The genesis of carcinoma of the Fallopian tube in hyperplastic salpingitis, with report of a case and a table of twenty-one reported cases / by E. R. Le Count.

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To Alban Doran
With compliments of the
author
E. R. LeCount.

THE GENESIS OF CARCINOMA OF THE FALLOPIAN TUBE IN HYPERPLASTIC SALPINGITIS, WITH REPORT OF A CASE AND A TABLE OF TWENTY-ONE REPORTED CASES.

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(*From the Pathological Laboratory of Rush Medical College.*)

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THE GENESIS OF CARCINOMA OF THE FALLOPIAN TUBE IN HYPERPLASTIC SALPINGITIS, WITH REPORT OF A CASE AND A TABLE OF TWENTY-ONE REPORTED CASES.

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Among theoretical conceptions of pathological processes [55]
to which disease is attributable are certain ideas that have at their inception the distinctness of a silhouette. With the advancement of knowledge, the margins of certain notions lose their definiteness and we find various processes uniting insensibly at their boundaries. The idea that necrosis means death of tissue remains firmly planted, but the exact limitation of its import is considerably blurred when the process of gradual death is screened behind the caption of atrophy. Any attempt deserves approval that has for its object the segregation and classification of morbid processes that lie in the boundary zone. It seems, however, that as time advances the narrow distance now separating the process of tissue hyperplasia from that concerned in the development of benign tumors will not be increased. Lubarsch,[1] after commenting on the close connection between tumors and infectious processes, notes this difficulty in the following words: "Suchte man daher nach anderen unterschiedenen Kriterien, so machte sich eine weitere [56]
Schwierigkeit, die Abgrenzung gegenüber die Hyperplasie bemerkbar." Still, it is evident that if a process of questionable character midway between tumor and hyperplasia

[1] Ergebnisse d. allg. Path. u. path. Anat., 1895, ii, p. 290, Wiesbaden.

[56] can be traced to an inflammatory origin, its position is no longer in doubt. It must of necessity be considered as hyperplasia or the meaning of the word tumor will require modification. In lesions of such uncertain species, in which the inflammatory origin is manifested by simply one of the inflammatory phenomena, viz., that of proliferation, the question seems surmountable in only one way—to admit without further discussion the existence of a firm bond uniting them. Such a solution of the problem is rendered easy by finding lesions which represent all transition stages from one process to another. An example of this kind is reported by W. W. Van Arsdale:[2] a growth developed on the upper right arm two days after several blows received during a sparring bout. A fluctuating swelling that increased the circumference of the arm 10 cm. was present two days after injury; one month later the mass had decreased to one-third its former size, but it had become hard and immovable. Two months after the injury, a growth 9 cm. in length and 3 cm. in its other diameters was chiseled from between the biceps and branchialis anticus; it was found to possess an outer shell of bone 1.5 cm. thick, the periosteum being closely adherent to its exterior, and a cavity filled with dark partially coagulated blood; its outer wall was true bone and its cavity devoid of bone-marrow proper; its inner wall was porous vascular bone.

It seems reasonably certain that in this case the clot of a subperiosteal hæmorrhage became ossified at least in its outer part. According to Klebs,[3] the process of bone-formation in this "Ossifying hæmatoma" would serve as an example of hyperplasia; for, he states, the line between hyperplasia and tumor-growth may be determined to some extent by the preponderance of the former in scars and granulation tissue and its proneness to spontaneously disappear. The growth would be inflammatory in origin, for the unabsorbed blood would excite an inflammation in the surrounding parts

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[2] Ann. Surg., 1893, xviii, p. 8, Phil.

[3] Die allg. Pathologie, etc., ii, p. 491, 1889, Jena.

(Cohnheim).[4] According to Lubarsch,[5] the apparently au- [56]
tonomous hyperplastic growths almost without exception follow inflammatory excitants. Notwithstanding these opinions, it is unreasonable to suppose that had ossification been allowed to continue throughout the entire coagulum, that the mass of new bone would ever have disappeared spontaneously; there would have resulted an osteoma—a benign tumor. Surgeons are well acquainted with the permanent character of the bony hyperplasia which occurs in a luxuriant callus and the osteomas that develop in the biceps and pectoral muscles from the kick of a gun (Tillmanns).

Another instance of lesions which represent transitions between hyperplasia and benign tumor is furnished by multiple adenomata of the liver. In proof of their mediate position is the fact that equally good authorities are arranged on opposite sides: Weichselbaum, Rindfleisch, Chiari and Kretz classify the condition with simple hyperplasia; Lubarsch, Thoma, Ponfick and Eppinger with adenomata. Orth[6] seriously considers the question of tumors arising from multiple nodular hyperplasia of the liver, and Schmieden,[7] in a recent review of the connection which exists between these lesions, declares that a sharp division between adenoma and hyperplasia in the liver cannot be made. He claims to have seen, as Van Heukelon did before him, the transition forms between hypertrophied liver cells and tumor cells. The relationship between hyperplastic processes and tumor is more important when it has to do with cells that possess great powers to proliferate and regenerate, *e. g.*, surface epithelium and the epithelium of superficial glands. In discussing this subject Birch-Hirschfeld[8] makes the statement that such atypical hyperplastic growths show in the excess of their regeneration certain points of similarity to tumors, and it may be accepted that they may

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[4] Vorlesungen über allg. Pathologie, p. 393, 1882, Berl.

[5] L. c., p. 297.

[6] Lehrbuch der spec. path. Anatomie, i, p. 957, 1897, Berl.

[7] Arch. f. path. Anat. (etc.), clix, p. 290, 1900, Berl.

[8] Grundriss der allg. Pathologie, p. 144, 1892, Leipzig.

[56] become changed into tumors; he also states[9] that the possible occurrence of growths which represent transition stages between hyperplasia and tumor can not be excluded.

The effect of a productive inflammation or inflammatory hyperplasia upon mucous linings is either a diffuse and uniform thickening or the formation of the isolated polypoid outgrowths. As the gross appearances change from a diffuse process to dispersed or widely scattered growths, the likelihood of the inflammatory origin lessens, for the conception of a tumor is connected with the local limitation of its early growth (Thoma). But to this there are exceptions, for " the inflammatory new growths, which are due to atypical proliferation of epithelium, tend to form either single, tumor-like protuberant growths or multiple growths over a considerable surface " (Birch-Hirshfeld).

The confusion which attends the word papilloma is no more attributable to its diversity of structure than to the question of its proper position in regard to tumors and the hyperplastic inflammations. Birch-Hirschfeld[10] states that in mucous membranes a diffuse or circumscribed polypoid thickening may result from chronic catarrhal inflammation; also, that in the nose[11] combinations of papilloma and hyperplasia of the mucosa occur. Klebs[12] uses the polypi of the stomach to illustrate the effect of hyperplastic inflammation in the production of papilloma. In the statement by Orth[13] concerning the papillomata of the Fallopian tube, that it is difficult to determine with certainty to what extent they are caused by inflammatory growths of the folds of the mucosa, we have further evidence of the confusion.

[57] Such uncertainty of classification leads naturally to the use of terms which are devised to bridge over the difficulty. Such a title, alluding both to the process of hyperplasia and to the admixture with tumor, is used by Hauser[14] in his

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[9] Lehrbuch der path. Anat., i, p. 180, 1896, Leipzig.

[10] L. c., p. 137.

[11] Lehrbuch der path. Anat., ii, p. 450, 1894, Leipzig.

[12] L. c., p. 615.

[13] Lehrbuch der spec. path. Anat., ii, p. 539, 1889, Berl.

[14] Deutsches Arch. f. klin. Med., lv, p. 429, 1895, Leipzig.

report of a case of "Polyposis intestinalis adenomatosa." [57] In this case there were disseminated polypi consisting largely of atypical epithelial growths not only throughout the intestinal canal but also in the stomach. Hauser refers to three other similar cases. Petrow [15] has added another in which there were numerous single or clustered, large and small polypous growths in the stomach and the entire intestinal canal, together with every evidence of a severe chronic inflammation in the mucous coats involved.

Quénu and Landel [16] have recently collected 42 cases in which the large intestine was the seat of a more or less extensive polypous hyperplasia. From the frequent history of diarrhœa, these authors believe that the process has its origin in inflammatory conditions, and this opinion is reached after a thoughtful consideration of the possibility that the intestinal disturbances might be secondary to the multiple adenomata. In a previous article by the same authors [17] there is even less doubt displayed respecting the identity of pedunculated adenomata of the rectum with hyperplastic processes, for the statement is made that "they are more or less directly dependent upon an inflammatory reaction."

Sklifossowsky,[18] after describing two benign papillary tumors in the mucous lining of the stomach, states that they originated from a hyperplasia of the mucous coat due to long-standing irritation; he likens them to the knob-like projections of the *état mamelonné*. His interest in these growths was largely due to the fact that all transitions were found in them between the diffuse thickening of gastritis proliferans and the tumors described.

Further evidence is not necessary to illustrate the fact that hyperplastic processes in the mucous lining of the

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[15] Bolnitsch. gas. Botkina, 1896, St. Petersburg. From the summary of Russian literature by Maximow and Korowin, Ergebnisse d. allg. Path. u. path. Anat., Lubarsch and Ostertag, v, p. 735, 1898, Wiesbaden.

[16] Les polyadénomes du gros intestine. Rev. de Chir., xix, p. 465, 1899, Paris.

[17] Rev. de gynéc. et de chir. abd., ii, p. 484, 1898, Paris.

[18] Arch. f. path. Anat. (etc.), cliii, p. 130, 1898, Berl.

[57] gastro-intestinal tract, like those of the liver, are closely allied to the processes of tumor-development; or that there are certain interposed lesions which might be accepted as proof of the continuity of processes having as their onset chronic inflammation, and, as their termination, tumor-growth. The analogy will be more complete with the demonstration of cases such as are hinted at by Birch-Hirschfeld [19] in the following proposition: "It is probable, but not proven, that certain forms of primary carcinoma of the liver may have their origin in a further atypical development of such liver adenomata." The fact that the hyperplasia of the gastro-intestinal mucosa has, as its end product, the evolution of *malignant* neoplasms, leaves no room for controversy such as has been noted with regard to multiple adenomata and nodular hyperplasia of the liver.

In 42 cases gathered by Quénu and Landel of polypous hyperplasia of the colon, there were 20 in which a carcinoma of the colon was also present. In the series of Hauser,[20] of carcinoma of the colon, five were associated with more or less extensive "polyposis," and in the stomach the same author reports one case in which the process was combined. (Case 25, p. 208.)

