THE UNIVERSITY OF MINNESOTA

GRADUATE SCHOOL

Report

of

Committee on Examination

This is to certify that we the undersigned, as a committee of the Graduate School, have given Merle Russell Hoon final oral examination for the degree of

Master of Science in Surgery

We recommend that the degree of

Master of Science in Surgery

be conferred upon the candidate.

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Chairman

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Verne P. Hunt

Fred L. Adair

W. W. Strachauer

A. C. Broders

Louis B. Wilson

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REPORT

of

COMMITTEE ON THESIS

The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by Merle Russell Hoon, for the degree of Master of Science in Surgery. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

E S Judd

A C Broders

Fred L. Adair

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THESIS

SOLID TUMORS OF THE OVARY

Merle Russell Hoon, A.B., M.D.

Submitted to the faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

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Primary solid tumors of the ovary may arise in either the connective tissue or the epithelial elements. Secondary tumors are metastatic growths from primary neoplasms located in any part of the body, more frequently, the breast, stomach,or large intestine. This group of tumors is composed of fibromas, sometimes called fibromyomas, carcinomas and sarcomas. Although this type of tumor is not rare, it is not nearly as frequent as the cystic variety of ovarian tumors. This is indicated by Briggs and Walker's report of a series and the number found at the Mayo Clinic between January 1, 1910, and August 1, 1921. The latter group forms the basis of study for this paper. Briggs and Walker had a series of 488 ovarian new growths, treated by operation during a period of twenty-one years. Of these thirty-nine were cystic and forty-nine were solid. The solid tumors included

31 ovarian fibromas
1 cellular spleen-like tumor
3 fibromas of the ovarian ligament
1 surface papilloma
3 adenomata
8 solid carcinomata
1 solid teratoma
1 round cell sarcoma.

The statements as to the relative frequency of cystic and solid tumors, and as to the various types of the solid tumors vary considerably among European and American writers. Griffith and Williamson state that "Sarcoma of the ovaries is commoner than carcinoma". Webster says that "primary sarcoma is less frequent than carcinoma of the ovary". This author adds that "secondary carcinoma is rare". Further discussion of this point will be given in the report of the literature in each respective type of tumor.

Fibromas-

In the Mayo Clinic from January 1, 1910, to August 1, 1921, fifty-five fibromas of the ovary, not associated with other pathologic conditions, were removed at operation. Diagnosis was confirmed by microscopic examination in all the cases in the series. During the same period a total of 4175 tumors of the ovary were removed. One hundred forty-nine (3.5 per cent) of these were fibromas, but ninety-four were associated with cysts, either benign or malignant, or fibromas of the uterus, and so forth, for which the operation was performed. The incidence of fibromas of the ovary is usually given in the literature as 2 per cent.

Cases reported from the literature.

Fibromas of the ovary were first mentioned by Astruc in 1740, and were later discussed by Baillie,in 1799, and Kiwisch, in 1845. Olshausen, in 1873, found six fibromas of the ovary in a series of 293 cases of tumor of the ovary. In 1876 Leopold collected fifty-nine cases from the literature, in some of which the diagnosis was questionable; in 1882, Coe reviewed twenty additional cases and in 1884, Wells found three such tumors in 1200 ovariotomies. In 1902, Peterson reported eighty-two cases from the literature with two of his own. Orthmann, in 1904, reported ten in a series of 527. In 1905, Basse reviewed four cases from Leopold's laboratory, and in 1913, Danforth reported a case in which the tumor complicated pregnancy. In 1914, Fullerton reported one case and Hellman, in 1915, reported six cases from the Frauenklinik of the Konigliche Charite, collected from a series of 41, 500 pathologic specimens. Clark and Gabe, in 1921, published a paper in which such tumors were discussed. The relative frequency of fibromata of the ovaries and uterus is shown by Hartz who notes that Kelly and Cullen found only three fibromas of

the ovary in a series of 534 cases of myomas of the uterus.

The primary origin of fibromas of the ovary has not been determined definitely, although these tumors have been referred to as similar to keloids. They do not have a tendency to recur, however, after removal as is characteristic of keloids. It is quite possible that they may arise from the stroma of the ovary, the corpus luteum, the corpus fibrosum, organized blood clots, the capsule of the organ, or the walls of the blood vessels. Klob, Peaslee, and Olshausen believe that their origin may be traced to inflammatory processes. Hemorrhage and hyperemia from mechanical causes are important factors. Infection plays a questionable part, but scirrhotic and retrogressive changes in the ovary at the menopause may be causes.

The tumors may occur at any age after puberty, but more often develop immediately before or just after the menopause. In the series of fifty-five cases, the greater number were found during the fourth, fifth, and sixth decades. The youngest patient was eighteen years and the oldest was seventy-three. Two patients were in the second decade eighteen and nineteen years respectively, five were between twenty and twenty-nine, fifteen were between thirty and thirty-nine, nine were between forty and forty-nine, fifteen were between fifty and fifty-nine, seven were between sixty and sixty-nine, and two were more than seventy. Twenty-six of the patients were menstruating, three were at the menopause, and twenty-six were past the menopause. Five patients were from one to five years past the menopause, ten were from six to ten years past, four were from eleven to fifteen years past, four were from sixteen to twenty years past, two were twenty-one and twenty-five years past respectively, and one was thirty years past and had had symptoms during that period.

A study of the series of fifty-five cases shows that menstruation is seldom influenced by the tumors. This is in agreement with Doran's conclusions from his study of eleven cases. In twenty-four the menses were regular and

practically normal. Five had irregular menses but three of these were at the menopause. In only four was the flow increased. One had increased flow for two years and one for two months. The youngest patient, eighteen years, had not menstruated because of the congenital absence of the uterus and vagina. The average age of the twenty-six patients past the menopause was fifty and nine tenths years. This is in accordance with Peterson's findings that fibromas of the ovary delay the menopause.

In Peterson's series forty-four patients were married and twenty-two were single. Of the forty-five in whom fecundity was mentioned, thirty-three (73.33 per cent) were sterile. In the fifty-five from the Mayo Clinic forty-one were married, four were widowed, one was divorced, and nine were single. Thirty of the forty-six had children, ten had one child each, four had two children each, three had three, three had four, three had five, five had six, one had seven, and one had ten. Thus, incidence of fibroma of the ovary was five times greater in married than in unmarried women. The number of children bears no relationship to the occurrence of the tumor.

Fibromas of the ovary may vary from 0.5 cm. to more than 30 cm. in diameter. The largest growth in the series measured 35 by 23 by 15 cm., and weighed 6023 gm. In one case in which the tumor was bilateral the growth in the right ovary was 17 by 15 by 9 cm., and that in the left ovary 18 by 17 by 11 cm. As a rule the tumor corresponds to the shape of the normal ovary, but its surface is nodular and irregular. Firmness depends on fibrous consistency or calcareous degeneration; the growths are softer with myxomatous degeneration. They are usually gray or grayish white. The cut surface is glistening white or yellowish white, owing to hyaline degeneration. If the blood supply is unusually rich they appear red or, in the presence of recent hemorrhage, they may be black.

Microscopically a certain regular arrangement of the individual fibrous cells which frequently form bands or strands is found. If muscle cells

are present, they may be derived either from the normal muscle cells of the hilum or the walls of the blood vessels. As a rule the muscle cells, if they are really muscle cells, are few in comparison with the connective tissue cells which are short and spindle shaped, with a slightly bent or pointed nucleus. In large tumors there are practically no muscle cells, because of the interference with the blood supply by the contraction of the fibrous tissue. Practically all forms of degeneration may be seen microscopically; fatty, myxomatous, hyaline, hydropic and calcareous are the most common. Large tumors contain extensive areas of necrosis. Fibromas may be distinguished pathologically from sarcomas by their less cellular structure and more regular arrangement and polarity of cells, and the absence of mitotic figures and embryonal types of cells.

The symptoms are subjective and objective. Among the subjective symptoms, which are comparatively few, is pain in the abdomen, usually dragging, unless the pedicle becomes twisted, when it is very acute and may cause collapse. The pain often radiates to the groin, when it simulates that of renal or ureteral stones. Occasionally pressure causes it to radiate along the distribution of the nerve trunks. Frequent and painful urination, constipation, and pain on defecation are sometimes complained of. Aching in the lumbar or sacral region is often noted. The patient, however, may not be aware of the tumor, even though it is large.

Objectively the tumor may be fixed by adhesions, but as a rule it is movable. The uterus, in some cases, moves separately from the tumor. Ascites is stated in the literature to be present in about 5 per cent of cases and may be due to irritation of the peritoneum. Olshausen believed it the result of mechanical irritation, Schauta attributed it to hyperemia, and Pfannenstiel and Schätzchen to a secretion of the degenerating tumor. The tumor may be present for several years before it becomes large or gives rise to marked symptoms. However, there

are a small number of cases in which the growth is more rapid and the tumor causes symptoms within comparatively few months.

In the fifty-five cases the tumor was known to be present from a few months to many years; in one case thirty years with comparatively few symptoms. Fifty-two of the fifty-five patients had symptoms. Seven had had symptoms from one to six months, five from seven months to one year, sixteen from one to two years, six from two to four years, six from six to ten years, one for twelve years, one for fourteen years, one for nineteen years, and one for thirty years. The duration was not stated in eight.

Pain, the most common symptom, was present in thirty-three cases, not mentioned in seventeen, and absent in five. As a rule, it was not present in the cases of the smallest or very largest tumors. The pedicle was twisted in two cases and caused severe pain and shock. Radiation of pain to the bladder and groin confused the clinical picture, but the paucity of urinary symptoms and the negative urinalysis and roentgenograms aided in the differential diagnosis.

Pressure on the bladder and rectum caused symptoms in twenty-six cases. Frequency of urination was present in fourteen of these. Desire to defecate frequently was present in two.

The tumor was definitely fixed in four cases and movable in fifty-one. It was located in the midline of the lower abdomen and pelvis in thirty-six cases; in the right side of the pelvis in twelve; in the left side of the pelvis in five; and in the culdesac in two. Ascites was present in fourteen cases (25 per cent). The amount varied from 0.5 to 16 liters. Two patients had also bilateral hydrothorax which disappeared after operation. When ascites is present the clinical picture may be confused with that of malignancy of the ovary, especially when loss of weight and strength are marked. However, the association of ovarian tumors and ascites should be remembered and exploratory operation

offered to patients with tumors of the pelvis and ascites unless metastasis is demonstrable.

