

A REPORT OF FOUR CASES OF MEMBRANOUS DYSMENORRHEA.

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The term "membranous dysmenorrhea" is applied to cases in which considerable portions of the endometrium are thrown off repeatedly at the menstrual period, usually with pains simulating those of labor. The cases vary in severity from the typical form in which a complete cast of the uterine cavity is discharged at each period with great pain, to the milder ones in which small fragments of the endometrium are passed with only slight symptoms at intervals of several months. Painless cases have occasionally been reported. The passage of a single membrane from the uterus does not constitute a case of membranous dysmenorrhea.

The affection is not a disease *sui generis*; but a condition which develops under varying circumstances, complicates different pathological processes, and presents a variety of microscopic appearances. Some writers have, therefore, suggested that the purely clinical term "membranous dysmenorrhea" be abandoned, and "exfoliative endometritis" (Wyder) (9), or "exfoliation of the menstrual mucosa" (Löhlein) (17) be substituted.

The etiology and pathogenesis of the condition are obscure, and the treatment has been attended with little success. This is due partly to the fact that the affection is in reality rare, and the specimens available for study still more infrequent. The milder cases are often not brought to the physician's attention, while, on the other hand, the diagnosis is frequently made on insufficient clinical data, and without a microscopic examination of the membrane. The latter point is illustrated by the fact that, of eleven specimens sent to the gynecological laboratory of the Johns Hopkins Hospital with the diagnosis of "membranous dysmenorrhea," only three proved, after investigation of the patients' history and examination of the membrane, to be genuine cases. The other specimens showed decidua in four instances, vaginal epithelium in two, and one example respectively of uterine polyp and blood-clot.

The disease was first recognized by Morgagni (1), who reported a case and gave an excellent description of its clinical course. Denman in 1791, also described membranes, but thought them identical with decidual casts, previously described by Hunter. The first microscopic study of menstrual membranes was made in 1842 by Ernst Heinrich Weber, and the term "membranous dysmenorrhea" was applied to the condition by Oldham and Simpson in 1846 (2). A certain resemblance to decidual tissue impressed observers more and more strongly, so that a prolonged discussion was carried on, especially in Germany, as to whether all cases of membranous dysmenorrhea were not in reality merely repeated early abortions. Only within the last thirty years have the two conditions been clearly differentiated. The first adequate histological study in the modern literature on the subject is that by Wyder (1878) (9). Von Franqué, in 1893 (23), reported five cases and made an elaborate study of the pathological

anatomy. Since his article numerous isolated cases have been reported, but little new information has been added to the subject.

The most important etiological factor in the condition is a preceding endometritis, arising after child-birth, an abortion or a gonorrhoeal infection. In other instances there is a retroflexion or some abnormality of the appendages. A considerable number of cases, however, occur in young unmarried women, with no history of infection and with pelvic organs apparently normal on examination. There is in this group, of course, the possibility of an overlooked vaginitis in childhood, or an endometritis accompanying the exanthemata.

The clinical history is usually somewhat as follows: Menstruation was regular and normal until after a labor or an abortion followed by fever, or after a gonorrhoeal infection. Dysmenorrhea then developed, followed in a few months by the appearance of membranes. These may be discharged only at intervals of three or four months. Usually, however, one is passed at each period; in exceptional cases two or more. Menstruation is accompanied by pain, and the expulsion of the membrane, which usually occurs on the third or fourth day, is preceded by intermittent uterine contractions, similar to those of labor. These cease after the discharge of the membrane, which is often followed by copious hemorrhage.

The prognosis as to recovery, either with or without treatment, is not good, as the condition usually persists until the menopause. Sterility is the rule, although a few patients recover and become pregnant.

The treatment most often adopted in cases where the underlying condition is obscure, is curetting a few days before menstruation, followed by the application of tincture of iodine or carbolic acid to the uterine cavity. This procedure frequently gives temporary relief, but the patients usually relapse within a few months. Any associated lesions of the uterus or appendages should of course receive appropriate treatment.

