellate arrangement of depressed lines; its surface is smooth and glistening with a few thin adhesions. Scrapings from its walls show that it was lined by ciliated cylindrical epithelium, the cilia having been seen in motion. Cultures from its contents show no growth of micro-organisms.

The left ovary measures 4, 2.5, and 1.5 cm. in its various diameters. Many adhesions bind it firmly to the tube. At its distal end is a freshly-ruptured corpus luteum; it contains numerous dilated follicles; one particularly, situated on its anterior sur-

face near its lateral end, is quite large, measuring 7 mm. in diameter and filled with clear fluid. Sections through this follicle reveal a most interesting condition, for we find a papillomatous mass 3 mm. in diameter, growing from its internal wall. This mass (*Fig. 4, a*) presents the typical arborescent appearance of a well-developed papillary growth, and a single glance is sufficient to demonstrate its relationship to the ordinary papillomata of the ovary. It is seen to spring from the wall of the follicle by a well-marked pedicle, through which its stroma becomes continuous with that of the rest of the ovary, as is well represented in the drawing. Most of its framework is composed of tissues identical with that of the ovarian stroma and very rich in spindle cells; though in some of its more outlying portions the tissue appears almost hyaline and contains very few cells (*Fig. 4, b*). The growth is covered by a single layer of polymorphous epithelial cells, most of which are cylindrical in shape and contain large oval nuclei, which occupy a great part of the cell and lie equidistant from its margins.

The lining of the follicle itself is also very interesting, for it presents all possible forms of epithelium and clearly demonstrates that one form may readily change to another; for in this case we find the typical cuboidal membrane granulosa cells arranged in several layers; then well-marked cylindrical and, lastly, flattened epithelial cells arranged in a single layer and following one another in close succession. The follicle is surrounded by typical ovarian stroma. Beside the well-marked papillary growth, we have indications at another point (*Fig. 4, c*) of more rudimentary papillary formation, similar to that noted in Case III. On none of the epithelial cells, either those covering the growth or those lining the follicle, was I able to demonstrate cilia. Their absence, however, is completely a matter of indifference, as I will show later.

That we have to do with a Graafian follicle in this case is clearly proved by the fact that in several places we found its interior lined by the typical membrana granulosa cells, in spite of the fact that I was unable to demonstrate an ovum within it.

I believe that no one who has carefully considered the facts brought forward in the last two cases, can have any reasonable doubt that papillary cysts of the ovary may in some cases arise from the Graafian follicle; and it is only necessary for a similar change to take place in several Graafian follicles in order to pro-

duce a typical multilocular papillary cystoma. As both of these cases occurred on or near the surface of the ovary, and as neither of them showed any signs of possessing cilia, I am aware that the statement, that papillary cysts of the ovary may be derived from the Graafian follicle, is open to two objections, and that it might be said that such a mode of origin is perhaps applicable to the simple non-ciliated papillary cystomata, which are not supposed to invade the folds of the broad ligament, but that it cannot possibly apply to those growths which lie within the folds of the broad ligament and are lined by ciliated epithelium. These objections are well taken, and I shall now proceed to prove that they are unfounded and that the ciliated intra-ligamentous papillary cystomata can also be derived from the Graafian follicle. In order to prove the correctness of this assertion, it will be necessary to prove that the Graafian follicle may under certain circumstances become lined by ciliated epithelium and grow between the folds of the broad ligament. And I am happy to say that I am able to prove both of these statements by my own observations.

In the first place I will consider the possibility of growths derived from a Graafian follicle growing within the folds of the broad ligament. In this connection we must be far more careful in distinguishing between intra-ligamentous cysts, which are developed from the ovary, and those of other origin. Heretofore, sufficient stress has not been laid upon this point, and I am sure that many cases described as intra-ligamentous ovarian cysts were not ovarian at all, but were derived from the parovarium and affected the ovary merely by pressure, as in the cases of Doran and Fischel, which I referred to in considering their work. For in several cases I have seen perfectly well marked papillary cysts developed within the folds of the broad ligament, which had absolutely no connection with the ovary, and which, when they had attained a greater size, might have readily flattened it out or caused it to atrophy.