One ovary only was affected in fifty-three cases (90 per cent). Both ovaries were affected in the other two. The growths reported in the literature were practically always unilateral.

Twenty-four patients complained of tumor; twelve of abdominal pain; six of pelvic pain and distress; two each of frequency of urination, falling of the womb and metrorrhagia, and one of menorrhagia.

The diagnosis depends on the presence of a unilateral tumor of the pelvis, nonfluctuating and separate from the uterus. Often no definite diagnosis other than "tumor of the pelvis" can be made before operation. In the differential diagnosis, must be considered pedunculated fibrous tumors of the uterus, solid carcinomas and sarcomas of the ovary, fibrous tumors of the tube, and adenomyomas. It should be remembered that sarcoma is more common in young persons. Solid carcinoma cannot be absolutely differentiated unless metastasis is present. If ascites is present cirrhosis of the liver, abdominal malignancy, tuberculosis, or other causes should be ruled out.

Treatment

The treatment should be surgical, as medical treatment is of no avail. Radium and roentgen-ray therapy should be reserved for cases in which operation is contra-indicated on account of coexistent conditions, such as serious cardiac lesions and nephritis. Operation should be advised for the removal of all ovarian tumors as soon as the diagnosis is made, since malignant change may occur, if it is not already present, or twisted pedicle with gangrene and peritonitis may occur.

The type of operation in the fifty-five cases varied according to indications found at operation. One ovary alone was removed in twelve cases,

one ovary with the tube on that side was removed in twenty-one cases. Both ovaries and tubes were removed in six cases. Subtotal hysterectomy with removal of one ovary and tube was performed in six cases, and subtotal hysterectomy with removal of both ovaries and tubes was performed in seven cases. When both ovaries were removed from patients who had not reached the menopause one ovary or a part of one ovary was transplanted. Total hysterectomy with removal of both tubes and ovaries was performed in three cases. The uterus was removed in these cases for various reasons, such as prolapse, multiple small fibroids, fibrosis, and chronic endometritis. The appendix was removed in thirty-seven patients; cholecystectomy for cholecystitis with cholelithiasis and gastro-enterostomy for duodenal ulcer were performed in one case each. In one case the tumor was found to be parasitic to the omentum and small intestine.

Prognosis

The prognosis, when solid carcinoma and sarcoma have been ruled out by microscopic examination of the tumor, is good. Preoperatively, and when the patient refuses operation, the prognosis is rendered uncertain by the possibility of twisted pedicle with resulting infection, gangrene and peritonitis, malignant change, and so forth.

In order to ascertain the results following operation, questionnaires were sent to the patients. Particular stress was placed on the effects on menstruation and on the occurrence of pregnancy. Twenty-six patients answered the questionnaires. Of these, ten had not reached the age of menopause and were anatomically able to menstruate. Nine of the ten menstruated regularly. One ceased menstruating after operation. In eight the flow was normal in amount; in one it was increased. Only one complained of dysmenorrhea. Of the twenty-six who answered questionnaires, six were married, still menstruating, and physiologically and anatomically capable of bearing children. Of these six

patients, three had children after operation; one had two children and the other two each had one child. Practically all patients reported freedom from the symptoms of which they had complained before operation, and general health and strength were good.

Conclusions

1. Fibromas of the ovary may occur at any age after puberty; they comprise 3.5 per cent of all ovarian tumors.

2. There may be comparatively few symptoms and the tumor may be present a long time without the patient's knowledge.

3. Ascites and tumor of the pelvis does not necessarily mean abdominal malignancy.

4. The treatment is surgical. All ovarian tumors should be operated on as soon as diagnosed.

5. The prognosis is good after operation.

6. Subsequent menstrual function is normal as could be expected following unilateral ovariotomy.

7. Normal pregnancy may occur in patients of child-bearing age, when only one ovary or one ovary and one tube have been removed.

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Solid carcinoma

In 1896, Krukenberg described a new growth of the ovary under the name of "fibrosarcoma ovarii mucocellulare (carcinomatodes)". As he was unable to demonstrate, by careful examination, proof of pre-existing epithelial elements which could be regarded as the source of these tumors, he concluded that they must arise in the stroma of the ovary. The tumors he described were large and solid. The surface was studded with many rounded nodules and a few small cysts. Microscopically the tumors were covered by a capsule composed of bundles of fibrous connective tissue. The body of the tumor was composed of two types of cells. The connective tissue cells were star-shaped, rich in nuclei and anastomosed with each other by means of long delicate processes. The interstitial substance in many places was abundant. Within the fine spaces between the connective tissue fibers he found large, pale, round, swollen cells. The nucleus usually is placed at one side near or at the periphery of the cell in the shape of a crescent, giving the cell the appearance of a signet ring. This type of cell varies considerably in size and Krukenberg believed the larger rose from the smaller by the process of mucous swelling. These cells are characteristic of this type of tumor. As the chief part of the tumor is composed of cells which arose in the connective tissue stroma he believed the tumor to be a fibrosarcoma. He concluded that the large swollen cells were not a proliferation of blood or lymph vessel endothelium but they represented a mucous degeneration of the large spindle shaped cells of the connective tissue. The adjective "mucocellulare" was added at Marchand's suggestion to indicate the occurrence of the latter type of cells.

At the autopsy of his first case, Krukenberg found metastasis of these tumor cells in the lymph spaces of the mesenteric and axillary lymph glands, liver, stomach, omentum, etc. This showed a similarity to carcinoma in the manner of metastasizing and he added the term "carcinomatodes" to indicate the

malignity of the tumor and the manner of metastasizing.

Krukenberg described five cases in his original paper. Two of these were laboratory specimens, without other data. Another gave a history of gastric symptoms and died after operation. No autopsy was made of this case. Two other cases went to autopsy. One of these had a carcinoma of the stomach--the stomach was negative in the other case.

Krukenberg believed these cases belonged to a definite type of ovarian tumor which occurs at any age, between youth and senility, apparently always bilateral, of slow growth and generally accompanied by ascites. As a rule, the tumor corresponds in shape to that of the ovary, usually firm, but softer in areas which have undergone myxomatous degeneration or where necrosis is marked.

Other pathologists had noticed similar tumors before the publication of Krukenberg's paper. In 1872, Waldeyer described such a tumor, Leopold in 1874 reported two cases. Schulz in 1886 wrote concerning the coexistence of ovarian tumors and carcinoma of the stomach. Seeger in 1888 reported two cases.

Krukenberg regarded these tumors as primary in the ovary. Since the publication of his paper much discussion has arisen over the occurrence and pathogensis and primary or secondary nature of these. One group of pathologists agrees with him in that they are primary in the ovary. Another group believes they are practically always secondary to a tumor located elsewhere, usually in the gastro-intestinal tract, more frequently the stomach, or the breast. Stickel reported thirteen cases of ovarian carcinomata associated with tumors of the stomach, colon and breast, and considered the ovarian tumors secondary. Glockner reported eighteen similar cases. In seven, the primary growth was in the pylorus.

Stauder in reviewing 295 ovarian tumors found three that showed the general characteristics of the Krukenberg tumor. One of these was associated with a gastric carcinoma, another was a "mixed" type (carcinoma and sarcoma).

The other he regarded as definitely primary in the ovary.

Major in 1918 reviewed the literature and reported a case with both ovaries involved and associated with "leather-bottle stomach" or "linitis plastica". The wall of the stomach contained many carcinoma cells. Between the time of the publication of Krukenberg's paper and his own, he found fifty-four cases in the literature, all of which were classified definitely as Krukenberg tumors. Of these eighteen were regarded as primary and thirty-eight as secondary. Thirteen of the former had a negative stomach on examination at the time of operation or later at autopsy. Major found eight other "probable" cases in the literature. In regard to his own case he states "histologically the tumor is a carcinoma. Some features suggest a fibro-sarcoma, but if this term is to be used it would be more logical to reverse the order employed by Krukenberg and call it a carcinoma mucocellulare fibro-sarcomatodes.-------This tumor is, in the majority of cases, secondary to a carcinoma of the intestines or stomach. The question of its primary or secondary nature can only be determined definitely by palpation of the stomach at operation or later at autopsy examination. Eighteen cases were collected in which the presence of a primary growth in the gastro-intestinal tract was demonstrated."

Ridout in 1919 reported a case of a unilateral Krukenberg tumor involving the right ovary, which was primary. The patient was only eleven years of age and showed no evidence of recurrence in six months. In July, 1920, Chapman reported a case in a fourteen year old girl which was apparently secondary to a carcinoma on the greater curvature of the stomach. His patient died three weeks after operation due to progressive cachexia and exhaustion. The clinical and pathological picture coincided with this type of tumor. Reel in 1921 reported another case which was considered as secondary although the primary tumor was not located. The patient died two months later but no autopsy was performed.

These cases would make a total of fifty-eight, seventeen of which were considered primary and forty-one as secondary. Stone in 1916, writing on "metastatic carcinoma of the ovaries" reviewed reports of 133 cases in the literature. From these he concluded that there was a definite causal relationship between tumors of the ovary and other organs and in which "with few exceptions the tumors of the ovary were undoubtedly secondary".

Thirty-seven cases of solid carcinoma and two cases of solid sarcoma of the ovaries were found in malignant tumors of the ovary at the Mayo Clinic between January 1, 1910 and August 1, 1921. These tumors were solid throughout or contained only relatively small cysts due to degeneration and necrosis or retention. All cases of benign or malignant ovarian cysts, dermoids,etc. were excluded. During this time there were 4175 tumors of the ovary removed. Thus solid malignant tumors comprise .93 of one per cent of all ovarian tumors. During this period 540 malignant ovarian tumors were removed. Of these .066 per cent were solid.

The youngest patient was eight, three years younger than any reported in the literature. Major found the average age of the fifty-five cases that he collected was thirty-six. In this series it was 44.2 years. Two cases occurred in patients under twenty, eight and sixteen years respectively. Three were between twenty-one and thirty, seven between thirty-one and forty, ten between forty-one and fifty, and fourteen between fifty-one and sixty and one at sixty-six. Twenty-six patients were married and four were widowed. Twenty-four of these had children varying in number from one to nine each. Seven of the patients were single.

The most common symptoms of this condition are pain, tumor, ascites, loss in weight and strength, anorexia, bladder and rectal disturbances. The pain varies in type and location. As a rule it is located in the lower abdomen and pelvis, but occasionally it may radiate down the groin, or located in the lumbar or sacral region of the back. The patients usually describe it as a

constant dull ache, bearing down or dragging. Occasionally it is sharp and severe due to twisting of the pedicle when it may resemble the colic of a renal or ureteral calculus. Pain was present in thirty patients.