One of the cases of benign tumor of the gastric mucosa which Sklifossowsky so positively ranks with the inflammatory hyperplasias, possessed at the same time a carcinoma, which was sufficiently interesting, on account of the early changes it showed, for Israel to report it under the title "Ueber die ersten Anfänge des Magenkrebs." [21] Also, in the case of Petrow, of diffuse gastro-intestinal polypous hyperplasia, death took place from invagination and spontaneous rupture at two places, where the growth had a similarity to adenocarcinoma.

To substantiate the view that the polypous growth occurs first and that the production of tumor follows, the following citations will suffice:

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[19] L. c., p. 743.

[20] Das Cylinderepithel-carcinom des Magens und des Dickdarms, p. 261, 1890, Jena.

[21] Berl. klin. Wchnschr., xxvii, p. 649, 1890.

Orth,[22] in considering similar growths in the Fallopian [57]
tube, writes as follows: "Among the recently reported cases of papillary new growths are some which may be correctly deemed benign and others which are malignant; from the great similarity of these to one another it is safe to accept the view that there is at least a danger of cancerous transformation. Hauser, in the report mentioned of a case of Polyposis intestinalis adenomatosa, claims (p. 446) that one must admit that the multiple warty growths have developed first and that these later underwent a carcinomatous change. Cullen,[23] after referring to the opinion of Lubarsch, that a benign tumor is never changed into a malignant one, says: "Case 4,262, which I have recently had the opportunity of studying, shows beyond a doubt that such a possibility exists." The case in question was that of a polypous adenoma of the uterine mucosa.

The investigations on inflammatory hyperplasia with tumor-formation in certain regions have been repeated by Stoerk [24] in the urinary tract. He describes a case of papillomatosis of the urinary bladder, ureter and pelvis, of the right kidney, and was able to find only two similar cases in the literature. He considers the process as an unusual form of chronic inflammatory hyperplasia, and compares it with Gastritis proliferans. More commonly the chronic inflammation in the urinary passages terminates in a hyperplasia associated with the formation of cysts. That certain cases should display both features of the process is not surprising. Litten [25] has described "Ureteritis chronica cystica [58]
polyposa." Cahen [26] has one case, and to this Stoerk adds three more, in which the hyperplasia of the mucous lining of the bladder was accompanied by carcinoma. Rehn [27] makes the interesting statement that in the majority of tumors of the bladder a substance in solution in the urine

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[22] L. c., p. 539.

[23] Cancer of the Uterus, etc., p. 355, 1900, N. Y.

[24] Beit. z. path. Anat. u. z. allg. Path., xxvi, p. 367, 1899, Jena.

[25] Arch. f. path. Anat. (etc.), lxvi, p. 139, 1876, Berl.

[26] Arch. f. path. Anat. (etc.), cxiii p. 468, 1888, Berl.

[27] Verhandl. d. deutsch. Gesellsch. f. Chir., xxiv, s. 240, 1895, Berl.

[58] causes the tumor-growth by its chemical irritation; he has observed three cases in which tumors of the bladder occurred in men employed in the manufacture of aniline dyes. Stoerk is inclined to lay strong emphasis upon gonorrhœa as an etiological factor, and Kaufmann [28] has described the occurrence of multiple polypi in the ureter from the passage through it of fæces from a fistulous connection between the pelvis of the kidney and the duodenum. As an example of the question which so constantly recurs—tumor or inflammation—and serving as an illustration of the apparent necessity to separate these conditions, the following quotation will answer: [29] "The condition described might be classed both as chronic cystitis and as tumor. . . . I am inclined to look upon the process as a chronic cystitis." This is in concluding an article on Cystitis Papillomatosa, where the cystoscopic examination left the observer in doubt. In the recent work by Cullen on Cancer of the Uterus, there is abundant evidence that a diffuse polypous hyperplasia of the uterine mucosa occurs and that this condition may be combined with carcinoma. The illustrations on pages 514 and 516 show its gross anatomy; some participation of the epithelium in the process is evident, since in many places it was many layers in depth in both cases, notwithstanding that no karyokinetic figures were found. Case 3,452 (p. 323) of "adenocarcinoma of the anterior cervical lip; commencing adenocarcinoma of the posterior lip, apparently independent of the former; papillary outgrowths of the uterine mucosa, with suspicion of commencing adenocarcinoma of the body of the uterus," is a striking analogy with the polypous hyperplasia with carcinomatous transformation observed in the intestinal mucosa and the urinary tract. Perhaps the best example of polypous hyperplasia described by Cullen is Case 6,659 (p. 401). Occurring in a young woman, aged 30, this author describes "a very unusual polypoid condition," in which "the mucosa, as a whole, presents a most unusual picture, consisting of large polyp-like masses springing from all parts and completely filling the enlarged cavity." His-

[28] Cited by Stoerk.

[29] F. Bierhoff, The Medical News, lxxvi, p. 810, 1900, Phil.

tologically, "one of the chief features is the preservation of [58] the lumina of the glands; few, if any, nuclear figures are to be made out," and "the uterine muscle has not been penetrated by the growth; in fact, at some points there still remains a small amount of normal mucosa separating the growth from the muscle." There had been no recurrence of tumor 11 months after the removal of the uterus. The diagnosis was adenocarcinoma. There is but little doubt, so far as one can judge from the report, that in this case the process was one of diffuse polypous hyperplasia which, so far as the examination shows, had not at the time of removal undergone carcinomatous change. That such a change would have occurred, had it been undisturbed, might be inferred from the continuity of process which has been shown so far to exist between the polypous hyperplasia and carcinoma.

But it is especially concerning tumors of the Fallopian tube that confusion has arisen; there has been quite a general failure to recognize that a diffuse hyperplastic inflammation is possible—a process which is strictly analogous to the polypous hyperplasia of other mucous surfaces—and that in certain typical examples it is as distinct from tumor-growth as gastritis proliferans is from carcinoma of the stomach. Part of the confusion is no doubt due to the fact that hyperplasia is so frequently combined with sacto-salpinx. Slawyanski[30] has recognized this fact, as is established by the frequency with which he uses the term *sacto-salpinx papillomatosa*, although he does not clearly distinguish between papilloma as a tumor and polypous hyperplasia due to chronic inflammation. He states that "with occlusion of the abdominal end, the tube appears larger, aside from the papilloma; products of the secretion both from the covering of the tumor and the diseased mucosa accumulate in the tube; thus sacto-salpinx becomes sacto-salpinx papillomatosa (p. 112)." Numerous investigations

[30] Special Pathology and Therapy of the Diseases of Women, vol. ii, Diseases of the Fallopian Tubes and Ovaries (Russian), 1897, St. Petersburg.

[58] in lower animals have proven that when the outer end of the tube is closed a retention cyst is the result.[31] Undoubtedly in many cases the inflammatory process which leads to the hyperplasia of the mucous lining of the tube causes the closure of the abdominal end. As a typical example, the case reported by Doléris and Macrez[32] will answer. He removed from a woman, aged 37, a growth of the right tube which was adherent to the liver and measured 20 by 30 cm. It consisted of a sac filled with grumous, viscid, yellowish fluid; its walls were 5 to 10 mm. and the lining was beset with pin-head to pea-sized papillary growths, which, on microscopic examination, consisted of villi with rarely more than one layer of epithelial cells as a covering. This is the second growth of this sort removed by Doléris; the other, in 1891,[33] being the first observed in France. The woman was 28 years old; the growth was in the right tube and the inner one-fourth of the sacto-salpinx contained no papillary growths. Clark has reported a similar case[34] of a cystic growth of the Fallopian tube 12 by 12 cm., or one-half the size of a man's head, in which the inner surface was studded with thick papillary growths except at one point, where the
[59] surface for an area the size of a palm was smooth. The wall of this cyst was thin; the warty growths were largely made up of connective tissue, and the epithelial covering of these was uniformly single-layered. Although Clark ascribes the process to inflammation, it is reported as the seventh instance of papilloma of the Fallopian tube. Another instance first reported on account of the concurrent appendicitis[35] was shown on later examination of the sac,[36] which was as large as a fœtal head, to contain the inner part of the tube as a curved cord on its outer surface. The lining

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[31] C. Gebhard: Pathologische Anatomie der weiblichen Sexualorgane, pp. 436–7, 1899, Leipzig; also: Ergebnisse d. allg. Path. u. path. Anat., 1898, v, 741 (work of Sadkowsky), Wiesbaden.

[32] La Gynecologie, iii, p. 289, 1898, Paris.

[33] Nouv. Archiv. d'Obstet. et de Gynec., vi, p. 11, 1891, Paris.

[34] Johns Hopkins Hospital Bulletin, ix, p. 163, 1898.

[35] Bull. Soc. Anat. de Par., 1897, xi, n. s., p. 518.

[36] P. Macrez: Des Tumeurs papillaires de la Trompe de Fallope, p. 61, 1899, Paris.

of the sac was beset with small growths covered with epithe- [59]
lium; the crypts between the growths extended outward so as to give to the section an appearance not unlike an adenoma. The condition described in this case might be considered as analogous to cystitis cystica of Stoerk and others, which led Aschoff to search for glands in the urinary tracts of newly born infants. It is essentially the same process—a hyperplasia of the lining (sacto-salpinx villosa et pseudo-follicularis). Both this case and that of Montprofit and Pilliet[37] are included by Macrez in the table of benign papillary tumors of the tube; in concluding the case above mentioned, the following interesting statement is made:

"L'origine irritative de ces productions dans la trompe ne doit pas surprendre, puisque l'on voit que dans les viscères comme le foie, le rein, la capsule surrénale, etc., les formations adénomateuses coexistent avec la sclérose et paraissent être un des modes de réaction des cellules parenchymateuses aux irritations qui amènent l'épaississement du tissu conjonctive."

The second case of papilloma reported by Doran[38] was double-sided; the right tube contained over a pint of fluid, the left a smaller amount. Both contained papillary growths which Doran describes as warts "similar in principle to those found in other structures, namely, overgrown papillæ, the result of continued irritation."

It is certainly of doubtful propriety to consider these growths, so clearly the products of an inflammatory action, as "papilloma." Sacto-salpinx papillomatosa might be altered with advantage to Sacto-salpinx polyposa, for the condition is one of diffuse polypous hyperplasia associated with the formation of a retention cyst and not one of tumor-growth. By some observers the diffuse villous hyperplasia associated with sacto-salpinx has been reported as carcinoma. W. L. Jakobson[39] has reported a case in which the papillary growths almost filled the sac. Although the epithelium had not proliferated so as to invade the musculature of the tube,

[37] Bull. Soc. Anat. de Par., 1893, vii, p. 505.

[38] Tr. Path. Soc., 1888, xxxix, p. 200, London.

[39] J. akush. i jensk. boliez., xii, p. 29, 1898, St. Petersb.