The menstrual membrane, when discharged entire, forms a triangular sac, having the shape of the uterine cavity, and sometimes showing rounded holes at the sites of the tubal openings. The outer surface (*i. e.*, towards the uterine wall) is ragged; the inner is smooth. The thickness of the membrane varies from that of tissue paper to two or three millimeters. Membranes of greater thickness suggest decidua. Complete casts of the uterine cavity are rarer in membranous dysmenorrhea than in pregnancy, the tissue in the former condition being usually passed in fragments.

A variety of microscopic appearances have been described in this condition. The membranous discharges from the uterus may be divided, however, into two groups (excluding decidua for the present): exfoliated mucosa and fibrinous casts.

In membranes composed of altered mucosa, two pictures

may be differentiated in a general way. The first is that of an interstitial endometritis. The stroma cells are of normal size and appearance, and there is an infiltration of lymphocytes. Hemorrhage, exudate, and fibrin are usually present in addition. In the second type the stroma cells show a strong resemblance to decidua. They are enlarged, oval or polygonal in shape, with a large vesicular nucleus and abundant protoplasm. All gradations may be traced between these decidua-like forms and the normal stroma cells. The entire membrane may be composed of these altered cells, or glands may also be present. Occasionally a compact and a spongy layer can be distinguished. The two pictures—interstitial endometritis and decidua-like areas—are often seen in the same membrane. It is these enlarged stroma cells which have given rise to so much confusion and to a prolonged discussion as to whether there is any criterion by which they may be differentiated from true decidual cells. They are usually interpreted in menstrual membranes, as the result of chronic hyperæmia and irritation. They are not, however, peculiar to this condition, being found also in glandular hypertrophy and œdema of the endometrium, where they are accounted for by circulatory changes.

Most membranes show signs of degeneration, varying from a hydropic appearance of the cells and inability to take ordinary stains, to coagulation necrosis. A "budding" of the interglandular tissue has been described by Von Franqué (23) and also by Hegar and Maier; *i. e.*, compact foci of stroma cells in which growth is more active, and which penetrate independently in different directions through the loose stroma. These authors found them also in the hyperplasia of the decidua associated with hydrorrhea gravidarum. They consider it a change which may be found in any plastic inflammation.

Amyloid change in the vessel walls has been found in membranes from a case of prolonged and severe pelvic inflammation. Large numbers of eosinophiles and also mitoses in the stroma cells have been reported by several observers.

Fibrinous casts are composed of a network of fibrin containing in its meshes red corpuscles, leucocytes, and remnants of the cells of the mucosa. There is some doubt as to whether these casts should be classified with true cases of membranous dysmenorrhea. Some authors exclude them entirely. They develop, nevertheless, in connection with endometric processes, and are passed with the same symptoms as the organized membranes. In fact, cases have been reported, in which the same patient passed at one time a fibrinous cast, and at another a membrane of altered mucosa. It is impossible, also, to separate the two varieties anatomically, as many transitional forms are found between the simple fibrinous cast and the well-preserved, exfoliated endometrium. Schönheimer (22) considers the process to be an acute fibrinous inflammation occurring under the influence of menstrual congestion, after a terminated endometritis, and subsiding at the end of the period.

The mechanism of separation of the membrane is obscure. The most generally accepted theory is that the hyperplasia

of the stroma cells causes an obstruction to the escape of blood into the superficial layers; hence it spreads out in the deeper portions of the mucosa. The tissue, friable because of chronic hyperæmia and its young connective-tissue cells, yields in its weakest part, and the membrane is dissected off by hemorrhage. The free bleeding which frequently follows the expulsion of the cast is thought to confirm this theory. An abnormal density in the superficial layers of the endometrium would also hinder the escape of the blood, and lead to the same result. Speaking against this mechanical theory of separation is the fact that the blood is often distributed equally through all parts of the membrane.

The degenerative changes found in the greater number of membranes must also be an important factor in causing separation,—possibly quite as important as they are in the separation of the decidua. Regressive processes in the decidua—chiefly coagulation necrosis with the appearance of fibrin—appear in the second half of pregnancy and are marked at term. The membranes from our first case show widespread coagulation necrosis in the stroma, and in the second case the process is beginning. In both cases there are pronounced changes in the blood-vessels,—many are occluded with fibrin and their walls degenerated.