In twenty-two patients the chief complaint was "tumor". In twenty cases, the patient herself had discovered the pressure of the tumor. Seven were discovered by the family physician and ten were not discovered until the time of examination at the Clinic. This illustrates the importance of a routine complete physical examination.

Thirteen cases or 35 per cent had ascites in amounts varying from 250 or 300 c.c. up to 6 or 7 liters. Seventeen of the patients were past the menopause varying from one to sixteen years. Prolongation of the period and increase in the menstrual flow was present in four. Ten others gave a history of metrorrhagia of two months' to two years' duration. Seven patients had noticed an irregularity in their periods.

Only two patients stated their general health was good. Twenty-two said it was below normal and thirteen that it was poor. Sixteen patients stated that the appetite was about normal, fifteen had noticed a loss in appetite and six that it was very poor or almost gone. Eighteen of the patients had lost weight varying from 5 to 36 pounds. Five patients showed marked cachexia with the "ovarian facies", a term used in many of the older textbooks. Seventeen complained of bladder symptoms--frequency or painful urination, burning on urination, or a more or less continuous sensation of pressure, dragging or weight in the bladder. One patient had had incontinence for six months due to the pressure of a large tumor. Sixteen patients complained of constipation and four of these had a sensation of fullness in the rectum with pain on defecation.

Physical examination of the patient reveals the presence of a tumor, usually in the pelvis but extending, frequently, above the brim of the pelvis, at times almost filling the entire abdomen. Fixation may be due to extension of

the growth to the pelvic wall or adjacent viscera or to inflammatory adhesions. The blood picture shows secondary anemia of varying degree as we find in malignancy in other parts of the body.

Bimanual examination in twenty-three of the thirty-seven patients showed the tumor was nodular. In three it seemed to be smooth. In the others no statement was made concerning this point. In seven patients it was fixed, while in the others it was more or less movable. The apparent consistency of the tumors varied considerably. Usually it was given as "firm or rather hard", occasionally "stony hard", while in two the clinical examiner thought the tumor was cystic.

The clinical diagnosis of solid carcinoma of the ovary is rarely, if ever made in a definite way. As a rule even the surgeon with the abdomen opened must wait for the microscopic diagnosis by the pathologist. The differential diagnosis includes the consideration of benign and malignant ovarian cysts, ovarian fibroids and dermoids, fibromas of the uterus, retroperitoneal tumors, etc. The preoperative diagnoses in the thirty-seven cases were as follows:

"Ovarian carcinoma"	10
Ovarian cysts	5
Dermoid cyst of the ovary	1
Uterine fibroids	7
Pelvic tumor	7
Uterine fibroids with carcinoma of the fundus	5
Retroperitoneal sarcoma	1
Carcinoma of the stomach with pelvic tumor	1

The treatment for this condition is the same as for any other type of ovarian malignancy, surgery associated with radiological therapeutics, radium and roentgen-rays. Exploratory operation should be offered all patients even in

the presence of ascites unless metastasis can be definitely demonstrated. Palpation of an enlarged liver with umbilicated nodules on the surface, enlarged hard inguinal or pelvic glands or extension with induration of the broad ligaments would indicate a condition hopeless of relief thru operation. X-ray of the chest and pelvic bones may enable us to reach the same conclusion. In such cases radium and x-ray may temporarily relieve the pain and suffering and prolong the patient's life for a short time. Periodic paracentesis abdominalis may be necessary on account of re-accumulation of fluid.

In the cases amenable to surgery, post-operative applications of radium in the vagina and rectum and x-ray applications to the abdomen and back are of value, if recurrence is to be feared on account of the inability to remove all the malignant tissue. When recurrence takes place, radium and x-ray treatments offer little even as palliative treatment.

If the patient's general condition will permit, both ovaries, tubes and uterus should be removed at operation unless the tumor is definitely encapsulated and limited to one ovary in a patient who is in the child-bearing period and anxious to bear children. In nineteen patients of this series a hysterectomy, either total or supravaginal with removal of both tubes and ovaries was done. Both ovaries and tubes were removed in eleven patients and one tube and ovary in seven. In the one case where the ovarian involvement was bilateral and associated with an inoperable carcinoma of the stomach, both ovarian tumors were removed on account of the danger of twisted pedicles.

Of the patients who developed recurrences as ascertained by subsequent examination at the Clinic, questionnaires and letters from the home physicians, three had (subsequent) secondary operations at the Clinic for same. One of these returned four months after operation and complained of severe neuralgic pain down the right leg. This was caused by advanced involvement of the inguinal glands which were removed with partial relief. Another returned at the same

interval with ascites and tumors of the omentum. The largest of these were removed and the patient was given x-ray and radium treatments. This patient lived eight months following the second operation. The third patient returned in three months' time with a small tumor on the head. This was removed for diagnosis and it showed carcinoma.

The study of the relationship of these tumors to carcinoma of the stomach and malignancy in other organs is interesting in that this series indicates clearly that the so-called Krukenberg tumor or solid carcinoma of the ovary is frequently primary in the ovary, which is in accordance with Krukenberg's belief. One case in this series as well as a review of the literature shows that the ovary may be the site of a tumor which is secondary to malignancy of the stomach or elsewhere. This patient was diagnosed clinically as inoperable carcinoma of the stomach and pelvic tumors. She gave a history of severe pelvic pain and insisted on an exploratory operation. At operation an inoperable prepyloric carcinomatous ulcer was found which had penetrated the serosa and was attached to the pancreas. Rosenstein has called attention to the fact that it is not necessary for the carcinoma of the stomach to penetrate the gastric serosa before metastasis may occur in the pelvis. In this case both ovaries were involved, the right ovary weighed 950 grams and the left 500 grams. Both were removed on account of the severe pain in the pelvis and the danger of twisted pedicle. Microscopic examination showed carcinoma with considerable fibrous tissue.

Another patient had a partial gastrectomy in July, 1909, for carcinomatous ulcer on the lesser curvature. In February, 1912 both ovaries were removed and showed carcinoma. No other evidence of involvement could be demonstrated at the time of operation in spite of careful examination of the abdomen. This patient died with pelvic recurrence in eight months' time. Another patient had a Billroth operation N. 2 for carcinoma of the stomach in June, 1910. In

December, 1912, both ovaries were removed and showed carcinoma on microscopic examination. Death occurred eight months later from abdominal recurrence. Both of these patients had both operations at the Clinic. These two cases are similar to the case reported by Hussy in which the ovarian carcinoma occurred five years after operation for carcinoma of the pylorus.

One patient had both ovaries and gallbladder removed in February, 1913. The left ovary showed carcinoma and the right ovary was normal. The gallbladder contained many stones and showed chronic inflammation with trabeculation. This patient died in August, 1919, six and one-half years later, from carcinoma of the stomach. Another patient had a squamous cell epithelioma removed from the nose in 1912. Four years later she had both ovaries, tubes and uterus removed. Both ovaries were involved and showed carcinoma which had extended to the uterus. At operation, which was difficult, marked local extension with numerous inflammatory adhesions between the tumors and the intestines, both large and small, were found. This patient was the only one in the series that died a surgical death. Exitus occurred five days post-operatively and was due to peritonitis, as a result of intestinal obstruction from pelvic adhesions, broncho-pneumonia and chronic nephritis. Autopsy showed metastasis to the left lung but the stomach and other viscera were normal.

Summarizing these we find that in one case the solid ovarian carcinoma was found with carcinoma of the stomach. In two cases bilateral carcinoma of the ovaries was found two and one-half years after operation for carcinoma of the stomach. A fourth patient died with gastric carcinoma six and one-half years after both ovaries had been removed for carcinoma. In the first of these a definite relationship is seen between carcinoma of the stomach and the solid ovarian carcinoma. But the time element in the second and third cases shows that the relationship in both is questionable. In the fourth case the ovarian malignancy preceded that in the stomach by six and one-half years and any relationship between the two is doubted seriously.

4-21 6M

The solid ovarian carcinomatous tumors in the series varied in size from 5 to 8 cm., up to 28, 30, and 35 cm. in diameter. The weight varied from 30 grams up to 11,000 grams, the largest. The average weight of the tumors was approximately 1250 grams. In the heavier tumors, calcification was a marked feature and their consistency was almost stony. In twenty-four cases or 65 per cent the involvement was unilateral and in thirteen bilateral. This is contrary to the frequent statements in the literature that the tumor is nearly always bilateral. This statement has been used also as an argument that the tumor is secondary on the premise that bilateral malignant involvement in paired organs, such as the kidney and ovaries, in most instances indicates a primary growth in some other organ.

The shape of the tumors corresponded roughly to that of the normal organ. The surfaces are usually somewhat nodular and spotted with many small cysts 1 to 7 or 8 mm. in diameter. The consistency varied according to the degree of degeneration and necrosis as well as that of calcium deposits. In the largest tumors necrosis was a marked feature on account of the poor blood and lymph supply in the center of the tumor.

In the microscopic study of these tumors an attempt was made to classify the degree of malignancy into four groups. No attention was paid to the clinical history until after the classification had been made. This was based on MacCarty's idea of primary, secondary and tertiary cellular differentiation which is also the basis of Broders' method of the classification of epitheliomas into Groups I, II, III and IV. That is the more highly the differentiation and specialization of the cells or tendency towards the adult type of cell, the less malignant. Conversely, the less the differentiation and specialization or tendency towards the embryonic cells, the more malignant.

In Group IV there was no attempt at cell differentiation and gland formation. This group was comprised of twelve cases. Of these, four were known

to be living and well, ten months, eighteen months, five and one-half and nine years respectively after operation. To correlate the microscopic classification and post-operative history, attention was paid to those patients who were definitely known to have died from recurrence. In the eight cases death occurred within two to sixteen months from the time of operation. The average interval in these eight was six and one-fourth months. One of these cases was a melanotic carcinoma.

Broders and MacCarty have called attention to the fact that the terms "melano-sarcoma", "melanomata", "melanotic-sarcoma", "chromatophoromata" etc. are misnomers. They have given good reasons why the pigmented malignant neoplasmata arising in the skin, choroid and other parts of the body should be called melanoepitheliomata. Cottam and Horzberg reported a case similar to the one in this series. Their patient was thirty-eight years of age. They were unable to demonstrate any metastasis or recurrence one month after operation, but gave a bad prognosis. Winternitz reported a case which he regarded as primary in the right ovary, in a patient twenty-six years of age. This patient had cerebral metastasis for which operation had been performed by Cushing three months previous to the discovery of the pelvic tumor. Andrews has reported a case of primary melanotic-sarcoma in the right ovary. This case was removed in a patient four months pregnant. The left ovary was normal.