[59] and notwithstanding that there were no metastatic growths, the condition of the tube was diagnosed carcinoma by both Jakobson and Petroff, who made the histological examination. In the case reported by Hofbauer [40] both tubes were closed externally, but retention cysts were absent. The lining of the right tube, in which the changes were more advanced, possessed small miliary and larger growths, some as large as two beans. From the gross changes and from the careful description of the histologic structure, this might also be considered as polypous salpingitis, did not the record point so well to tuberculous salpingitis. The sac in the case operated by Leopold and described by Fearne [41] measured 5 cm. in diameter and occupied the infundibulum and ampulla of the tube. It was filled with a soft vascular papillary growth. The lining folds have hypertrophied, branched, and then, according to Fearne, undergone malignant transformation. The muscle fibers had disappeared by atrophy and a firm connective-tissue wall had so successfully limited the process that there were no metastatic growths and the patient was well 1½ years later.[42] The case reported by Sänger and Barth,[43] over which they hesitated long before concluding that it was one of carcinoma, which diagnosis has constituted one of the principal factors of the present confusion, was one in which the tubal mucosa was thickened so that it resembled the cerebral convolutions in miniature. The accompanying illustration, showing the macroscopic appearance of the lining, resembles greatly the mammillated appearance of the stomach in gastritis proliferans. This thickening affected the outer one-half of the tube uniformly; there were numerous nuclear figures in the epithelial cells which covered the villi in a single layer, and largely from this histologic similarity with "Adenoma malignum" of Ruge and Veit, these authors concluded finally that it also was carcinoma. The diffuse character of the process in this case, and

[40] Arch. f. Gynäkol., lv, p. 316, 1898, Berl.

[41] Über primäre Tubencarcinom. Geburtshülfe u. Gynäkologie, ii, p. 337, 1895, Leipzig.

[42] Tr. Obstet. Soc. (London), 1898, xl, p. 202.

[43] Die Krankheiten der Eileiter, A. Martin, p. 253, 1895. Berl.

the uniformity with which the tubal mucosa was involved, [59]
point to a hyperplasia similar to that seen in other mucous coats—to a condition resulting from inflammatory reaction with excessive proliferation or the early disappearance of all other changes but proliferation—a process which Adami, following Klebs, refers to as "neoplastic hyperplasia," and which Hauser, as before noted, connects with tumors by the term "polyposis adenomatosa."

It does not always happen that the outer end of the tube becomes closed by the inflammatory process; the subsequent invasion of the adjacent peritoneum, by papillary or warty growths, however, is no proof that the process is one of tumor-growth; for, in condyloma acuminata an exactly similar process occurs—extension of a hyperplastic inflammation by direct continuity of surface. The classical case of Doran [44] is of this nature. The outer part of the right tube was dilated and filled with cauliflower-like growths; these were formed by villi covered by a single layer of epithelium of which some cells were ciliated. There was also an enormous ascites and pleural effusions which required frequent tapping; although it was impossible to remove the entire [60]
growth, no recurrence had taken place 16 years after the operation.[45] It is more reasonable to believe this case to be one of hyperplastic salpingitis than of tumor. Doran, in his original report, likened it to the venereal condylomas and to the inflammatory polypi of the tubal mucosa described by Rokitansky and Hennig.

Another condition has been described by Schirschoff [46] as papilloma. It is that of a single pedunculated tumor which arose from the lining of the tube 5 mm. inside the fimbriæ; the abdominal os was wide and gaping. The growth was 5 cm. in length and made up of a cluster of smaller masses. The exact pathologic position this growth should occupy as

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[44] Tr. Path. Soc. (London), 1880, xxxi, p. 174; Idem., 1882, xxxiii, Supplementary Reports, p. 49.

[45] A System of Gynecology, by many writers, edited by T. C. Allbutt and W. S. Playfair: Diseases of the Fallopian Tube by Alban Doran, p. 806, 1897, London.

[46] Bolnitsch. gas. Botkina., Nos. 42–44, 1898.

[60] regards the Fallopian tube will always be in doubt, since there is but slight mention of the large (wt. 410 g.) papillary cystoma which was situated just below the outer end of the tube. In other cases such localized growths have been catalogued as carcinoma. Stroganoff [47] has described a single pedunculated growth which arose from the mucosa by a pedicle 1 cm. in diameter. The tube containing it was closed externally and held about 50 ccm. of the usual serohemorrhagic fluid. The structure of this growth was such that a diagnosis was made of "carcinoma cylindro cellulare." There is no mention of regional invasion, glandular involvement or recurrence; the woman was 39 years old. Tuffier [48] found in a tube, which was closed externally, pear-shaped and as large as a fœtal head, a dark, soft and friable mass which was at first supposed to be free; in examining it a narrow pedicle was found. The lining of the sac containing this growth was, for the greater part, smooth and devoid of epithelium. The examination of this growth alone, which, like that of Strogonoff, was largely necrotic, led to a diagnosis of carcinoma (epithelioma).

Falk [49] also described a localized growth as carcinoma. On the left side the tube formed a sac that contained a sanious, semi-purulent fluid and in its outer part gelatinous cysts; the sac formed by the right tube was as large as a child's head. It contained a similar fluid, free, grayish, villous masses, and on the posterior wall springing from the mucosa, a growth the size of a walnut; this contained gland-like structures, and from its histologic resemblance to the case of Sänger and Barth, a diagnosis of carcinoma was reached. It is obvious that in this instance the chronic inflammation on one side caused sacto-salpinx with hyperplasia of the lining and the formation of pseudocysts; on the opposite side, sacto-salpinx with the production of a localized growth. In cases of this nature, the effort to separate tumor and hyperplasia meets, in the localized nature of the growth, an ob-

[47] Collection of works in Obstetrics and Gynecology, dedicated to Prof. K. F. Slavyanski (Russian), p. 227, 1894, St. Petersburg.

[48] Ann. de Gynéc. et d'Obst., 1894, xlii, p. 203, Paris.

[49] Berl. klin. Wchnsch., 1898, xxxv, p. 554.

stacle which is at present insuperable. If there occur in [60] such localized growths evidences of the multiplication of cells—nuclear figures—or if alterations are found in the morphology and staining reactions of the cells which would indicate that they have not reached an adult type, the process is certainly more like tumor than like hyperplasia. But between hyperplasia and carcinoma there is a considerable gap. Hauser, after describing the multiplication of the glands in the polypi of the intestine, makes the statement [50] that it should not be understood that all such growths are of necessity precursors of carcinoma. With the article of Schmieden [51] there are portrayed atypical karyokinetic figures in the liver cells which form the adenomata. In short, it seems to me that the case described by Falk does not correspond to carcinoma so much as it does to a benign and localized growth; here it is necessary to recur to a proposition made earlier—that it is doubtful whether the narrow distance now separating hyperplasia from benign tumor will be increased. It is reasonable to believe that there should occur in the lining of the Fallopian tube regenerative processes, similar to those of glandular organs and structures possessing glands, the products of which are closely allied to adenomata.

The foregoing considerations demonstrate the imperceptible transition of hyperplastic processes of the tubal mucosa—belonging properly to the salpingitides—into those of true tumor growth; and that these may terminate in the production of benign tumors. The literature of tubal tumors also contains abundant evidence that the transition of villous hyperplasia into growths that at least possess some indications of malignancy is an equally gradual one. The tumors demonstrated by Kaltenbach as double-sided tubal carcinoma [52] were later elaborately described as papillomata.[53] Carcinoma is positively excluded in the following words: "Aber nirgends lässt sich doch ein Anhaltspunkt für eine

[50] L. c., p. 447.

[51] L. c.

[52] Centralbl. f. Gynäk., xvi, p. 357, 1889.

[53] Ztsch. f. Geburtsh. u. Gynäk., 1889, xvi, p. 364, Stuttg.

[60] wirkliche Carcinombildung finden, auch da nicht, wo die Neubildung mehr einen parenchymatösen Character hat, und von einer Zerstörung des bindegewebigen Papillärkörpers durch eingedrungene Epithelmassen ist nichts zu sehen." Notwithstanding this statement, there was a recurrence within 18 months.[54] In Eckhardt's[55] case the cyst formed by the dilated outer portion of the tube had small elevations on its external surface which, on microscopic examination, were found to consist of solid outgrowths of epithelium. In a report by Fabricius,[56] the left tube was removed and the growth that it contained pronounced papilloma by Paltauf. The right adnexa appeared normal and were left in place. Five months later a large growth occupied the right side of the pelvis, and masses removed from where the left tube had been amputated were declared by Paltauf to be carci-
[61] noma. In the instance chronicled by Michnoff,[57] the folds of the lining of the left tube were thickened by many strata of epithelium and the muscular layers in some places were invaded through their entire thickness. The condition in the right tube considered by Michnoff as papilloma corresponds very well with sacto-salpinx villosa; the epithelium, rarely more than a single layer, covered papillary growths 1 cm. tall, and these filled the canal near the outer end of the tube; the os abdominale was closed and a cyst had formed there the size of a small hen's egg. In a case reported by Kretz as papilloma,[58] sacs had formed on both sides that exhibited externally small, white, soft, flat nodules. By the study of serial sections, these were found to be produced by the growth outward of the crypts between villi; the diverticula produced in this manner usually possessed a single layer of tall epithelium; where the epithelium was in two or three layers the cells were shorter and nuclei more spherical. Such cystic formations were found within the lymph channels.

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[54] Doran Tr. Obstet. Soc., 1898, xl, p. 200.

[55] Archiv f. Gynäk., 1897, liii, p. 183, Berl.

[56] Wien. klin. Wchnsch., 1899, xii, p. 1230.

[57] Meditsina, iii, p. 181, 1891, St. Petersb.

[58] Wien. klin. Wchnsch., 1894, vii, p. 572.

Although it is not within the scope of this article to insist [61] on the glandular character of the epithelial tubal tumors, certain facts may be pointed out. It is obvious that the five cases above cited as examples of growths that were removed during the transition between hyperplasia and tumor are very similar to proliferating papillary cystoma of the ovary. This similarity with ovarian tumors has been dwelt upon by many writers. Gebhard [59] compares them with uterine carcinoma in the following words: "Obwohl ich selbst, wie eingangs erwähnt, keine eigene Erfahrungen über das Tubencarcinom besitze, so bin ich doch bei der Durchsicht der in der Litteratur niedergelegten Beschreibungen des mikroskopischen Verhaltens dieser Geschwuslt zur überzeugung gekommen, dass dieselbe histologisch durchaus mit dem malignen Adenom u. Adenocarcinom des Uteruskörpers auf eine Stufe zu stellen ist."