The diagnosis of membranous dysmenorrhea, although it may be very probable from the clinical history, should not be made without a microscopic examination, as there are two other discharges from the genital tract, which may simulate menstrual membranes macroscopically. These are vaginal casts, or fragments of vaginal epithelium, and decidual casts. The former are thrown off, either as the result of an exfoliative vaginitis, or treatment of the vagina with strong chemicals, such as silver nitrate. The tissue in exfoliative vaginitis may be passed either during menstruation or independently of it. If the pieces are passed with pain during the period, the case may be considered one of membranous dysmenorrhea. This was the case in two specimens sent to the laboratory, with the diagnosis of "membranous dysmenorrhea," and proving, on microscopic examination to be of vaginal origin. An exfoliative vaginitis may accompany a true membranous dysmenorrhea. Leopold (11) reports a case of this kind, and considers the cause of the two processes the same, *i. e.*, a superficial hemorrhage, arising from extreme hyperæmia, and extending through the cervix into the vagina. Hoggan (6) describes a membrane, the upper part of which was composed of uterine mucosa, the lower of vaginal epithelium. If small portions of vaginal epithelium are passed together with endometrium, the former may be overlooked, in case only the larger pieces in the specimen are examined.

As a rule vaginal casts and pieces of vaginal tissue are thinner, tougher, and more parchment-like than membranes from the uterus, and no glandular openings are seen on the surface. The diagnosis can be made immediately with the microscope.

Decidual casts are expelled in abortion, extra-uterine pregnancy, and in the rare cases of pregnancy in one horn of a double uterus. The typical decidual cast is larger, thicker,

and more vascular than the dysmenorrhic membrane. If chorionic villi are found on microscopic examination, the diagnosis of intra-uterine pregnancy is of course clear. If decidua alone is present, the only diagnosis that can be made, from consideration merely of the cast, is that of the existence of pregnancy,—either in a normal uterus, a rudimentary horn, or a tube.

The greatest difficulty, however, has arisen over the differential diagnosis of an early abortion from a menstrual membrane containing large decidua-like cells. The question arises chiefly in cases of early pregnancy, before the decidua has reached its full development and typical form. Cells, which in size, form, nucleus, and staining properties closely resemble true decidual cells are found apart from pregnancy, not only in menstrual membranes, but also in œdema of the endometrium, glandular hypertrophy, and inflammatory conditions of the mucosa. There may be no difference in size between these enlarged forms and decidual cells, as was proved by Von Franqué (23) in a series of measurements; but the former do not show the epithelioid appearance found so often in the mature decidual cell, which has more abundant protoplasm and a much more sharply-defined outline. The protoplasm of the decidual cell also loses its fibrillated appearance and takes a deeper eosin stain. Although the differential diagnosis of a menstrual membrane from typical decidua is usually clear on microscopic examination, there are many confusing cases, in which the question of early pregnancy cannot be excluded without the aid of the clinical history.

There are specimens from three cases of genuine membranous dysmenorrhea in the collection of the gynecological laboratory of the Johns Hopkins Hospital, and also one specimen of a fibrinous cast, which, from the patient's history, should be included in this group.

The cases are as follows:

CASE I.—L. R., age 20. Gynecological history No. 12,427. Sent by Dr. G. K. Vanderslice, Phoebus, Va. Was admitted to the Johns Hopkins Hospital, October 11, 1905, and discharged October 20, 1905.

Complaint.—Pain in left side, painful menstruation and backache.

The family history was unimportant.

Past history and present illness.—Patient has always been well, aside from the present trouble. There is no history of severe infectious diseases.

Had a tumor removed from the right breast in 1904. Menstruation began at twelve years, is regular every four weeks, lasting seven days, and has been painful and profuse from the beginning. Ever since the onset, so far as patient can remember, she has passed with each period "pieces of flesh." Dysmenorrhea is severe on the first day, less on the second, and on the third day the membrane is passed during a paroxysm of pain, lasting about one hour. This pain, which is always located a little to the left of the mid line, is sharp, and, as patient expresses it, "feels like raking over a raw surface." It is relieved immediately by expulsion of the membrane, which is sometimes followed by considerable hemorrhage; at other times none.