In Group III microscopic examination showed little differentiation of the cells. In places slight tendency to gland formation was shown. This group comprised fourteen cases. Four of these were known to be living and well, two, three, five and one-half and seven and one-half years after operation. One patient died five days after operation. The other nine died in from two and one-half to twenty-one months after operation. The average interval between operation and death was eight and one-half months.

Group II was composed of ten cases. The microscopic sections in this

group showed the cells partially differentiated and forming glands. The cells of some of these contained some mucus. The cells of some of these glands also showed varying degrees of cell migration. In this group it was impossible to follow up one case. The other eight died in from four to fifty months after operation, the average time of death was fifteen months after operation.

Only one case fell in Group I. The microscopic examination showed comparatively well differentiated cells. There was only slight tendency of the cells to migrate. This patient was alive and well two years after operation and had gained eight pounds.

Thus we see that twenty-six cases or 70 per cent fell into Groups III and IV, from the microscopic examination. This bears out the clinical histories and shows that solid carcinoma of the ovary is highly malignant. Broders estimates that 75 per cent of epitheliomas of the cervix fall into Groups III and IV. Thus solid carcinoma of the ovary is only a little less malignant than that of the cervix.

The prognosis in solid carcinoma of the ovaries is comparatively poor. Formerly it was stated that this tumor was relatively benign, but all the recent writers agree that it is more malignant than previous reports would indicate. In this series only three patients were living and well after the five year period--five and one-half, seven and one-half and nine years respectively after operation. Two were living and well after three years, two at two years, two at eighteen months, and two at ten months. In contrast to these eleven cases, fifteen of the patients were dead within a year, of these six died within six months of the time of operation. Four others died within the two year period.

From this series of thirty-seven cases of solid tumor of the ovary and a review of the literature, we may conclude that

1. Solid carcinoma of the ovary may occur at any period of life from childhood to senility, the most common period being in the fourth and fifth

decades.

2. They are highly malignant.

3. As Krukenberg believed they are frequently primary, more so than the recent literature would indicate.

4. Solid carcinoma of the ovary may be bilateral but in 66 per cent of this series the tumor was unilateral.

5. Melanotic carcinoma is occasionally primary in the ovary.

6. Melanotic carcinoma of the ovary is highly malignant as is the same type of tumor located elsewhere.

7. The general history is similar to that of ovarian fibromas with the additional symptoms of malignancy, loss in weight, strength and appetite, with a secondary anemia. The growth of the tumor is usually more rapid.

8. Ascites cannot be considered a criterion for malignancy as it was present in 35 per cent of the solid carcinomas and in 25 per cent of the benign fibromas.

9. The treatment of solid carcinoma of the ovary is surgical removal followed by x-ray and radium treatments if total removal of malignant tissue is impossible.

10. Metastasis and local recurrence indicate a hopeless prognosis.

11. X-ray and radium are the treatments for metastasis and local recurrence but at best, are only palliative.

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Solid sarcoma of the ovary

A study of the literature reveals the fact that most sarcomata of the ovary occur in young individuals. Although the occurrence of this tumor during the third and fourth decades or after the menopause is comparatively infrequent it is by no means rare. An idea of the relative frequency of ovarian sarcomas is given by Kaufman. For a given period sarcomas were found in 160 autopsies (1.25 per cent of all the autopsies) at the Basler Pathological Anstall. Of these, twelve or 7 per cent were sarcomas of the ovary. Porter collected from the literature 2,995 cases of ovarian tumor. From these he concluded that 20 per cent of all ovarian tumors are malignant and 5 per cent are sarcomas.

In regard to the age incidence Bland-Sutton states, "The ovary is prone to become the seat of sarcoma in early life, followed by a period of comparative immunity, followed by a second period of renewed but diminished liability. He adds that they are rather frequent under five years of age and occur with decreasing frequency until about the time of onset of puberty. In adults there are two common periods, between the twentieth and thirtieth years and after the menopause. One-half the cases are bilateral, grow very rapidly, often attain formidable proportions and quickly destroy life. Removal is attended with a high mortality and in patients who recover from the operation quick recurrence is the rule. This author collected 100 cases in which ovariotomy was done in children under fifteen years. Of these twenty-one were sarcomas. Seven of these died after operation and four more of the ones he was able to trace died within a year.

Doran reported a case which was bilateral in a seven months fetus which lived only a few minutes after birth. He described the tumor as round cell in type and regarded it as "the persistence and hyperplasia of the entire embryonic tissue of the ovary of an earlier age". Hayd and Schwartz each report cases in patients aged twenty-three months. Involvement in both cases was uni-

lateral. Smith and Motley's case was bilateral in a girl of three years. Death occurred in seven months from recurrence. Higgins reported three cases in patients aged five, seven, and twelve years respectively. He calls attention to the chief symptoms of this condition as insidious onset, unexplained colicy pain, precocious menstruation, steady enlargement of the abdomen with fever and extension or metastasis. From the literature one concludes that occurrence is less frequent than in the adult.

Stewart reported a case in a patient thirty-one years of age. The tumor had been present for two years. The patient complained of dysmenorrhea and increase in menstrual flow. She died three days after operation from ileus. The microscopic diagnosis of the right ovarian tumor was round cell sarcoma. The left ovary was cystic and showed angio-sarcoma. Foerster's case was unilateral in a patient twenty-three years of age. Microscopically it showed fibrosarcoma of low grade malignancy. Palale's case was nineteen years of age and showed lymphosarcoma of both ovaries which he considered primary although the same pathology was present in the right breast and right supraclavicular glands. Brodhead reported a case in a negress of eighteen years of age. The involvement was unilateral and the tumor was removed eight days after delivery of a living child. It had produced symptoms of "the acute abdomen" due to the twisting of the pedicle. He believed that conservative surgery should be followed and only the involved organ be removed when the patient is in the child bearing age and wants more children. Judd had a similar case in a patient sixteen years of age. The tumor was unilateral and acute symptoms were due to a twisted pedicle. Discussion of this case indicated that it had been the experience of some surgeons that it was not necessary to do a pan-hysterectomy.

In the case reported by Briggs and Walker, the patient was twenty-nine years of age. Symptoms of lower abdominal pain, swelling of the abdomen and menstrual disturbances had been present for three months. Involvement was

bilateral and ascites was present. It was impossible to remove all the malignant tissue and death occurred nine months later from abdominal recurrence. L. Pick collected twenty-three cases of sarcoma of the ovary. He concluded that it frequently occurs in young women and metastasis does not occur until late.

Jones and Jessett each reported a case in a patient fifty years of age. In both cases, microscopic examination showed spindle cell sarcoma. Lockhart found seven sarcomas in a series of sixty-five ovarian tumors.

Two cases of solid sarcoma of the ovary were found in the thirty-nine cases of malignant solid tumors of the ovary at the Mayo Clinic between January 1, 1910, and August 1, 1921. One of these was a patient forty-eight years of age who was one year past the menopause. The tumor was noticed by the patient two years previously. Her only symptoms were pain in the lower left quadrant of the abdomen and dysuria with frequency. Microscopic examination showed spindle cell sarcoma. A letter five years later states that she has gained twenty pounds and her general health is good.

The other patient was twenty-eight years of age and single. Her chief symptom was pain in the right side of the abdomen and gave a history of three attacks of acute appendicitis in the preceding six years. On physical examination a movable pelvic tumor, of firm consistency to the left of the uterus, was found. At operation the appendix and left ovary were removed. Microscopic examination of the left ovarian tumor which was 6 cm. in diameter, spindle cell sarcoma. A questionnaire answered three years after operation indicated that she had no symptoms of recurrence and had gained 30 lbs. in weight.

The history of the patient with solid sarcoma of the ovary is little different than in cases of solid carcinoma. Physical examination likewise demonstrates a pelvic tumor which on palpation gives a sensation of solidity and firmness in contrast to the sensation of elasticity and fluctuation usually present with ovarian cysts.

The diagnosis of solid sarcoma of the ovary is seldom, if ever, made clinically. As in solid carcinoma it is usually made by the pathologist. The treatment is the same in both conditions. In cases of sarcoma of the ovary, Coley's serum (dead cultures of erysipelas and B. prodigiosis) may be of some value. Coe and Coley report a case in a woman thirty-two years of age who had an exploratory laparotomy and was diagnosed as inoperable ovarian malignancy on account of the size of the growth and local extension and adhesions. She was given forty-seven injections of Coley's serum and twenty-two x-ray exposures. These caused a decrease in size of the tumor and it was removed at operation. Menses then became regular and she conceived in six months time followed by a normal birth of a living child. Death occurred two years later with questionable recurrence in the lungs and broncho-pneumonia.

The prognosis of operable solid sarcomas of the ovary in adults is much better than in solid carcinoma. Inoperable sarcoma in adults has practically as hopeless a prognosis as carcinoma. The prognosis of solid sarcoma in children as shown by case reports in the literature is much less favorable than in adults. In 80 to 90 per cent of cases death occurred from recurrence in six months to one year. The relative difference in prognosis of children and adults is what we would expect from the (pathologic) microscopic findings as the sarcomas in adults are usually of the spindle cell type or fibro-sarcoma, while those in children are usually of the small round cell type or lymphosarcoma, which is the most malignant tumor of all types of sarcomas. The operative mortality in young children with this condition is high. Various authors estimate it from 25 to 35 per cent. Porter found only three cases in his series who remained well for three or more years.

Conclusions.

1. Approximately 20 per cent of all ovarian tumors are malignant.

2. Solid sarcoma of the ovary is the rarest type of ovarian new growths. One per cent would be the approximate incidence of solid sarcomas.

3. Review of the literature shows this tumor is most common in young children under three years of age and is found with decreasing frequency up to fourteen or fifteen years of age.

4. The two periods of usual occurrence in adults is during the third decade and after the menopause.

5. Diagnosis and differential diagnosis offer the same difficulties as the other solid tumors of the ovary. The diagnosis is seldom made except by the pathologist.

6. The treatment of this condition is the same as in solid carcinoma of the ovary with the possible addition of Coley's serum which may have a questionable value.