The classification of tubal carcinomata into purely papillary and papillo-alveolar by Sänger and Barth [60] is but a makeshift for adenocarcinoma; as Cullen says,[61] concerning adenocarcinoma of the uterus, "I am strongly of the opinion that where the papillary arrangement is most marked, the growth has started in the surface epithelium; whereas it seems probable that when the gland-like arrangement is more pronounced, the process has started first in the glands. The simpler plan would be to consider all these merely as variations in one disease." Slavyanski [62] would limit the term adenocarcinoma to the latter form of Sänger and Barth. He separates them into two forms—carcinoma papillomatosa villosum and carcinoma cylindrocellulare seu adenocarcinoma.

From the description of the following case it may be seen that the view of Cullen relative to the two methods of growth in the adenocarcinoma of the uterus is equally applicable to tubal carcinomata; that there is a disposition to grow towards the lumen in the form of branching villi as well as outward into the muscular coat as sacs, diverticula or al-

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[59] L. c., p. 455.
[60] L. c., p. 272.
[61] L. c., p. 360.
[62] L. c., p. 116.

[61] veoli, and that these methods of growth are part of the same process.[63]

I received, June 22, 1899, from Dr. Henry P. Newman of Chicago, a tumor which was removed by him at the West Side Hospital. I am deeply indebted to him for the opportunity to examine it. The following abstract of the clinical history was also obtained from him:

Mrs. F., age 47, admitted to the West Side Hospital June 20th; in her early married life she had two miscarriages at the third and fourth months of pregnancy respectively. Subsequently, she gave birth at term to a child, which is now 21 years of age; delivery was instrumental and severe. Since then she has been unable to carry a child beyond the third or fourth month of pregnancy. In spite of many miscarriages she has enjoyed a fair degree of health until two years ago, when menstruation became painful. The pain was referred to the sides and lower abdomen; it began just before the flow and continued during the entire period; there was also experienced general weakness and exhaustion on slight exertion. One year ago she first noticed a protrusion from the vagina which she took to be the womb; this has gradually enlarged, becoming more prominent after standing, straining, and coughing. It has never been painful, but has proved annoying in walking or sitting from its large size. There has also been an enlargement of the abdomen until it is now as large as a pregnancy at full term. She complains of a frontal headache; she has a fair digestion; there is no constipation or urinary trouble, but there is a constant leucorrhœa and the discharge is often streaked with blood.

Operation.—Incision in the median line of the abdomen 8 cm. long; over two gallons of ascitic fluid escaped; the left tube was very much enlarged and thickened; the ovary was not involved. The tube was excised close to the cornu of the uterus. The right adnexa appeared normal; wound closed with catgut and silk in layers. The protruding cul-de-sac of Douglas was then opened from below, emptied of

[63] This case was briefly reported at the Chicago Gynecological Society, December 15, 1899, by Dr. Newman and myself.

FIG. 1.—Tubal carcinoma—anterior surface—natural size.
a.—Accessory tube.

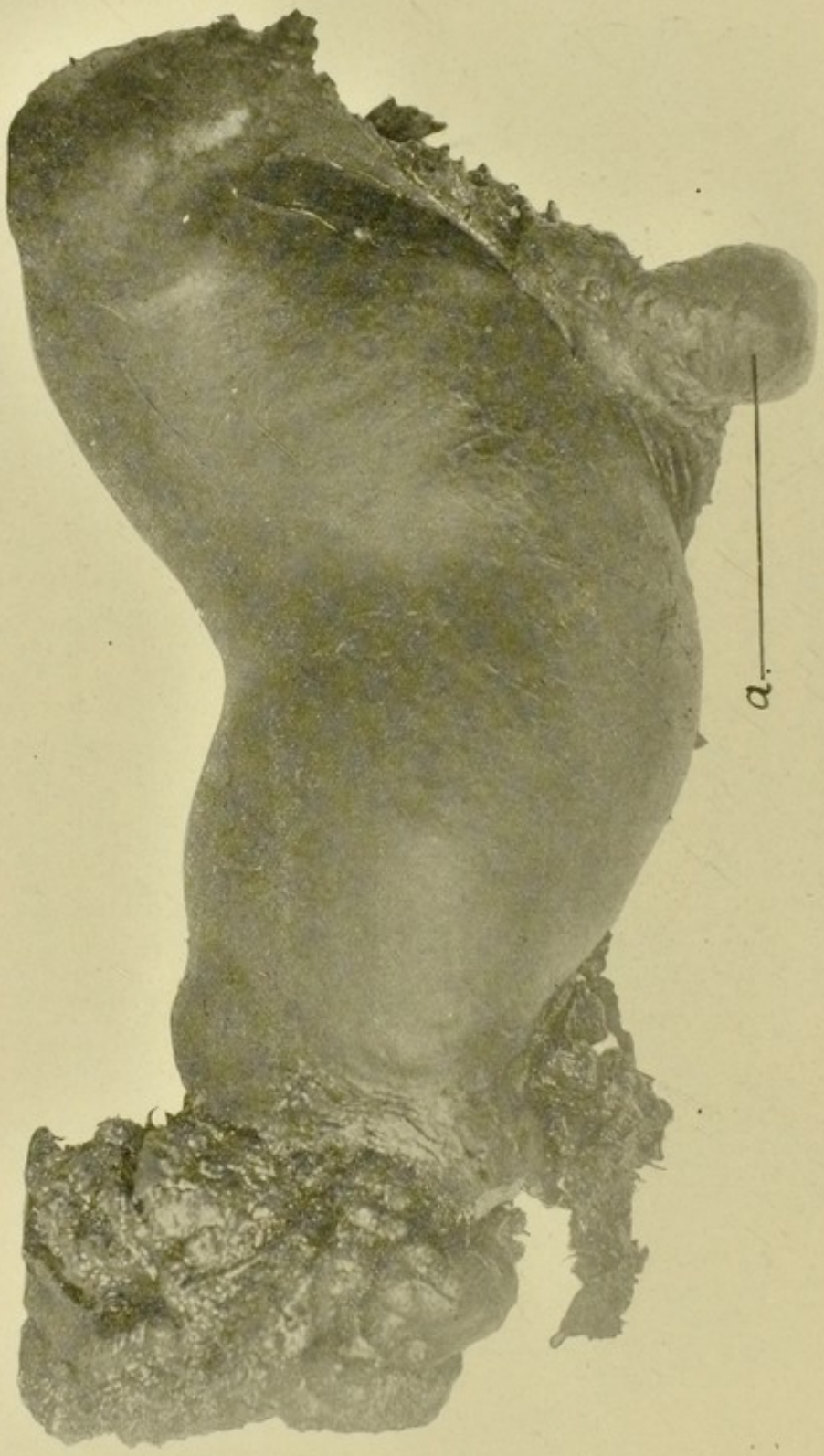

FIG. 2.—Tubal carcinoma—posterior surface—natural size.
a.—Ovary.

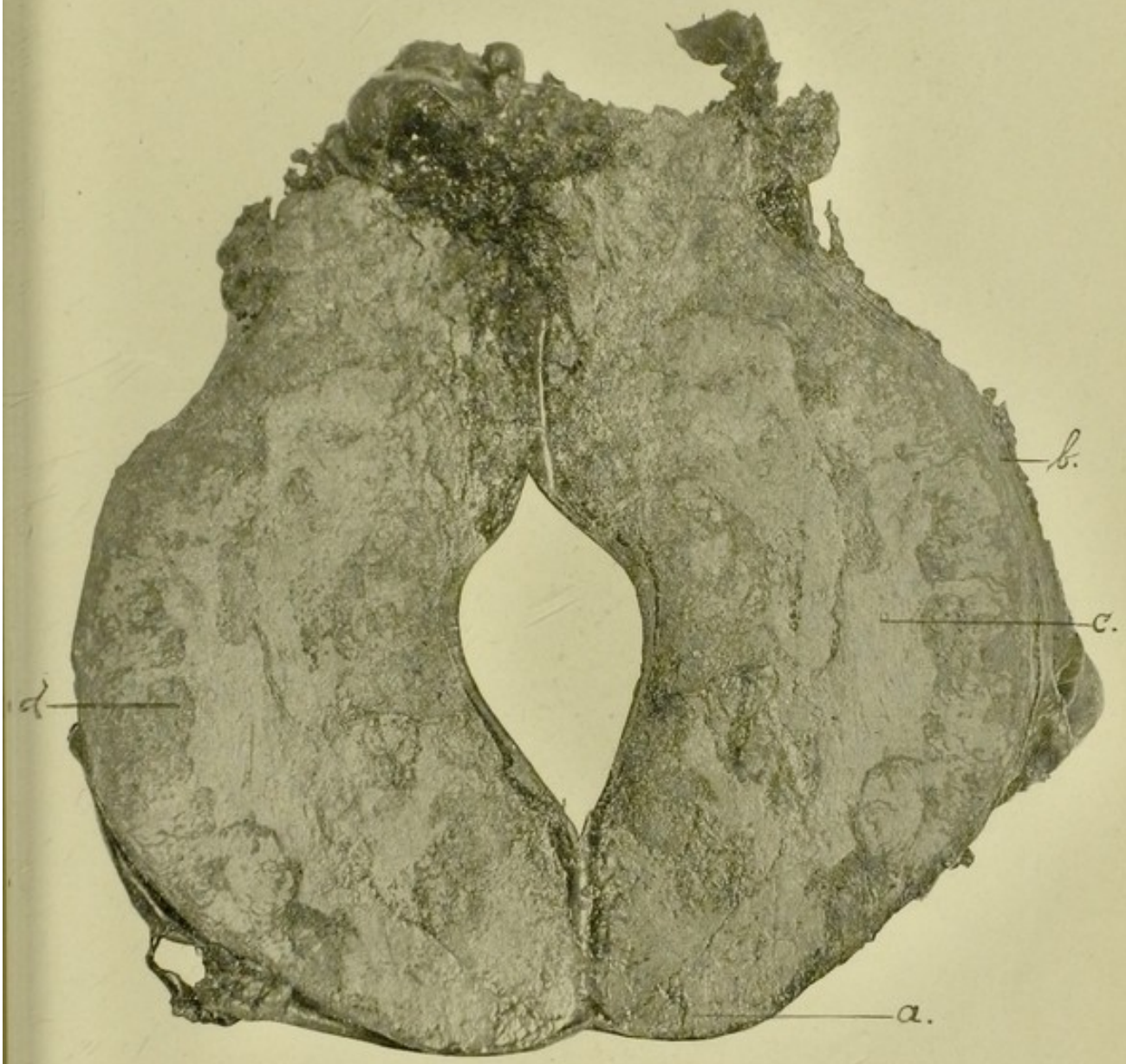

FIG. 3—Tubal carcinoma sectioned longitudinally (three-fourths of natural size).

a.—Uterine end.

b.—Muscular wall.

c.—Necrotic tissue.

d.—Papillary growth of the lining toward the lumen of the tube.