I also desire to call attention to the fact that Olshausen's^{13, 15} statement, that the great majority of papillary ovarian cysts are developed within the folds of the broad ligaments, is greatly exaggerated and will sustain my position by Doran's figures. He found 9 cases developed within the folds of the broad ligament and 4 cases without it, which possessed regularly formed pedicles. Now, when we take into account the fact that he certainly reckoned among his intra-ligamentous ovarian tumors, several of other

origin, it will be evident that considerably less than one-half of his cases were developed within the broad ligament. This accords with my own experience, for I have lately seen three cases, none of which were intra-ligamentous.

Having thus shown that the intra-ligamentous development of these growths is less common than is generally supposed, it now becomes necessary to ascertain whether it is possible for a cyst developed from a Graafian follicle to grow within the folds of the broad ligament. Theoretically, there is no possible objection to an enlarged Graafian follicle, situated near the hilum, growing down in the direction of least resistance between the layers of the broad ligament. But, practically, as far as I can learn, there is no undoubted case on record in which such a mode of growth has been observed.

I have been fortunate enough to have observed such a case, which I will record in this connection.

CASE V.—*Miliary Tuberculosis of the Fallopian Tube; Intra-ligamentous Hydrops Folliculi.*

Mrs. C., both ovaries and tubes removed by Dr. Kelly, February 21, 1891; recovery. Description of specimens: Right side—was so mutilated that examination was impossible. Left side—the specimen consists of the tube, ovary and a clear transparent cyst in the broad ligament. The tube measures 7 cm. in length, 0.5 at thinnest, and 1 cm. at thickest part; the fimbriated end is occluded and the tube covered with numerous adhesions.

The tube appears to lie in a depression between the intact portion of the ovary and the clear intra-ligamentous cyst beneath it; the peritoneal covering of the tube spreads out over the cyst, which is therefore intra-ligamentous. A portion of the ovary, measuring 4, 3 and 2 cm. in its various diameters, is present above the cyst, and presents numerous follicles and adhesions, while its lower margin appears to be continuous with the cyst wall. The cyst is 5 cm. in diameter, with thin, almost transparent walls, and is situated between the folds of the broad ligament. Extending across the anterior and inferior surface of the cyst is the thinned-out parovarium, which is about 8 cm. in length. The cyst contains a clear yellow fluid, containing many whitish particles in suspension, which under the microscope are seen to be very fatty compound granular bodies.

The cyst is unilocular, of a glistening white color interiorly, with numerous ecchymotic patches. Scrapings show it to be lined by cuboidal and roundish epithelial cells, with large vesicular nuclei; many of the cells are fatty.

Microscopic sections of the tube show most exquisite miliary tuberculosis of the mucous membrane, in which the tubercle bacilli were demonstrated in small numbers. Sections through the wall of the cyst show it to be a typical hydrops folliculi; for it is lined by cuboidal epithelial cells, with large nuclei, which are arranged in several layers over the greater part of the interior of the cyst; though here and there they are arranged in only a single layer.

This case, as far as I can learn, is unique, and proves absolutely that growths developed from the Graafian follicles may invade the broad ligament; and teaches us that all tumors within the folds of the broad ligament are not of Wolffian body origin.

Having thus proved that a Graafian follicle growth may become intra-ligamentous, it only remains necessary to prove that under certain circumstances its epithelium may become ciliated in order to fulfil all the requirements necessary for the development of the ciliated papillary intra-ligamentous cystomata from the Graafian follicle.

Fortunately, I am also able to confirm from my own experience the observation of Von Velits, that the epithelial lining of the Graafian follicle may be ciliated.