7. The prognosis in adults is better than in children.

8. The prognosis in adults is better than in solid carcinoma of the ovary.

9. The prognosis in children is very bad on account of the high operative mortality and the frequency of early and fatal recurrence.

10. In adults when the tumor is unilateral and encapsulated and the patient is in the child bearing period and anxious to bear children, conservative surgery should be employed and only the involved ovary and adjacent tube be removed.

11. As shown by one case in this series and a review of the literature menstruation may be regular and normal in amount following unilateral ovariotomy for this condition.

12. Normal gestation and delivery may also follow.

13. Solid sarcoma may be accompanied by the same complications as other ovarian tumors.

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BIBLIOGRAPHY

1. Andrews, H. R.: Primary melanotic sarcoma of ovary. Trans. of the Obst. Society of London, 1902, xliii, 228-231.

2. Astruc, J.: A treatise on all the diseases incident to women. Translated from a manuscript copy of the author's lectures read at Paris, 1740. London, M. Cooper, 1743, 480 pp.

3. Baillie, M.: A series of engravings, accompanied with explanations, which are intended to illustrate the morbid anatomy of some of the most important parts of the human body. London, J. Johnson, 1799, 228 pp.

4. Basse, G. L.: Beitrag zur Kenntnis der gutartigen bindgewebigen Neubildungen des Ovariums, insbesondere der Myome. Arch. f. Gynak., 1904, lxxiv, 70-101.

5. Bland-Sutton, Sir John. Tumors innocent and malignant. Cassel & Co., London & New York, 1917, VI Edition, 628-31.

6. Briggs, H. and Walker, T. E. Solid ovarian tumors of which thirty-one were fibromata. Jour. of Obst. and Gynec. of the Brit. Empire, 1908, 1, 1083.

7. Broders, A. C.: Squamous cell epithelioma of the skin. Ann. Surg., 1921, lxxiii, 141-160.

8. Broders, A. C.: Squamous cell epithelioma of the lip. Jour. A. M. A., 1920 (March), lxxiv, 656-664.

9. Broders, A. C. and MacCarty, W. C. Melano-epithelioma. Surg., Gynec. and Obst., July 1916, xxxiii, 28-32.

10. Brodhead, G. L.: Sarcoma complicating puerperium. Med. Rec., 1916, lxxxix, 650.

11. Chapman, T. L. Krukenberg Tumor. Surg., Gynec. and Obst. July 1920, xxxi, 58-59.

12. Clark, E. D. and Gabe, W. E.: Fibroma of the ovary. Am. Jour. Obst. and Gynec., 1921. vi, 603-608.

13. Coe, H. C.: Fibromata and cysto-fibromata of the ovary. Am. Jour. Obst., 1882, xv, 858-879.

14. Coe, H. C. and Coley, Wm. B.: Sarcoma of the ovary. Med. Rec., 1907, lxxi, 436.

15. Cottam, G. G. and Herzberg, Mortimer.: Primary melano-sarcoma of the ovary. Prelim. Clinical Report, 1915, Jour. Lancet, xxxv, N. S. 435-439.

16. Cullen, E. K.: Combined adeno-carcinoma and mixed cell sarcoma of the ovary. Bull. Johns Hopkins Hosp., 1911, No. 298, 367-369.

17. Danforth, W. C.: Ovarian tumors in pregnancy with report of a case of a

solid tumor. Surg., Gynec. and Obst., 1915, xx, 319-324.

18. Doran, A.: Cases of fibroma of the ovary and ovarian ligament removed by operation; with a series of after-histories of cases reported in the transactions since 1879. Am. Jour. Obst., 1896, xxxiv, 405-411.

19. Doran, A.: Large ovarian tumors in a 7 months child. Trans. of the Path. Soc. of London. 1899, xl, 200-208.

20. Foerster, F.: Fibro-sarcoma of the ovary. Amer. Jour. of Obst., 1914, lxix, 350-352.

21. Forssner, G.: Carcino-sarcoma. Quoted from an editorial. Jour. A. M. A., 1909, lii, 1335.

22. Fullerton, W. D.: Fibroid tumors of the ovaries. Surg., Gynec. and Obst., 1914, xviii, 451-455.

23. Griffith and Williamson,: A System of Gynecology. Allbutt, Playfair and Eden, 1906, 445.

24. Gibson, C. L.: Sarcoma of the ovary. Ann. of Surg., 1920, xxxi, 763.

25. Glockner, A.: Ueber Secundares Ovarial Carcinom. Arch. f. Gynäk., 1904, lxxii, 410-469.

26. Hartz, H. J.: Report of a case of an ovarian fibroma undergoing sarcomatous degeneration. Am. Jour. Obst., 1912, lxvi, 544-548.

27. Hayd, H. E.: Sarcoma of the left ovary in a child twenty-three months old. Trans. Am. Assn. of Obst. and Gynec. 1918, xxxi, 50-56.

28. Hellman, A. M.: Ovarian fibroids, with report of six cases. Surg., Gynec. and Obst., 1915, xx, 692-699.

29. Higgins, T. T.: Ovarian sarcomata in children. An account of three children. Brit. Med. Jour. of Children's diseases. London, 1915, xii, 161-165.

30. Hussy, P.: Beitrag zur Kenntnis der Krukenbergschen Ovarialtumoren. Hegar's Beitrage z. Geb. u Gyn. 1911, xvi, 481.

31. Jessett, B.: Spindle cell sarcoma. Brit. Gyn. Jour., 1906-07, xxii, 68-69.

32. Jones, A. T.: Case of large sarcoma of ovary; great amount of fluid in abdominal cavity; improvement in general condition since operation; prognosis good for several years in this type of case. Trans. Amer. Assn. Obst. and Gyn. 1914, xxvi, 246-248.

33. Judd, A. M.: Sarcoma of the ovary. Amer. Jour. of Obst. and Gyn., 1920-21, ii, 383-385.

34. Kaufman, E.: Spezielle Pathologische Anatomie. 5 Auflage. 936-937.

35. Kelly, H. A. and Cullen, T. S.: Myomata of the uterus. Philadelphia, Saunders, 1909, 725 pp.

36. Kiwisch, F. A.: Klinische Vortrage über specielle Pathologie und Therapie der Frankheiten des weiblichen Geschlechtes. Prag., J. G. Calve, 1845-1855, 3 vol.

37. Klob: Quoted by Hellman.

38. Krukenberg, F.: Ueber das Fibrosarcoma ovarii Mucocellulare (Carcinomatodes). Arch. f. Gynäk. 1896, l, 287-321.

39. Kruger, M. Muenchen. Med. Wchnschr. 1909, lvi, 2606.

40. Leopold, G.: Die soliden Eierstocksgeschwulste. Arch. f. Gynäk. 1874, vi, 189-278.

41. Lockhart, F. A. L.: Sarcoma of the ovaries. Jour. Obst. and Gynec. of the Brit. Empire. 1909, xvi, 73-83.

42. MacCarty, W. C.: Clinical suggestions based upon a study of primary, secondary (carcinoma) and tertiary (carcinoma) epithelial hyperplasia in the breast. Surg., Gynec. and Obst. 1914, xviii, 284-289.

43. MacCarty, W. C.: The histogenesis of cancer (carcinoma) of the breast and its clinical significance. Surg. Gynec. and Obst. 1913, xvii, 441-459.

44. Major, R. H.: A study of the Krukenberg tumor. Surg., Gynec. and Obst., 1918, xxvii, 195-204.

45. Marchand: Quoted by Onterbridge.

46. Onterbridge, G. W.: "Krukenberg Tumor" of the ovary. Amer. Jour. of Obst., Dec. 1911, lxiv, 925-952.

47. Olshausen: Quoted by Hellman.

48. Orthmann: Quoted by Hellman.

49. Palale, J. O.: Primary sarcoma of the ovary. Med. Rec. 1915, lxxxvii,167.

50. Peaslee: Quoted by Hellman.

51. Peterson, R.: A consideration of ovarian fibromata based on a study of two recent cases and eighty-two collected from the literature. Am. Gynec., 1902, i, 45-68.

52. Pfannenstiel: Quoted by Hellman.

53. Pfannenstiel: Ueber die papillären Geschwülste des Eierstocks; anatomische und klinische Untersuchungen zur Klärung der Frage ihrer Malignität. Archiv. f. Gynäk., 1895, xlviii, 507.

54. Pick, L.: Zur Symptomatologie und Prognose der Sarcome des Eierstodes. Centralbl. f. Gynäk., Leipzig, 1894, xviii, 940-946.

4-21 6M

55. Porter, M. F.: Sarcoma of the ovary. Trans. West. Surg. Assn. 1913, 329-341.

56. Reel, P. J.: Krukenberg cancer of the ovary. Interst. Med. Jour., 1917, xxiv, 520-523.

57. Reel, P. J.: Krukenberg cancer of the ovary. Ann. of Surg., April, 1921, lxxiii, 481-486.

58. Ridout, C. A. S.: Primary carcinoma of the ovary at the age of eleven. Brit. Med. Jour., 1919, ii, 380.

59. Rosenstein, Julius.: A contribution to the question of metastasis of carcinoma in the ovaries and Douglas' culdesac. Surg., Gynec. & Obst., 1910, xi, 113-123.

60. Schatzchen: Quoted by Hellman.

61. Schauta: Quoted by Hellman.

62. Schultz: Quoted by Onterbridge. Magenkrebs im jungenlichen alter. Inaug. Diss. Breslau, 1886.

63. Schwartz, L. S.: Primary sarcoma of the ovary. Amer. Jour. of Obst., 1917, lxxv, 513-515.

64. Seeger, R.: Ueber Solide Tumoren des Ovarium. Inaug. Diss., Muenchen, 1888.

65. Smith, F. H. and Motely, J. C.: Sarcoma of both ovaries in a child of three years. Surg. Gynec. and Obst., 1915, xx, 419-424.