Patient has also less marked paroxysms of pain in the intermenstrual interval. These attacks last frequently but a few minutes, and may occur several times a day, or at intervals of several days. The pain is located in the same spot as during

menstruation. Patient thinks that the pieces of membrane passed at present are smaller than formerly, and that she is gradually improving.

About a year before admission patient noticed that the uterus was situated low down, and since then she has been troubled with backache and leucorrhœa.

Physical examination on entrance showed a well-nourished girl. The heart, lungs, and abdomen were normal.

Pelvic examination under ether gave the following: Outlet, virginal; no signs of infection; cervix low, $1\frac{1}{2}$ in. from the outlet; fundus in ante-position; freely movable; both ovaries easily felt and apparently normal.

A dilatation and curetting were performed, and a very small amount of endometrium, normal in appearance, was obtained (nineteen days after the last period). The specimen unfortunately was not saved.

Patient made an uneventful recovery, and was discharged ten days after admission. She sent to the laboratory some material passed during the period in November, which on microscopic examination showed nothing but blood clot.¹

The laboratory possesses three specimens from this patient, the first passed when she was fifteen years old, the second in August, 1902, at the age of seventeen, and the last in March, 1905. There is a certain similarity in the membranes, all of which show marked vascular, inflammatory and degenerative changes, and the first two also glandular hypertrophy.

The first membrane (gyn. path. No. 8315), has been imper-

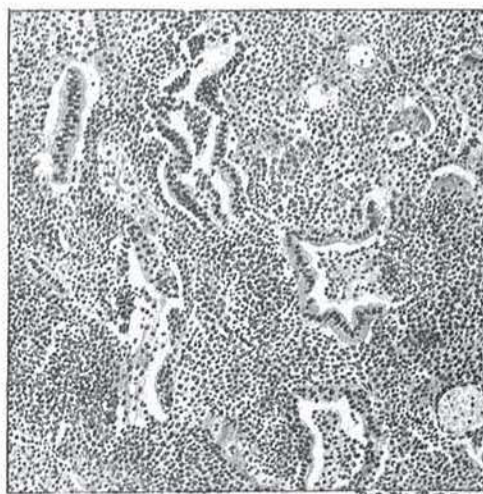


FIG. 1.—Case I. Gyn. Path. 8315. Showing glandular changes and areas of beginning necrosis in stroma.

fectly preserved and stains poorly. Surface epithelium is absent. The glands, which run parallel to the surface, are irregularly distributed. In the upper half of the membrane they are scarce, and lacking altogether in large areas. In the lower part of the membrane, however, they are increased in number, and in some places form a tortuous mass, separated by only scanty stroma. The epithelium is sometimes reduplicated and projects into the lumen in the form of tufts. The dilated lumina contain desquamated epithelium; red corpuscles and fibrin.

The stroma cells are not increased in size, and aside from a degenerated appearance, due partially to the poor preservation, show no abnormality. Small areas of beginning necrosis, from which networks of fibrin radiate, are scattered through the

¹ A letter from patient's physician dated April 15, 1906, states that she is again passing membranes, but with less pain.

stroma. The blood-vessels are numerous and comparatively large. Some are filled with well preserved red corpuscles; others with fibrin. Shadows of red cells are found throughout the tissue; also numerous leukocytes.

The membrane passed in August, 1902 (gyn. path. No. 8399),



FIG. 2.

FIG. 2.—Case I. Gyn. Path. 8399. Section through entire thickness of membrane, showing glandular dilatation, changes in blood vessels and degeneration in stroma.

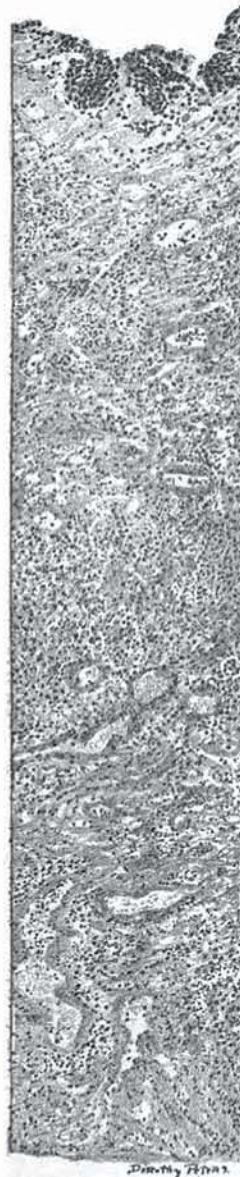


FIG. 3.