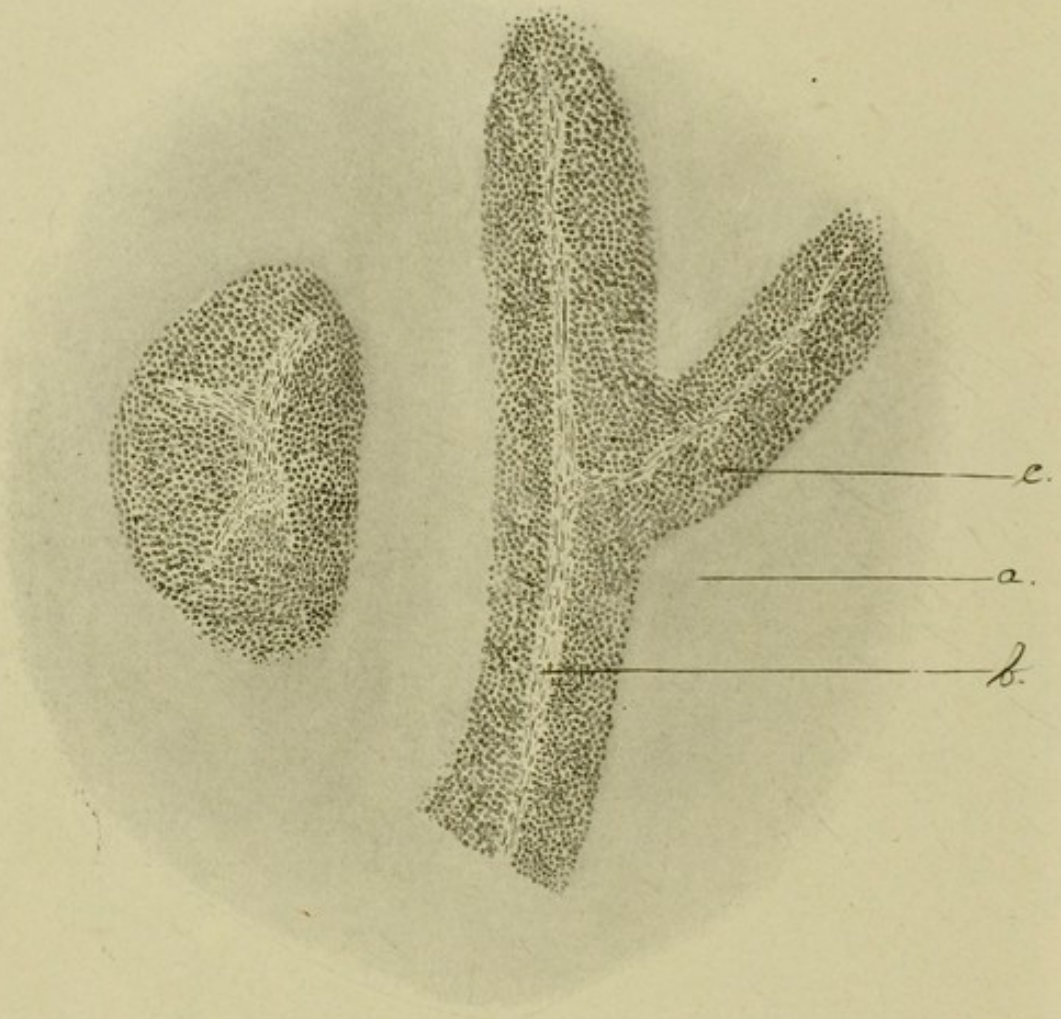

FIG. 4.—Villi that have been sectioned longitudinally and transversely; from the more central part of the growth.

a.—Necrotic tissue.

b.—Connective-tissue stalk.

c.—Epithelial cells in many strata.

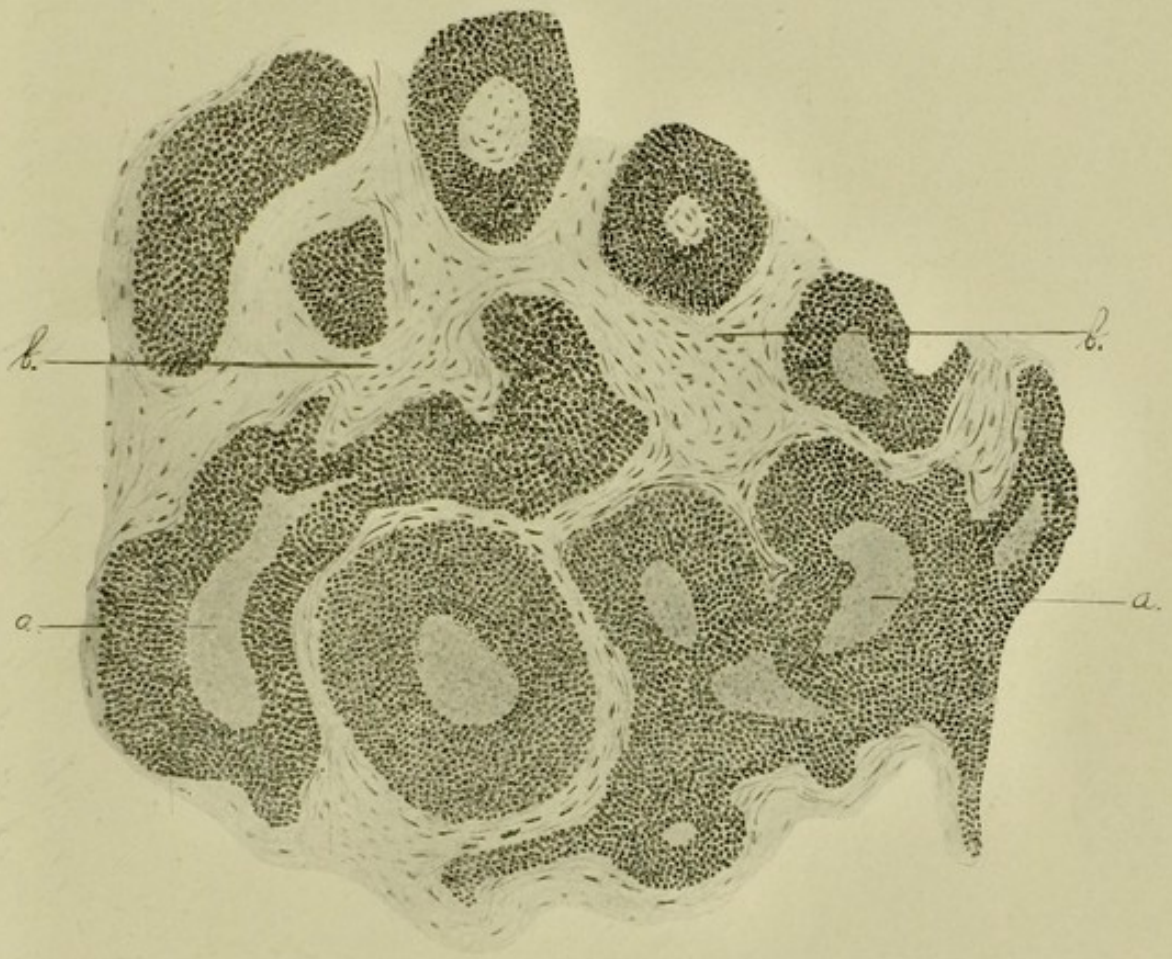

FIG. 5.—Intricate arrangement of stroma and epithelium in which it is difficult to interpret the appearances without the study of serial sections.

a.—Necrotic tissue.

b.—Stroma.

FIG. 6.—"Inverting type" of proliferation. The epithelium between the papillary growths has proliferated outward toward the muscular wall.

a.—Necrotic tissue.

b.—Stroma.

c.—Epithelium.

d.—Masses of epithelium lining cavities that have not been opened in this section.

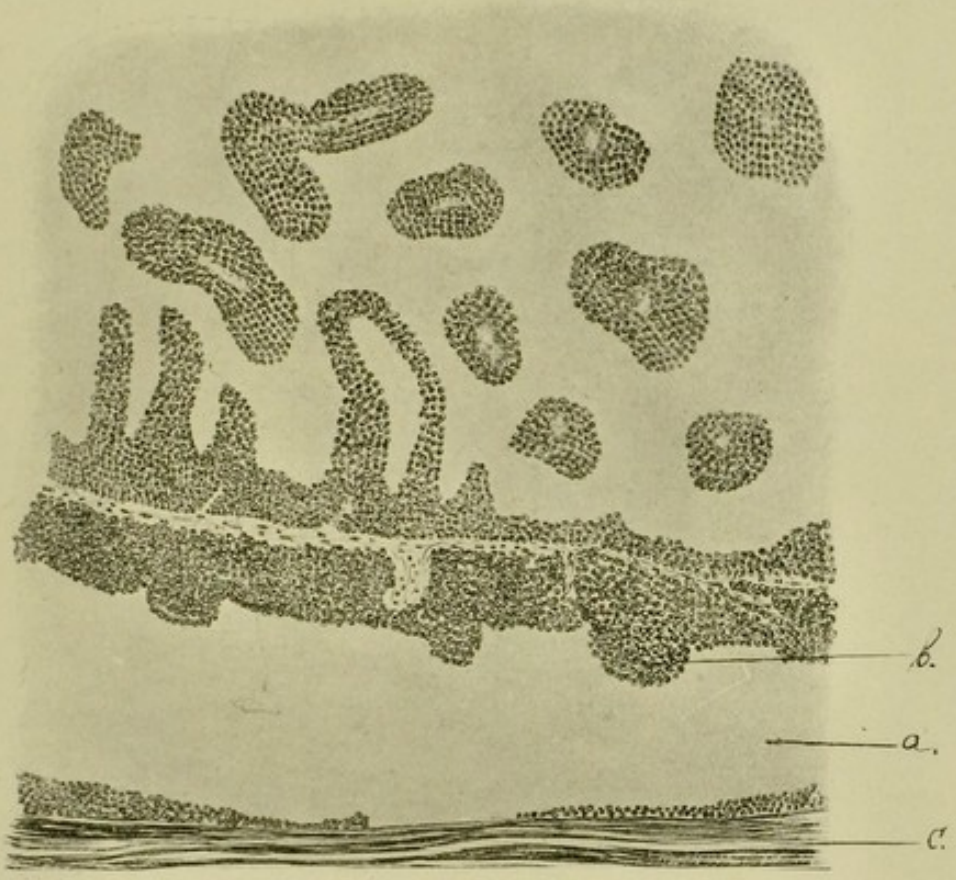

FIG. 7.—Showing the outward growth of intervillous epithelium and the flattening of the thereby produced diverticula against the muscular wall of the tube.

a.—Diverticulum filled with necrotic tissue.

b.—Beginning papillary proliferation of epithelium into the diverticulum (cyst).

c.—Muscular wall of tube—only a part of which is shown.

its contents—a large amount of ascitic fluid—and the vaginal [61]
fornix, which was so redundant as to protrude at the vulva, was removed and its edges closed with catgut sutures. The uterus was curetted and packed with iodoform gauze. There was nothing removed from the uterus which led to any suspicion of its containing a neoplasm. The patient, though fractious and unmanageable, made an uninterrupted recovery, leaving the hospital at the end of the third week.