66. Stauder, Alfons.: Ueber Sarkome des Ovariums. Zeitschr. f. Geb. u. Gynäk, 1902, xlvii, 357-400.

67. Stewart, F. T.: Sarcoma of the ovary. Ann. of Surg., 1906, xliv, 306-307.

68. Stone, W. S.: Metastatic carcinoma of the ovaries. Surg. Gynec. and Obst., 1916, xxii, 407-423.

69. Stickel, M.: Ueber doppelseitige metastasche ovarialcarcinome. Arch. f. Gynäk., 1906, lxxix, 605-663.

70. Waldeyer, G.: Die Entwickelung des Carcinome. Arch. f. Path. Anat., 1872, lv, 130-131.

71. Webster: Quoted by Briggs and Walker.

72. Wells: Quoted by Peterson.

73. Winternitz, M. C.: Primary melanotic sarcoma of the ovary. Johns Hopkins Hosp. Bull., 1909, xx, 314-318.

74. Wolfson, W. L.: Primary sarcoma of the ovary. Long Island Med. Jour., 1915, ix, 291-293.

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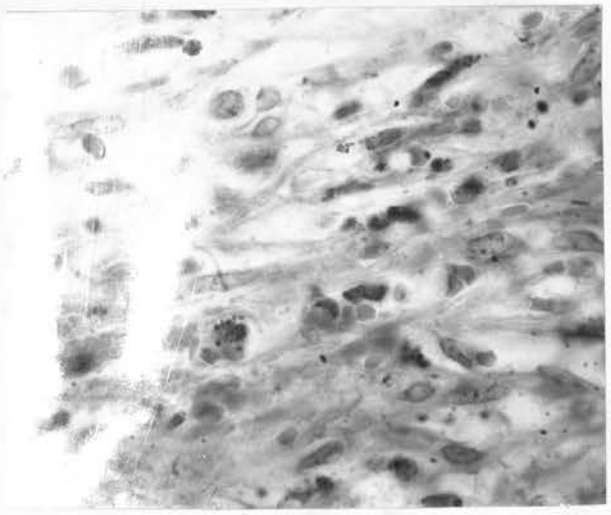

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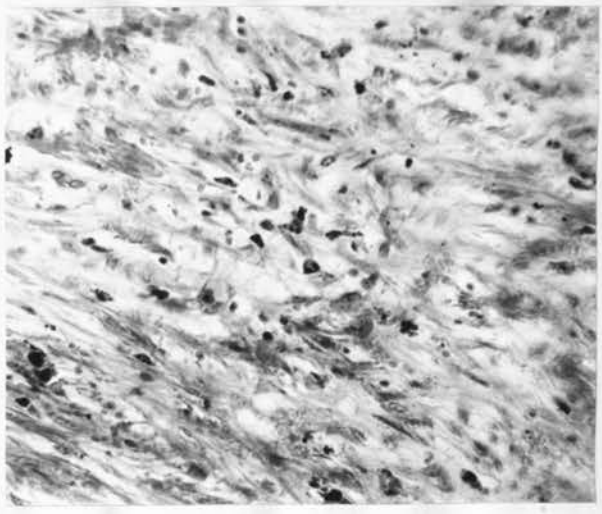

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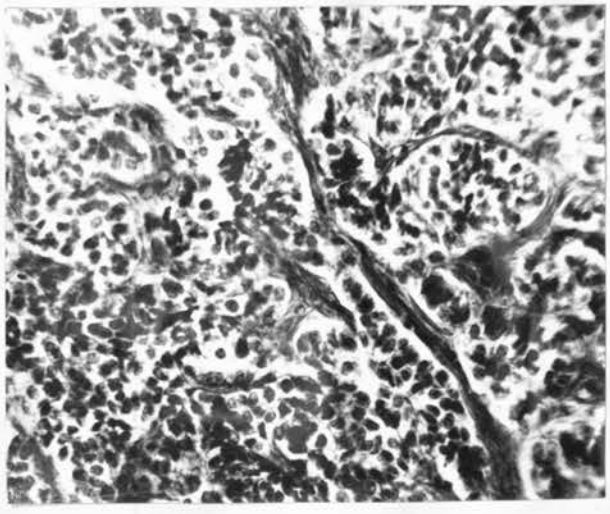
Melanotic carcinoma. Pigment lying within and between the cells. Marked absence of cell polarity. Prominent nucleoli.



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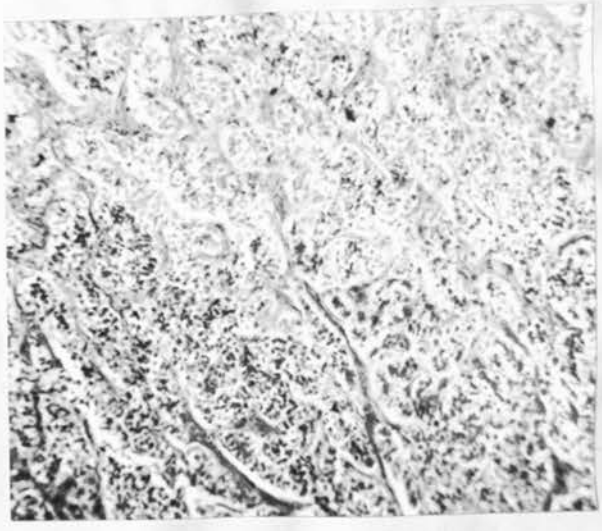

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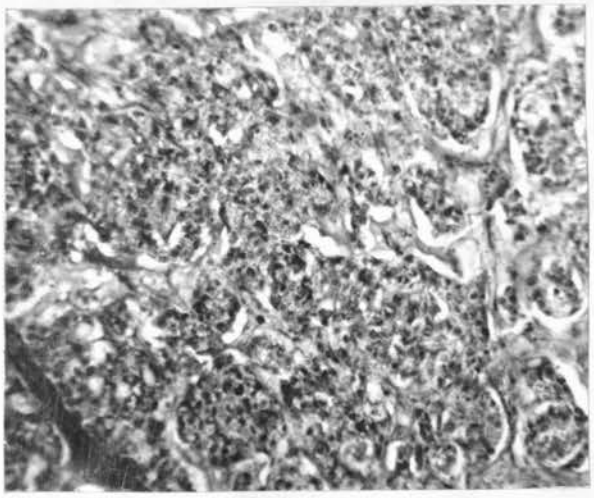
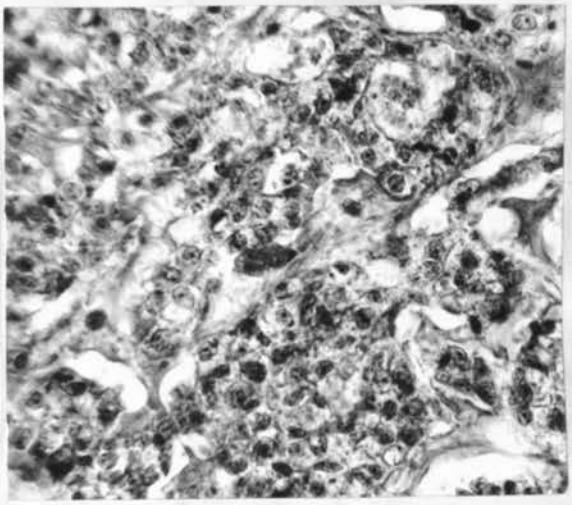
Solid carcinoma, Group IV. No tendency to cell differentiation or gland formation. No cell polarity.





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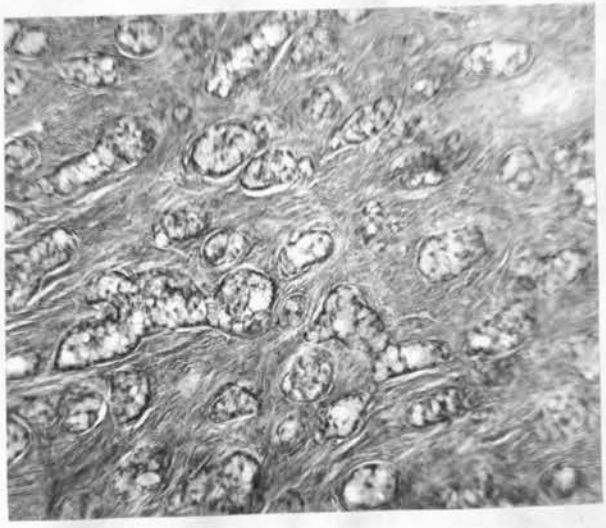
Carcinoma, Grade 3. Very slight cell differentiation with some tendency to gland formation.



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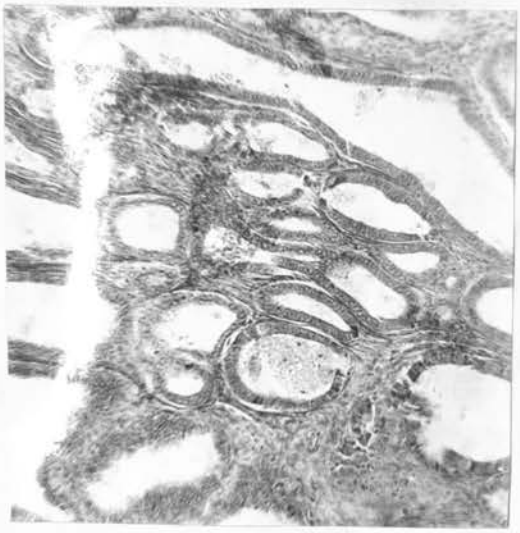
Carcinoma, Grade 2. Cells fairly well differentiated with gland formation. Migration of cells limited in degree.



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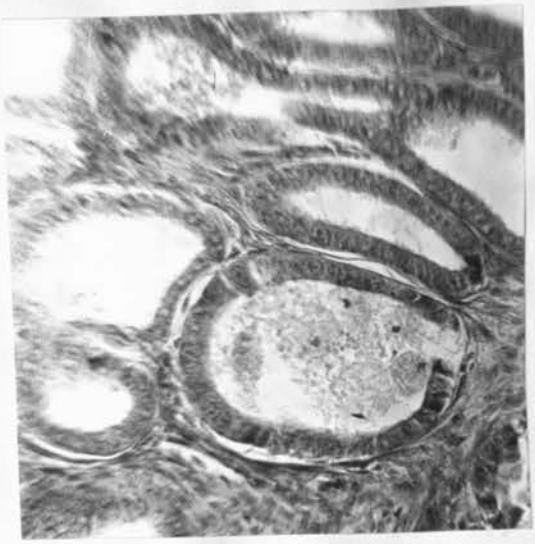

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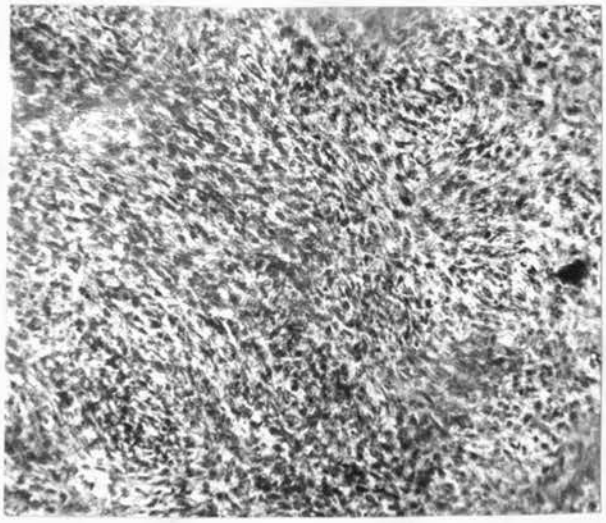
Carcinoma, Grade 1. Cells comparatively well differentiated with gland formation. Migration of cells seen in occasional areas.