FIG. 3.—Case I. Gyn. Path. 8400. Section through entire thickness of membrane, showing extensive necrosis and changes in blood vessels.

consists of a piece of tissue about 3 mm. thick, and approximately the size and shape of the uterine cavity. Microscopically it presents a striking picture, on account of the marked glandular hypertrophy and the extensive degenerative changes.

The surface epithelium is mostly lacking, being represented only by a few groups of cuboidal cells. The stroma immediately

beneath the surface is thickened, and contains compressed and atrophied glands, which run parallel to the surface. In the deeper portions of the membrane are groups of tortuous and greatly dilated glands. They are lined with a single layer of low-cylindrical epithelium, and their lumina are filled with fibrin, red cells and leukocytes. In the neighborhood of these glands are numerous very large thin-walled vessels distended with blood. The stroma cells are somewhat enlarged. In a few areas near the large blood-vessels they stain clearly. For the most part, however, the cell outline and nucleus are indistinct and stain faintly and diffusely. Many of the cells are swollen. Some nuclei are shrunken and take an intense stain; others are undergoing fragmentation. The stroma cells are widely separated by fresh hemorrhage and exudate, and there is everywhere an abundant network of fibrin and a thick infiltration with polymorphonuclear leukocytes. The blood-vessels are numerous and large. Many are filled with fibrin and the walls of some of the smaller stain homogeneously with eosin, as if undergoing hyaline change.

The membrane expelled in March, 1905 (gyn. path. No. 8400), shows more advanced degenerative changes than the preceding. It is composed of thickened stroma, showing areas of coagulation necrosis, especially in the region of the blood-vessels. Clinging to the edges of the membrane are fragments of well preserved glands and stroma. The cells of the membrane are somewhat larger than normal. They all stain diffusely, are indistinct in outline, and show shrinking or fragmentation of their nuclei. The blood-vessels, which are numerous in the deeper portions of the tissue, show marked degeneration, their walls stain homogeneously with eosin, and their lumina are filled with fibrin. The entire membrane is traversed with a network of fibrin and thickly infiltrated with polymorphonuclear leukocytes.

CASE II.—The membrane from this case was sent to the laboratory February 7, 1905, by Dr. J. B. Beeson, of Livingston, Montana, with the following history: The patient, age 30, is a well-formed, healthy-appearing woman, married five years. Her menstrual history was normal until the appearance of the membranes. She had one or two abortions (probably artificially induced), during her early married life; for the past two or three years, she has not been pregnant. She began to pass membranes eight or nine months ago, and since then has discharged one at each period. Severe dysmenorrhea, confining her to bed for two or three days, developed coincidentally with the appearance of the membranes. No pelvic examination was made and the patient has been lost sight of.

The specimen (gyn. path. No. 8239), consists of a few shreds of grayish-red tissue. Microscopically it is composed almost entirely of stroma. The surface epithelium is absent, and only an occasional remnant of a gland is seen. The stroma varies much in density; the cells in some areas being more closely set than normal; in others separated by exudate and their character changed. The rarified areas are, as a general rule, near the free surface of the membrane; the denser areas in the interior, where they occasionally surround the blood-vessels. The largest of the altered stroma cells have round, vesicular, faintly staining nuclei, two or three times the size of those of the usual stroma cells. The cell outline cannot be defined; but the protoplasm is small in amount and stains very faintly with eosin. Every gradation can be traced between them and the normal stroma cell. Numerous thin-walled vessels are present throughout the section, most of them occluded with fibrin. From them a delicate network of fibrin spreads out into the surrounding tissue. Indeed, the abundance of fibrin, both within and without the vessels is a striking feature. Scattered everywhere throughout the membrane are foci, in which the fibrinous network and the leukocyte infiltration are denser, and the stroma cells are indistinct and stain diffusely. In a few

places the process has advanced to actual necrosis. There is everywhere a marked infiltration with small round cells, especially about the thrombosed vessels.