Macroscopical Appearance.

The mass consists simply of the left Fallopian tube. Its uterine end tapers abruptly and the abdominal end is the seat of an exuberant, cauliflower-like growth of new tissue which appears to have burst forth from the tube (Fig. 1). The tube forms a small U-shaped bend, the convexity of [62]
which is upward. The middle of this convolution measures 1.5 cm. in diameter. It then bends downward and becomes greatly dilated. Its external surface is covered with a smooth, glistening, unbroken serous membrane which contains many circularly arranged blood-vessels. All signs of fimbriæ at the outer end have disappeared. At the external end is an abrupt termination of the smooth serous covering which is overrun with tissue grown out of the abdominal ostium. This new tissue consists in part of small, smooth nodules which vary from .6 and .8 to 1.5 and 2 cm. in diameter and of shaggy, rough tissue between the rounded parts. This outgrowth is spread over more of the under surface of the tube than elsewhere; it is very friable. The ovary and its ligament form a pedunculated appendage to the tumor mass and is small as compared to the large tube (Fig. 2). The length of the growth is 13.5 cm. The ovary contains a large corpus luteum; the external surface is smooth. Just in front of the tubo-ovarian ligament is a small accessory tube measuring 28 mm., springing directly from the serous covering of the main tube; its stalk is 1 mm. in diameter; its outer end is dilated (Fig. 1). The weight of the entire mass is 250 grammes. The tumor was hardened entire, and without cutting, in Mueller's fluid and formalin (4 per

[62] cent), except a small, irregular mass detached from the external end; this was hardened in strong alcohol (95 per cent). When the hardening was completed the tube was sectioned through its long axis. The center was found occupied by a soft material of a gray color; it filled the canal, and extends between the projecting masses of tissue which fringe the lining (Fig. 3). The muscular coats are thin, but the mucosa by its proliferation has invaded the necrotic content of the tube for a distance which averages·1 cm. in all parts of the tube. The proliferating lining is dotted over with grayish, necrotic débris. The greatest accumulation of this material has occurred in the middle of the tube where it measures 2 cm. in diameter; at this point the remaining 5 cm. of the diameter of the tube is occupied mainly by the proliferating mucous membrane. The muscular and fibroserous coats measure from 1 to 3 mm. in thickness. At the uterine end of the tube there is a large amount of necrotic material in the lumen and but slight proliferation of the lining; at the abdominal end this condition is reversed.

Microscopic Appearance.

Sections were cut from points along the whole length of the tube and stained by various methods. The structure is essentially the same in all portions. Set upon the muscular coats, which are thin, are many papillary or villous growths. They are usually tenuous stalks of connective tissue covered with epithelium (Fig. 1), which branches and rebranches to form a tassellated lining (Fig. 4). The epithelium consists of many strata, of which only the deeper layers have a columnar type. The nuclei are oval and irregular and do not stain very strongly. The absence of a nuclear membrane and the arrangement of the chromatin in certain nuclei betokens poorly preserved karyokinetic figures. This assumption is made certain by finding, after some search, certain masses of chromatin which are plate-shaped and, in other cells, the double plates of metakinesis. Such nuclei in process of division are quite numerous; they are as abundant in the outer strata as in the inner. In sections stained after the iron-hæmatoxylin method, these nuclei in

various stages of division form black masses. In some of the [62]
dividing nuclei, in spite of the unfavorable fixation, the centrosomes and the pointed ends of the groups of achromatic threads may be seen. There are no more irregularities in these dividing nuclei than might be accounted for by the hardening process. The layers of cells often number ten to twenty and in the outer parts of the tumor near the abdominal end they are even more numerous. The many-layered appearance of the epithelium is not due to the thickness or obliquity of the section, for in very thin sections cut in paraffin and not more than one cell in thickness, at least four to six layers are present, and this is true for regions where the outer layers have undergone considerable necrosis, where, in fact, the tips of papillæ are buried in necrotic débris. In no place are any single rows of epithelium upon a basement membrane found, such as occurs in the normal folds of the tubal mucosa. With low powers of the microscope the epithelial character of these cells is not clearly evident because of the large size of the nuclei as compared with the scanty amount of protoplasm surrounding them. Even with the immersion objective some appear to possess very little protoplasm. The nuclei alone average about seven mikrons in diameter when they are circular; the nuclei of the columnar cells measure in their long diameter ten to eleven mikrons. Exceptionally very large nuclei may be found which measure 15 to 20 mikrons in diameter. In practically every nucleus of the resting cells there may be found small oval bodies colored a pale green, with the hæmatoxylin and eosin staining; with the iron and hæmatoxylin and considerable differentiation, these bodies are much darker. Very rarely two occur in the same nucleus; they are undoubtedly nucleoli; the peculiarity consists in their large size. Very often they equal in diameter one-third or one-fourth of the diameter of the nucleus; exceptionally they occupy one-third of the entire nucleus. The columnar shape of the cells close to the stroma is manifested more by the shape of the nucleus than by the cell body; in this region the nuclei are more closely arranged in palisade form.

[62] On the edges of these villous growths where the epithelium is in contact with the necrotic material, and in places where the edges of papillæ are in contact, the epithelial cells have undergone degenerative changes. Here occur occasional nuclei, usually smaller, in which the chromatin is collected in a few granules which stain intensely with nuclear dyes, and such granules commonly festoon the inner margin of the nuclear membrane or form a few crescent-shaped masses on its lining. Such nuclei may appear devoid of cell bodies. More frequently the necrosis has resulted in shrunken and
[63] irregular nuclei which stain deeply throughout. Some nuclei also have long, twisted and irregularly tortuous extensions. Upon the ultimate border occurs a zone composed of dust-like granules of chromatin. In the necrotic tissue in which the free ends of the papillæ are embedded, there may be found occasionally cells distinguishable by their shape and size which have, however, lost all power to react to nuclear dyes; they assume the same tint with eosin as the granular material in which they lie. Leucocytes are present in the epithelial covering of the papillæ, but only as isolated cells; they are never accumulated in foci. Although often of the polymorphonuclear type, there are also many with small round nuclei. In the layers of epithelium they are easily distinguished from the epithelial cells in process of division, but in the outer bordering zones of necrosis they lose their identity. The leucocytes are often present in the walls of the vessels of the stroma.

The stroma or connective-tissue stalks upon which the epithelium is arranged to form papillary growths is very delicate (Fig. 4). It consists of but little more than a vessel wall. On each side of the lumen of the vessel are from three to six layers of parallel long cells which resemble the cells of involuntary muscle. Their nuclei are slender and from 20 to 30 mikrons in length and possess rounded or abrupt, blunt ends. The margins of these cells are obscure when in contact; but in advantageous places it is possible to see that the cells, like the nuclei, are spindle-shaped. Where papillæ have been cut across, the ends of the divided nuclei of these cells appear round and the nuclear membranes

are much darker than when in longitudinal planes. Elastic [63]
fibers (Weigert's stain) are present neither in the walls of the blood-vessels of the connective-tissue stalks nor in the layers of cells which surround the vessels. The endothelial lining of the vessels is well preserved and shows no changes. There is some fibrin in some of the vessels and a small quantity in the necrotic tissue between the papillæ; in either case it never consists of more than a delicate network, extremely irregular. In sections from all parts of the tube examined it is possible to find villous outgrowths, the epithelium of which has become completely necrotic, but in which the stroma has not entirely lost its staining properties. Such papillæ, stained with Van Gieson's stain, show prolongations of the stroma extending for even long distances into the necrotic material before their nuclei, too, suffer chromatolysis. In some papillæ the epithelium is entirely necrotic upon both sides for only a short segment of its extent, the fuchsin-stained stroma bridging over the defect.

It is evident from the foregoing description that the papillary growths in this tumor consist mainly of an epithelial covering of many layers and that the proliferation of these has been so marked that they have filled the tube entirely, distended it to a marked degree and have undergone a considerable necrosis. The necrotic tissue has filled the enlarged channel. These growths have been referred to as stalks, as villous growths; when cut directly across, their outline is circular. Such circular bodies lying in the midst of the necrotic tissue have a striking appearance, since in certain sections they are found at considerable distances from any other tissue. Their outer margin is bordered by the dark circle of pycnotic nuclei and chromatin granules; the larger part of the body consists of the mass of epithelium with the radially disposed nuclei, and a small vessel containing numerous red blood-cells forms the center.

As might be expected, these villous growths have no regularity in their arrangement. The study of many sections cut in series shows that the entanglement is very intricate (Fig. 5). Arising from the wall of the tube, their course may be directly toward the lumen or oblique or even par-

[63] allel to the wall. To complicate the arrangement, the villous growths frequently join one another as well as branch; consequently, in certain sections there may be seen at short distances from the muscular walls regions made up entirely of masses of epithelium, each mass consisting of a papilla cut obliquely or transversely, and containing in its center the blood-vessel. The edges of these clusters of epithelium may be in contact and the line of division difficult to find; in other places a narrow row of necrotic cells separates the epithelium of different papillæ; in yet other places the necrotic material has accumulated between them so that they appear well separated.

In deeper zones nearer the muscular walls still another peculiar appearance is obtained. Here the condition is reversed; the stroma borders the epithelium on the outside, and the epithelium lines a cavity filled with necrotic tissue (Fig. 6). The examination of serial sections shows that such cyst-like collections of cells are due to the growth outward, toward the muscular layers, of that part of the mucosa which intervenes between the villous prolongations; these outward growths, when cut across, appear like small cysts filled with necrotic tissue. As a rule the lining of these cavities at the inner margin is sharp and distinct. The layers of the epithelium are the same in character and number as those which cover the papillæ. It is essentially the same epithelium; the proliferation toward the lumen has resulted in villous growths; toward the muscular wall, in cavities; and these, when sectioned, appear like cysts. The necrotic material which fills them usually stains lightly and with eosin, but some are met with which are quite filled with chromatin granules; such cysts (so-called for convenience) have a darkly stained content. Naturally, such cavities are not always sectioned directly across; they often appear long and parallel to the muscular wall, or they are short and more oval. The muscular wall is bordered in this manner with but little interruption. It is obvious that the interpapillary proliferation outward toward the muscular wall has met with an obstruction; the distention of the tube has not been able to keep pace with the proliferation of the

epithelium. Sections occasionally show the following con- [63]
dition: the inner border of the muscular wall of the tube is covered with the same epithelium in strata as has been described upon the papillæ. This epithelium lines a cavity the opposite wall of which is quite distant (the width of the field, Obj. 3, Ocular 3, Leitz) and from the opposite wall [64]
small villous growths project toward the muscular wall; the remainder of the cavity is filled with necrotic tissue (Fig. 7). These cystic formations in some sections, with the tissue in which they lie, form a zone of considerable width just inside the muscular coats.