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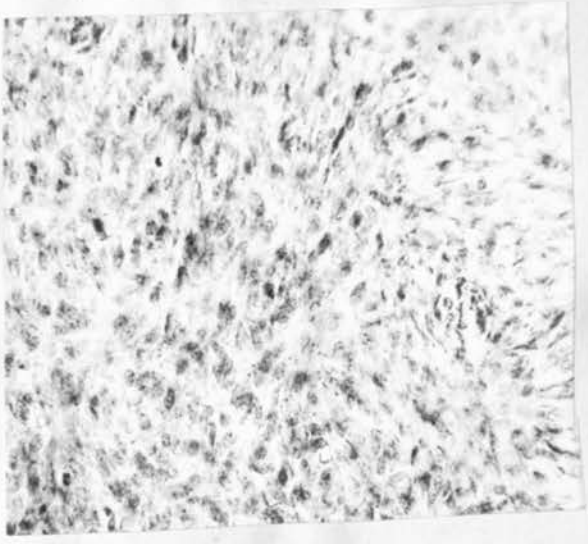

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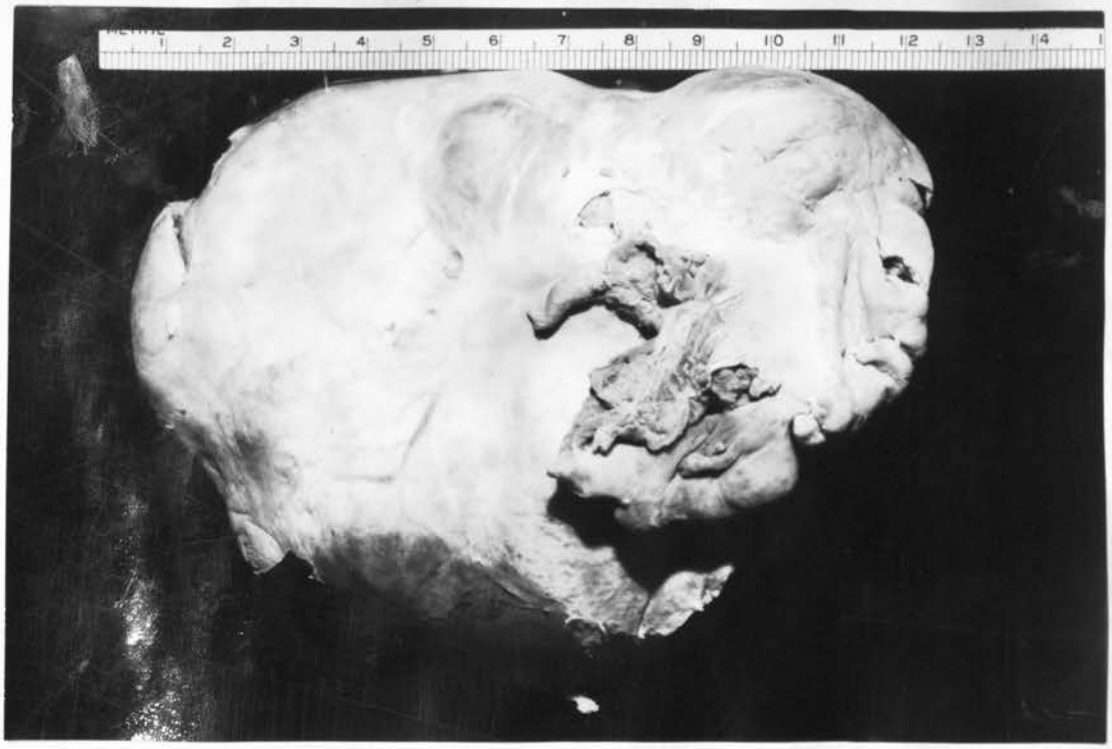
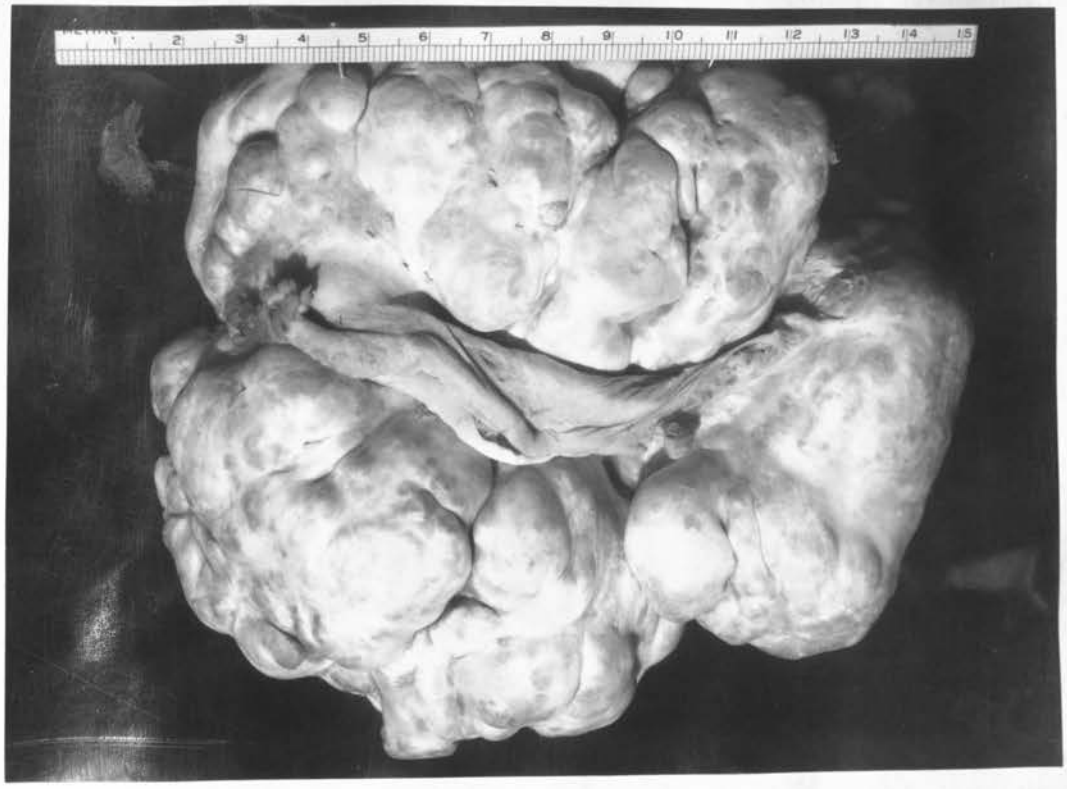
Solid (spindle-cell) Sarcoma of Ovary.



A32574. Miss P. A. Age 28. Sarcoma. Surface View.

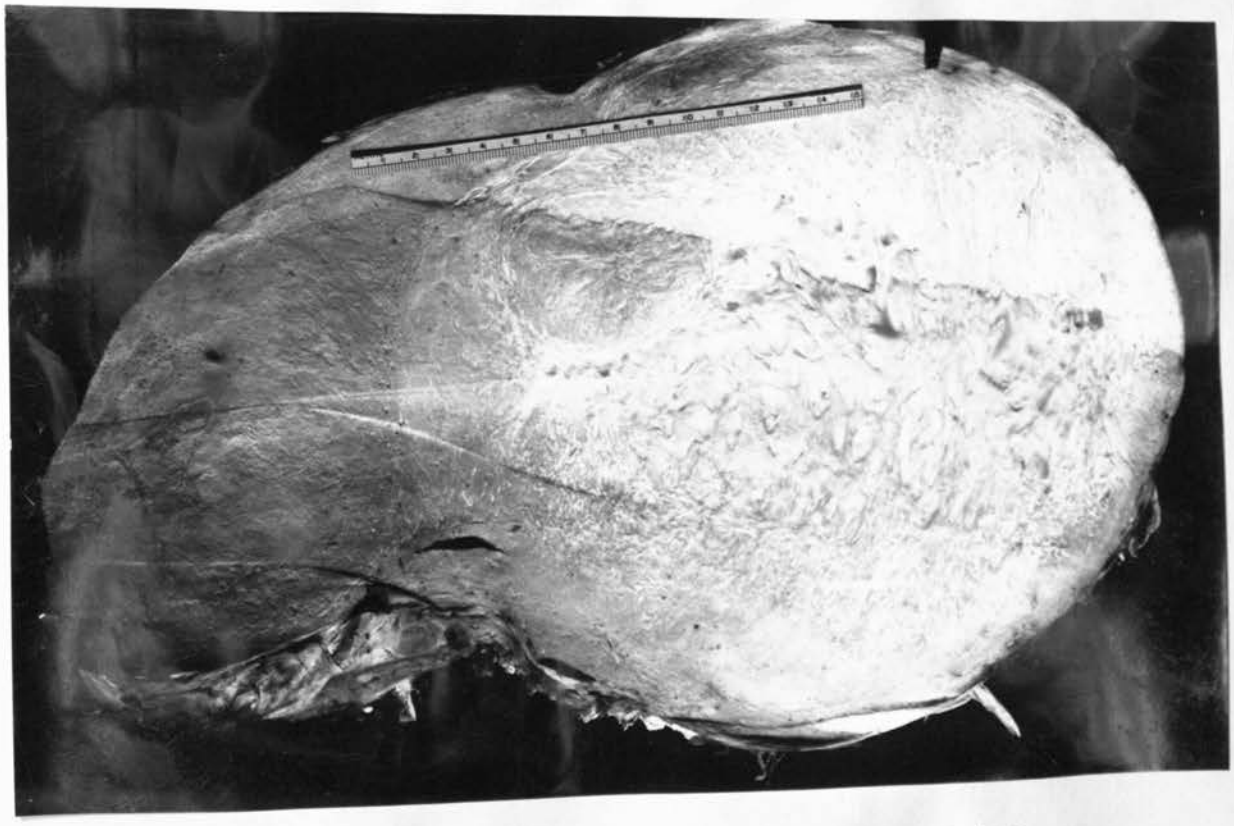
A32574. Miss P. A. Age 28. Sarcoma. View of Cut Surface.