Even in the absence of a pelvic examination, both the clinical history and microscopic appearance of the membrane point to an inflammatory origin in this case.

CASE III.—The following history is obtained from Dr. C. D. McLeod, of Chatfield, Ohio, who sent the specimen to the laboratory. The patient, age 38, was married at 16 years of age, and has four children. No history of puerperal infection. She has had marked dysmenorrhea for the past seven years, and during the last two or three years has passed shreds of membrane. She has also been subject to severe pain in the pelvis about ten days after menstruation. About twelve years ago she had some nervous trouble, diagnosed as "cerebro-spinal meningitis," which has left her with a partial paralysis of the left side.



FIG. 4.—Case III. Gyn. Path. 8648. Showing enlarged stroma cells. (Drawn by Miss Young.)

The physician when called to the patient in November, 1904, found her having alarming hemorrhage and severe intermittent pains. He removed a complete cast of the uterus (the present specimen), which he took at the time to be an abortion sac. Pelvic examination showed a prolapsed, enlarged and softened uterus. The two periods following this one were also attended by profuse hemorrhage. The patient then improved temporarily, and would pass two or three periods without discharging membranes. She has relapsed since, however, and membranes have again appeared.

The specimen (gyn. path. No. 8648), is composed of the upper portion of the endometrium, about 1 mm. in thickness, and

gives the impression of having been separated en masse. The appearance is perhaps due partially to the fact that manual aid was given in the removal of the cast. The inner surface is smooth and the epithelium fairly well preserved. The surface towards the uterine wall is ragged and shows parts of glands, some of them abruptly torn across, projecting beyond the stroma. The glands are convoluted and dilated. Their epithelium shows no abnormality. The stroma is denser towards the surface; in the lower layers separated by exudate. The cells are considerably enlarged, oval or stellate in outline, and have a round, pale-staining nucleus and an increased amount of protoplasm. Many have a swollen and hydropic appearance. They are pushed apart by serous exudate and in some areas by a small amount of hemorrhage. Numerous lymphocytes are scattered everywhere throughout the membrane. The blood-vessels are abundant, and are filled with well-preserved red cells. The degenerative changes and fibrin, so conspicuous in the other membranes, are absent in this specimen.

CASE IV.—There is in the gynecological laboratory only one example of fibrinous cast of the uterus. This was sent by Dr. E. C. Seufert, of Chicago, with the following history: M. S., single, age 24. Born in Poland and came to America at the age of 18. Has worked in tailor-shops for the past five years.

Had diphtheria and scarlet fever at about eight years of age, with perfect recovery from both. She was very stout at the time of puberty. Menstruation began at thirteen and was irregular for several years. The flow has been slight, lasting for three days, and from the onset accompanied by dysmenorrhea. The pain has increased in severity, and on the third or fourth day of each period during the last three years she has passed stringy mucous and shreds of membrane. No leucorrhœa.

Patient consulted the physician in January, 1905, for the increasing dysmenorrhea. She brought with her a complete fibrinous cast of the uterus,—the first one which had been expelled entire.

Physical examination at that time showed the patient to be well-nourished, and the chest and abdomen negative. The uterus was normal in size and position, and movable. Patient refused the treatment recommended, and it has been impossible to trace her subsequent history.