The tissue between the cysts is made up of the same elements as those described in the stroma of the villus, except that between the cysts it is abundant, whereas in the villi it is insignificant. It contains the long spindle cells, in all respects identical with those found in the villi; also many vessels in which are little more than loose-walled sinuses. Scattered leucocytes are seen frequently both with round and with irregular nuclei. The greater part of the stroma is apparently formed by fibers; some of them stain red with Van Gieson's stain; most do not. There are no elastic fibers among them. Numerous slender capillaries, which are so delicate that a single red corpuscle fills the lumen completely, are conspicuous in some sections in the stroma; with the iron-hæmatoxylin stain, by which the red blood-cells are made almost black, such capillaries, filled with blackened cells, form a distinct delicate network.

Very peculiar appearances are caused by the occurrence in the stroma, in certain places, of collections of blood-serum[64]—œdematous regions. The coagulated serum usually has small holes in it, oval in shape, which resemble the holes in the cells of a fatty liver; often leucocytes are found in the holes. The margins of the serum are beset with semicircular spaces; both the oval holes and the marginal defects are due to the shrinkage of the coagulated serum. In such œdematous situations, and in the tissue of the border-

[64] The fluid of the blood is readily coagulated by hardening in solutions which contain chromic acid or its salts.

[64] ing zones, are found large swollen cells in all stages of dropsical degeneration; the wall of the cell forms a bag for the network produced by the vacuoles. Such vacuoles do not have the clear outline of holes which at one time contained fat. Often considerable fibrin occurs in the œdematous spots, and in places œdema is combined with hæmorrhage. Plasma or mast cells are not present in the œdematous districts or in the stroma elsewhere.

The question naturally presents itself: Are there any loose, unconnected, wandering epithelial cells in the stroma? A careful search for these was made in different ways. Many cysts were examined to see if at their outer margins there could be found any evidences of the proliferation of the epithelium outward into the stroma. Also many serial sections were examined to see if any of the collections of epithelium which form cysts were entirely unconnected and cut off; a third evidence of such a process was sought for, viz., cells in the stroma with nuclei in mitosis. All of these signs of invasion of the stroma by loose and wandering epithelial cells were absent. The proliferation of the epithelium has been *en masse;* by the proliferation of the tubal lining as a membrane; also by the production of a lining of many strata.

The muscular wall of the tube averages 1 to 2 mm. in width. The muscle fibers are few in number; sections stained by the picrofuchsin mixture reveal a large amount of fibrous connective tissue which takes a brilliant red color; this preponderance of fibrous tissue is especially marked in the inner half of the wall. The circular coat has undergone the greatest atrophy; only occasional strands of it are present.

The outer half of the fibro-muscular wall is more loosely arranged. There are many large, flattened blood-vessels in this portion and around them small aggregations of fat. In the inner one-half of the wall occur occasional clusters of lymphoid cells that show the effects of pressure, being greatly elongated and parallel with the fibers. Such lymphoid nodes made up entirely of cells that correspond to small lymphocytes occur in all sections. In a few sections there are

islands of cells that present a different appearance; closely [64]
aggregated cells with pale nuclei form an elliptical clump that possesses a very definite margin. Careful examination fails to reveal any nuclear figures in these cells; their nuclei possess very little chromatin; their arrangement is quite irregular; for these reasons and the fact that no lining cells can be found for the spaces in which they lie, a conclusion was reached that these islands have resulted from the proliferation of the endothelial lining of lymph channels. Still other islands of cells leave no doubt but that the proliferating epithelium has penetrated deeply within the fibro-muscular wall. In a few sections, lying nearer the inner border of this wall, are irregular tubules lined with epithelial cells. The nuclei of the cells are long, occupy most of the cell and stain deeply. The cells are columnar and in places two or three strata in depth. Some of these tubules occur within lymph channels, for outside the deeper and more columnar cells the endothelial lining of the channel is easily recognizable. Since these deeper prolongations of the epithelium were found so seldom, no effort was made to prove their connection by serial sections with the more centrally located parts of the tumor. The ovary contained no tumor tissue.

From Dr. W. W. Sheppard, the family physician, it was learned that for some time after the operation the patient was "nervous and hysterical," but improvement was steady and she was soon able to be up and around the house a part of each day. About nine or ten weeks after the operation ascites reappeared and upon vaginal examination a tumor, the size of an orange, was found on the left side. The ascites was relieved by tapping two or three times, the first being done on November 1st. During the month of December Dr. Byron Robinson was called in consultation. He has informed me that he found the abdomen enormously distended by a large tumor and considerable ascitic fluid. The patient was sitting up and able to walk about the house; her general appearance was cachectic, pulse 120, temperature 100° F. The tumor arose from the small pelvis and upon vaginal examination was found to be fixed, except

[64] its uppermost portion, which was slightly movable. It was
[65] located chiefly on the left side. The uterus was slightly enlarged.

Operation (by Dr. Robinson).—Upon opening the abdominal cavity with a long median incision the entire peritoneum was found studded with papillomatous growths which varied in size from those barely visible to some as large as a hen's egg. The larger ones were located in the lower, left quadrant of the cavity, and in this position were adherent to one another so as to form an irregular mass. There were approximately two gallons of a clear ascitic fluid, similar in tint to pale ale, in the cavity. The irregular tumor on the left side was firmly adherent to the left lateral wall of the small pelvis; it extended upward so as to be in front of the sigmoid; the omentum was firmly adherent to it, and in the omentum near the tumor and also in the adjacent mesentery were many small shot-sized and pea-sized warty growths. Most of these growths had a pale yellowish color and were like a fresh brain in consistency; some of the smaller growths appeared very vascular. All of the larger growths were removed.

Recovery followed the second operation without any special events. At present she is able to perform some of her customary household duties. The ascites returned gradually so that about five months after the second operation paracentesis was necessary for the patient's comfort; and it has been practiced every two or three weeks since. At one time eleven quarts were removed, at another twelve quarts; the fluid maintains its former characteristics. A sample of this fluid showed on examination the following features: sp. gr. 1007, alkaline reaction, a large amount of albumin, absence of sugar, a moderate amount of proteids (biuret reaction), absence of bile, and .3 of 1 per cent of urea. I received the tumor masses removed by Dr. Robinson after they had been in a weak aqueous solution (4 per cent) of formalin for several days.

Macroscopic.—They consist of three large masses and about a dozen smaller; altogether they weigh 1,350 grammes. The largest piece measures $16 \times 13.5 \times 4$ cm.

and is disk-shaped; on section it presents a granular surface [65]
which resembles somewhat adipose tissue. Its external surface is smooth except for tag-like, torn adhesions. Its concave side has a furrowed and trabeculated appearance. The next smaller in size is very irregular in form, measuring 12 × 10 × 5 cm.; it is very rough and nodular externally and in spots has been torn. The smallest of the large pieces measures 11 × 7.5 ×4.5 cm., and on section is found to possess a much softened, necrotic center. One of its flat surfaces is quite smooth. All of the smaller masses are very irregular; some appear to be little more than fibrous tissue, others resemble the larger masses.

Microscopic (continued).—Sections were made of all the large growths, and some of the smaller, and stained by various methods. A large part of all the growths consists of necrotic tissue; many sections contain little else. The necrosis is most marked in and around the central portions; such necrotic tissue stains lightly or darkly according to the degree of chromatolysis; varying degrees of œdema and quantities of fibrin occur as well as small hæmorrhages. In sections where necrosis is less marked, the appearance of the innermost parts of the tubal tumor are duplicated; here occur cross-sections of papillæ lying in the necrotic tissue which are in all respects similar to those in the tube in size, shape, paucity of stroma and number of epithelial strata; the epithelial cells contain similar large nucleoli. Karyokinetic figures, however, are much more numerous; often three, four or six dividing nuclei are present in a single field of the immersion objective (celloidin sections, 15 to 20 mikrons thick). The stroma of the papillæ—connective-tissue stalks—has its origin in a capsule which surrounds each metastatic growth more or less completely. The capsule is formed by long cells arranged parallel to the circumference whose oblong nuclei contain nucleoli which are barely visible; these cells are not arranged in layers, for the nuclei have been cut in all possible diameters; the cells resemble the "fibroblasts" of organizing granulation tissue. In sections of the various metastatic growths, and even in different sections of the same growth, the capsule shows

[65] large blood-vessels, regions of necrosis and of hæmorrhage and thrombosed vessels. In regions just internal to the capsule, where the papillomatous growths have been so luxuriant that the papillæ are in contact and a tissue has been produced which appears solid and granular, if the stroma be examined in such places *the connective-tissue cells are also found with mitotic figures.* They are never as abundant as the dividing nuclei of the epithelium; that the stroma or supporting tissue contains cells which are multiplying is beyond doubt; that these cells are the same as those which constitute the stroma is also certain, since all stages of multiplication by indirect division may be found and also for the reason that there are no other cells in the stroma with resting nuclei than those described. It may be inferred that this difference between the stroma of the papillæ in the primary tumor and that in the papillæ of the metastatic growths is due to more favorable conditions of nutrition; it is also possible that the more rapid proliferation of the epithelium, as is shown by the abundance of dividing nuclei, has in itself led to a proliferation of the cells of the framework, and that this has been sufficient in amount to allow the observation of occasional dividing nuclei in the stroma cells.

This condition of embryonal stroma and embryonal epithelium, since both contain dividing nuclei, has resulted in a line of demarcation where epithelium and connective tissue meet, which is much less distinct than similar lines of contact in the primary tumor. In regions close to the capsule, where there has been a rich growth of papillæ and necrosis has not occurred, the indistinct line of contact and the entanglement of papillæ renders it difficult to distinguish between epithelium and connective tissue. Some aid may be had from the columnar position of the nuclei of the epithelium on the stroma, but this does not always obtain; in other places the epithelium has contracted away from
[66] the stroma so that a narrow space is present. The blood-vessels in the stroma have very little wall; they resemble the vessels commonly encountered in a small spindle-celled sarcoma.