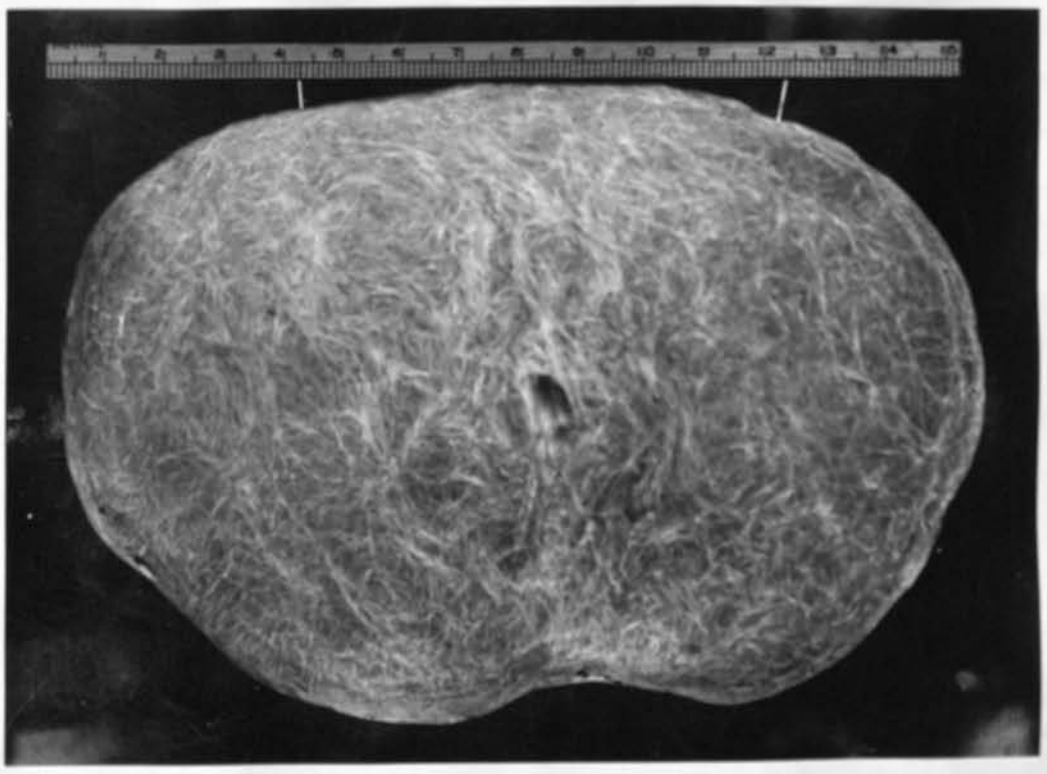
A-25985. Mrs.N. D. M. Age 34. Carcinoma. Fallopian tube attached.

A-247965. Mrs. G. W. L. Age 60. Carcinoma. Fallopian tube attached. Surface View.

A205277. Mrs. N. R. Fibroma. 35 x 23 x 15 cm. Weight 13¼ lbs.
Surface View.

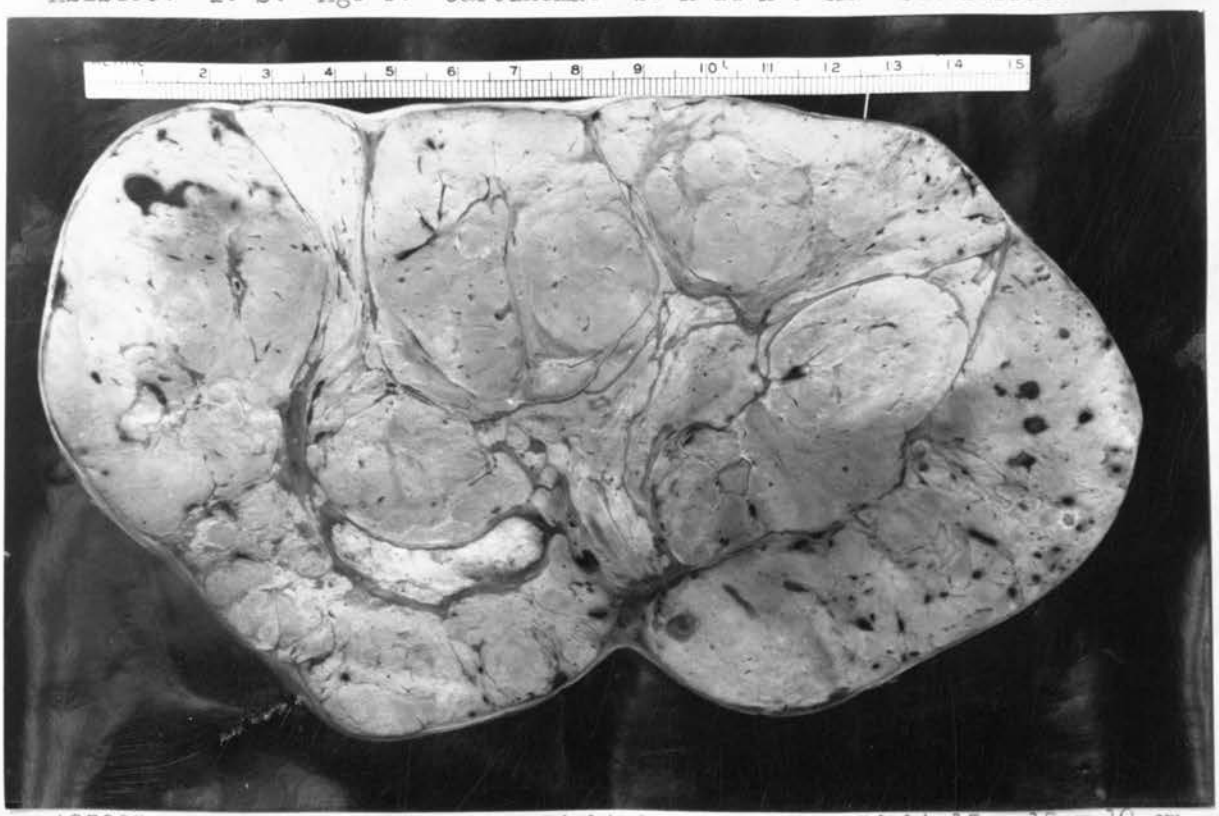


A205277. Mrs. N. R. Fibroma. 35 x 23 x 15 cm. Weight 13¼ lbs.
View of Cut Surface.



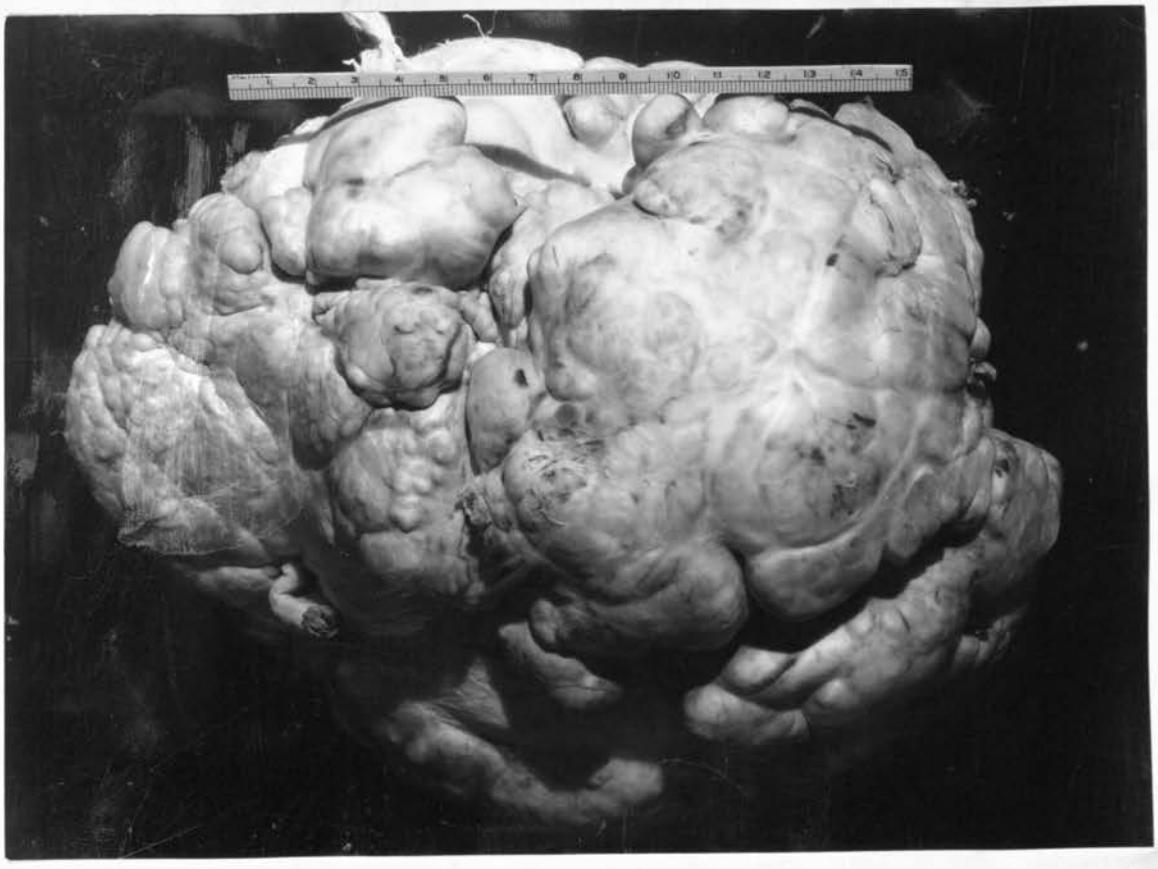
A-115013 Fibroma. 15 x 11 x 10cm.Striations on cut surface with small cyst in center of tumor.

A212409. I. S. Age 8. Carcinoma. 20 x 14 x 9 cm. Cut Surface.



A25985. Age 34. Cut Surface Right Ovary. Tumor Right 15 x 13 x 10 cm.

Left 9 x 7 x 5 cm.



A337037. Miss K. L. Carcinoma. 24 x 18 x 14 cm. Surface View with Fallopian Tube.

A158717. Carcinoma. 37 x 32 x 15 cm. Weight 34 lbs.