The specimen from the cast (gyn. path. No. 8470), shows mi-

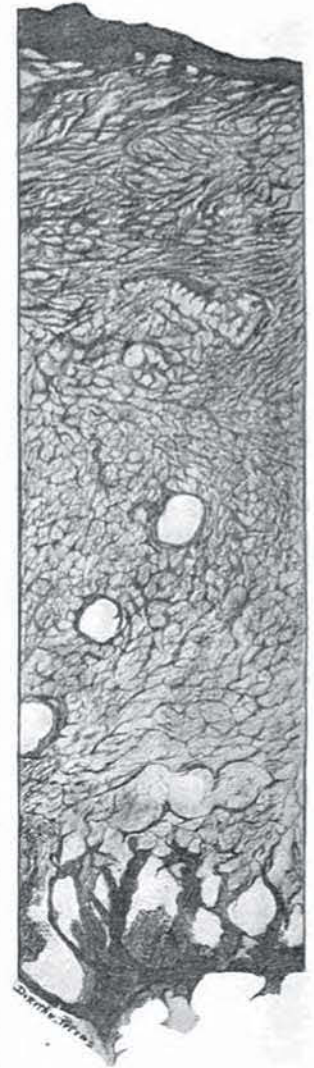


FIG. 5.—Case IV. Gyn. Path. 8470. Section through fibrinous cast from uterus.

microscopically a heavy, loose-meshed network of fibrin, in which remnants of cells are in places visible. There is a wide band of fibrin on the surface; below that a layer of finer network; and in the lowest stratum are numerous rounded openings, some of which are artefacts, and others of which seem to have been blood-vessels. The cells which are scattered throughout the network are so degenerated that no idea of their nature can be obtained.

In conclusion I must express my gratitude to Dr. Howard Kelly, who suggested the subject for this paper; to Dr. Elizabeth Hurdon for her constant help and interest; to Mr. Max Broedel for superintending the illustrations; and to the physicians in charge of the cases for their courteous and detailed replies to numerous letters.

BIBLIOGRAPHY.

1. Morgagni: "Seats and Causes of Disease." Bk. III, Sec. II, 48th Letter.
2. Oldham: London Medical Gazette, 1846.
3. Simpson: Edinburgh Medical Journal, 1877.
4. Mandl: Thesis. Wien, 1869.
5. Haussmann: Mon. f. Geburts. Bd. XXXI, 1867.
6. Hoggan: Arch. f. Gyn. Bd. 1876, s. 301.
7. Gautier: Path. of Memb. Dys. Thesis. Geneva, 1878.
8. Finkel: Virchow's Arch. Bd. LXIII, 1875, s. 401.
9. Wyder: Arch. f. Gyn. Bd. XIII, 1878, s. 39.
10. Haussmann: Beiträge z. Geb. and Gyn. Bd. I.
11. Leopold: Arch. f. Gyn. Bd. X, 1876.
12. Leopold: Arch. f. Gyn. Bd. XI, 1877.
13. Cohnstein: Arch. f. Gyn. Bd. XVII, 1881.
14. Ruge: Cen. f. Gyn. Bd. V, 1881.
15. De Sinety: Soc. de Biol., 1880.
16. Ruge: Zeitschr. f. Geburt. Bd. VII, 1882.
17. Löhlein: Zeitschr. f. Geburt. Bd. XII, 1886, s. 465.
18. Meyer: Arch. f. Gyn. Bd. XXXI, 1887.
19. Du Tremblay: Thesis. Paris, 1887.
20. Coquard: Thesis. Lille, 1887.
21. H. Meyer: Arch. f. Gyn. Bd. XXXI, 1887.
22. Schönheimer: Arch. f. Gyn. Bd. XLIV, 1893.
23. V. Franqué: Zeitschr. f. Geburt. Bd. XXVII, 1893.
24. Winkel: Lehrbuch. 1890.
25. Küstner: Grundzüge der Gyn. Jena, 1893.
26. Winter: Lehrbuch. 1896.
27. Amann: Micr. Gyn. Diag. 1897.
28. Dunning: Amer. Journ. Gyn. and Obs. 1897.
29. Cook: Am. Journ. Obs. Vol. XXXVII, 1898.
30. Gebhard: Veits' Handbuch. 1898.
31. Ries: Jour. Am. Med. Assn. March, 1896, p. 552.
32. Madden: Jour. Am. Med. Assn. March, 1896.
33. Dewitt: Am. Journ. Obs. Vol. XLII, 1900.
34. Fothergill: Brit. Med. Jour. Feb., 1902.
35. Lawrence: Jour. Am. Med. Assn. Vol. XLIV, Dec. 10, 1904.
36. Schottländer: München Med. Wochenschr. Bd. LII, 1905, s. 775.