The investigations of Leod,³⁷ Leydig,³⁹ and Nussbaum³⁸ on the ovaries of the lower animals, showed that the granulosa cells of the frog and others of the lower animals were always ciliated during the period of "heat;" and the theoretical deductions of Marchand and Fleischlen prepared the way for the discovery of cilia in the Graafian follicles in man.

Over a year ago, in a case of small cystic ovaries, I found several of the dilated follicles lined by ciliated epithelium. This was soon followed by several others, some three or four cases in all. In one instance, the ovary contained at least five or six follicles in which cilia in motion were demonstrated. Unfortunately, these observations were made at a period in which I did not keep accurate records of my work, so that I am unable to give all the minutiae concerning the specimens.

About the same period, but little independently of one another, Von Velits made similar observations, and was fortunate enough

in several cases to obtain sections of Graafian follicles in which ova were still visible. The follicles were lined by a single layer of cylindrical ciliated epithelium, of which he gave excellent drawings.

These observations prove beyond all doubt that not only the simple papillary cysts may develop from the Graafian follicles, but also the ciliated papillomata and even the ciliated intra-ligamentous papillomata. For, in the third and fourth cases, we proved that the non-ciliated papillomata might, in some cases, develop from the Graafian follicle; and in the last two observations, that under certain circumstances the Graafian follicle might become ciliated and even grow within the folds of the broad ligament. Now, we have only to suppose the papillary formation, going on in Cases III and IV, to occur in a Graafian follicle with a ciliated membrana granulosa, in order to have a ciliated papillary cystoma developed; and if the follicle should happen to grow within the folds of the broad ligament, as in Case V, we would have a ciliated intra-ligamentous papillary cyst produced.

In view of these observations, I feel no hesitancy in concluding with Marchand that there is no generic difference between the ciliated and non-ciliated papillary cystomata, for their origin is the same, namely, from the Graafian follicle.

I desire to call attention to the fallacy of supposing that the sand body, "psammon-koerperchen," is pathognomonic of the papillary cystomata, as has been stated by Flaischlen,²³ Von Velits²² and others; for in several cases which I have examined they were entirely absent from the growth. And the fact, long since demonstrated by Virchow,⁴⁰ that similar growths occur in the brain and other organs, completely robs their presence of any significance whatever.

It was upon their presence near the ciliated Graafian follicles, that Von Velits²² based his statement that these follicles represented the earliest stage in the development of the papillary cystomata, even though they exhibited no trace of papillary growths. In view of these facts it can not be considered that Von Velits demonstrated the development of the papillary cystomata from the Graafian follicle, as he claimed; and therefore it is believed that the first proof of this mode of development is presented in this article.

In conclusion, I will sum up the results of my work, and in so doing will not commit myself to any single theory of development to the exclusion of all others; for I believe that they may be de-

veloped from one of several sources; and it is not impossible that different portions of the same growth may have developed from different structures, though I am unable to state positively that this is ever the case.

As the result of my observations, I would almost entirely reject the Wolffian body theory and consider the growths to be purely ovarian. The papillary ovarian cystomata may be derived from the following sources:

1. The Graafian follicle. This is probably the usual point of origin for the development of these growths; and according as the membrana granulosa is ciliated or not, so the growth will be of the ciliated or non-ciliated variety; and according as the affected follicles grow within the folds of the broad ligament or not, so the growth will be intra-ligamentous or not.

2. The germinal epithelium. This is the most frequent and perhaps the only source of origin for the superficial papilloma, and probably is frequently the starting point for the usual form of the multilocular papillary cystomata.

3. The tubal epithelium. From a consideration of the conditions in Case I, it is probable that some cases are developed from ingrowths of the epithelium of the tube into the stroma of the ovary. This mode of origin is, however, not yet absolutely proven.

These conclusions tend to prove that the work of all the later investigators in this direction, except those who accepted the Wolffian body theory of development, has been accurate and of real scientific value; but no one observer seems to have met with all of the different forms of development presented in this article.

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