Among the tumors of the Fallopian tube that can be con- [66]
sidered as carcinomata, this case is unique in the following particulars: The os abdominale was evidently open, since there was not formed the usual sac, and invasion of the peritoneal surface and adjacent tissues probably took place via this opening by continuity of surface. The case is also remarkable in that large secondary tumor masses were removed from the abdominal cavity, the patient still living, although slowly succumbing to the disease.[65] The similarity in method of growth and general histologic structure to proliferating cystadenomata of the ovary is continued in the comparative benignancy of the peritoneal metastases.

The appended table comprises 21 cases of carcinoma that were selected from 52 cases that have been reported as papilloma or carcinoma. 15 of the 52 were excluded by reason of insufficient data; of the remaining 37 some have been shown to be instances of hyperplasia of the tubal mucosa due to inflammation, a process usually combined with sacto-salpinx, that leads to the formation of benign localized growths whose position in the domain of tumors is very questionable, or to more diffuse growths that may possess some of the characteristics of malignancy; the latter resemble the carcinomata that develop in scars, burns or fistulæ from long-continued irritation.

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[65] The patient died February 18, 1901; through the kindness of Dr. Sheppard, a necropsy was secured, the details of which will be shortly published.

AUTHOR, TITLE AND PLACE OF PUBLICATION.	BILATERAL OR UNILATERAL.	CONDITION OF THE OPPOSITE TUBE.	CLOSURE OF OS ABDOMINALE AND FORMATION OF A SAC.	RECURRENCE OR RECOVERY. DEATH SOON AFTER OPERATION.	CONCERNING METASTASIS, INVASION OF ABSCESS CAVITIES, ETC.	CONDITION OF THE OVARIES.	REMARKS.
E. Senger: Ueber ein primäres Sarkom der Tuben. Centralbl. f. Gynäk., 1886, X, p. 601, Leipzig.	Bilateral.		In both tubes there occurred two dilatations or sacs.	Tumor found at necropsy.	In Douglas's pouch a small growth.	Both normal.	Reported as sarcoma.
E. G. Orthmann: Ueber Carcinoma Tubæ. Ztsch. f. Geburtsh. u. Gynäk., 1 88, XV, p. 212, Stuttg.	Right tube.	Pyosalpinx.	The outer end, greatly dilated opened into an abscess cavity.	Death on sixth day after operation.	The tumor had invaded two abscess cavities. A small nodule in the "excavatio vesico-uterina." A swollen lymph gland in the small pelvis.	Abscesses in both ovaries.	
A. Doran: Primary Cancer of the Fallopian Tube. Tr. Path. Soc. (London), 1888, XXXIX, p. 208.	Right tube.	Left tube at operation appeared small.	Outer end closed: a sac formed.	Recurrence; lived nearly eleven months after operation.	Lumbar glands invaded.	R.—cancerous.	At necropsy, tumor found in the uterine vesical and vaginal mucosa.
C. J. Eberth and R. Kaltenbach: Zur Pathologie der Tuben. Ztsch. f. Geburtsh. u. Gynäk., 1889, XVI, p. 357, Stuttg.	Bilateral.		L.—dilated to size of thumb. R.—larger (faustgrösse.)	Recurred in 18 months.	Subperitoneal nodules noted on the right tube.		Demonstrated first as carcinoma. Reported later as papilloma.

T. Landau and J. Rheinstein: Beiträge zur pathologischen Anatomie der Tube. Archiv f. Gynäk., 1890-91, XXXIX, p. 273, Berl.	Right tube.	Outer end closed and a sac formed that contained 500 ccm of bloody, thin fluid.	Sac formed on right side.	Recurred in 10 months.	Ascites after the operation, with hard masses in the abdomen.	Normal.	
S. D. Michnoff: A Case of Primary Carcinoma of the Fallopian Tubes (Russian). Meditsina, 1891, III, p. 181, St. Petersb.	Left tube.	Sacto-salpinx papillomatosa.	Left tube formed a sac as large as a large fist.	Recurrence in 7 months.	A cyst occurred at junction of right tube and ovary, size of a hen's egg; it was filled with clear fluid.	L.—ovary left in body, it was imbedded in adhesions. R.—normal.	
P. Zweifel: Vorlesungen über klinische Gynäk., 1892, p. 139, Berlin.	Bilateral.		Large sacs on both sides. L. tube 20 cm. long and 8 cm. thick.	Presumably recurrence, since patient died 1½ years after operation.		Normal.	
F. J. E. Westermark and U. Quesnel: Ett fall af dubbelsidig kancer i tubæ Fallopii. Nord. Med. Ark., 1892, XXIV, Nr. 2, p. 1, Stockholm.	Bilateral.		Sacs formed on both sides—larger on left.	Recurrence: death in five months.	Invasion of cyst of right ovary. No exudate in peritoneal cavity at necropsy. Lymph glands of small pelvis invaded. T.—nodules found in the liver at the necropsy.	L.—ovary cystic. Monolocular cyst size of an orange.	Carcinoma of the cervix found at the necropsy.

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R. Kretz: Zur Casuistic der Papillome der Eileiter. Wien. klin. Wchnsch., 1894, VII, p. 572.	Bilateral.		L.—tube 17 cm. long and 6 to 8 cm. in diameter. R.—tube similar. Both closed externally.		Small subperitoneal nodules noted, externally on both tubes. Invasion of the lymph channels, (histologic examination).	Unknown.	Reported as papillomata. Kretz considers the case similar to that of Eberth and Kaltenbach.
W. Fischel: Ueber einen Fall von primärem papillärem Krebs der Muttertrompeten. Laparotomie, Heilung, Ztsch. f. Heilk., 1895, XVI, p. 143.	Bilateral (?)	Condition of left tube not positively known. It was imbedded in adhesions and not removed.	R.—tube formed a sac 8 by 4.5 cm.	Recurrence: death seven months after the operation.	Small nodules on external surface of right tube. Abdominal cavity contained clear as itic fluid.	Unknown.	Part of the cyst of the right tube possessed a smooth wall covered by a single layer of short epithelium.
A. Rosthorn: Primäres medulläres Carcinoma tubæ. Ztsch. f. Heilk., 1896, XVII, p. 177.	Right tube.	At necropsy left tube found to contain metastatic (?) tumor nodules.	Sac formed by right tube supposed to be pyosalpinx.	Recurrence: death six months after first operation.	Inguinal glands removed at a second operation. Retroperitoneal glands found invaded at the necropsy.	Cyst of right ovary.	Necropsy by Chiari.
T. J. Watkins (and E. Ries): Exhibition of unique microscopic sections of papilloma and carcinoma of the tubes, etc. Am. Gyn. and Obst. J., 1897, XI, p. 272, N. Y.	Bilateral.		Both tubes large and formed by four convolutions; both closed externally.	Recurrence: death seven months later.	Ext. end of the right tube connected to a mass 4 × 4 × 5 cm. This contains a central cavity beset with several warty growths. Metastatic carcinomata on the ovaries and on post. surface of right tube. Collections of tumor cells found in lymph channels of wall of left	L.—ovary many corpora candicantia.	Condition of right ovary not clear.

E. Falk: Fortschritte u. gegenwärtiger Stand der vaginalen Operations technik. Therap. Monatsh., 1897, XI, p. 313, Berl.	Left tube.	Unknown.	Left tube closed externally. Sac formed.	Recurrence: death seven months after operation.		L.—ovary normal.	Tumor found in the uterus in mucosa near right ostium and diagnosed as sarcoma was supposed to be responsible for recurrence and death.
K. Eckardt: Ein Fall von primärem Tubencarcinom. Arch. f. Gynäk., 1897, LIII, p. 183.	Left tube.	Normal. (Doran).	Sac formed by the left tube size of child's head.	Healthy a few months later. Subsequent history unknown.	Subperitoneal elevations, size of hazel-nut, make external surface irregular.	Both normal.	Broad ligament shortened by invasion of the tumor.
A. H. Pilliet: Épithélioma de la trompe utérine. Bull. Soc. Anat. de Par., 1897, XI, p 956.	Right tube.	Unknown.	Cavity in the right tube opposite ovary.	History not known.	Invasion of the lymph channels, (histologic examination.)	Condition of left ovary unknown. R.—invaded by tumor in its outer part only.	
C. H. Roberts: A Case of Primary Carcinoma of the Fallopian tube. Tr. Obst. Soc. London, 1898, XL, p. 189.	Right tube.	"The left tube inflamed and closed."	Outer end of right tube closed: sac formed.	Well ten months later.		Normal.	Very brief histologic description.
J. Fabricius: Beiträge zur Casuistik der Tubencarcinome. Wien. klin. Wchnsch. 1899, XII, p. 1230.	Left tube.	At first operation the right adnexa appeared normal; at second, thickened.	Supposed to be a pyosalpinx until it was cut.	Recurrence five months later when a large mass filled the right half of the pelvis.		Unknown.	At the first operation masses removed were pronounced papilloma. At the second operation when radical removal was found to be impossible, masses were removed that were pronounced carcinoma.

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J. Fabricius: Idem.	Right tube.	L.—adnexa appeared normal at the operation.	Abdominal opening leads into a cyst.	Recurrence: five months after first operation left adnexa and uterus were removed.	Carcinomatous invasion of the cyst on right side. At the second operation it was found that the entire peritoneum was beset with small tumor nodules. The metastatic nodules on the outer surface of the uterus were examined and pronounced adenocarcinoma.	Right ovary enlarged but otherwise normal.	After second operation a large cyst developed that reached upward to the navel and finally evacuated through the rectum.
(98) Danel: Essai sur les Tumeurs malignes primitives de la Trompe Utérine, 1899, Paris.	Left tube.	Appeared healthy at operation. Not removed.	Left tube formed a sac.	Recurrence took place on the right side.	Many peritoneal growths on the uterine end of the tube. Enlarged glands in the adhesions around left tube. Tumor cells found in the lymph channels. (Histologic examination.)		
B. Friedenheim: Beitrag zur Lehre vom Tubencarcinom. Ueber ein primäres, rein alveoläres Carcinom der Tubenwand. Berl. klin. Wchnsch., 1899. XXXVI, p. 542.	Left tube.	Unknown.	No sac formed.	History subsequent to operation unknown.	Left tube and tumor adherent to colon. Left parametrium infiltrated with tumor masses.	L.—smooth externally, size of a walnut, contained small cysts.	Tumor said to have had its origin in an accessory tube.
E. Mercelis: Primary carcinoma of the Fallopian tube. N. Y. Med. J., 1900.	Right tube.	Left tube removed. Condition not described.	Right tube 4 cm. in greatest diameter. Outer end	Recurrence on right side 18 months later.	Outer end of right ovary invaded by tumor.	L.—ovary small and firm—not removed.	