

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 Arthur Edwin Mahle
final oral examination for the degree of
Master of Science in Pathology
We recommend that the degree of
Master of Science in Pathology
be conferred upon the candidate.

W. Carpenter MacLeod
Chairman

E. T. Bell.

J. O. Fitzberg
James C. Mason.
Geo. B. Custerman.

Date May 16, 1922

REPORT
of
COMMITTEE ON THESIS

The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by Arthur Edwin Mahle, for the degree of Master of Science in Pathology. 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 Pathology.

Wm. Carpenter MacCarty.
James E. Passon.
Geo. B. Keisterman

THESIS

THE MORPHOLOGICAL HISTOLOGY OF ADENO-CARCINOMA OF THE
BODY OF THE UTERUS IN RELATION TO LONGEVITY.

(A Study of 186 Cases)

Arthur Edwin Mahle, B.S., 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
Pathology.

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In the mortality statistics among wage earners, compiled by Dublin, from 1911 to 1916, cancer of the female genital organs ranks second in importance as regards cancer mortality, with a death rate of 14.7 per one hundred thousand persons, or 20.9 per cent of all cancer deaths. Cancer of the stomach and liver constitutes the largest group, with a death rate of 26.3 per one hundred thousand persons, or 37.6 per cent of all cancer deaths. Among white females, however, cancer of the female genital organs accounted for 28.6 per cent of all cancer deaths. Among colored females the rate is somewhat higher. The largest number of carcinomas of the female genitals affected the uterus, with the ovaries and tubes next.

The following table, taken from Dublin and from Hoffman, indicates that under the age of twenty-five there is no significant mortality from carcinoma of the female organs.

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Mortality Table of Cancer of Female Genital Organs
According to age and color per 100,000, from Dublin and from Hoffman

Age	All Females* 1903-1912	White Females 1911-1916	Colored Females 1911-1916	All Females U. S. Reg. Area 1910-1915
All ages	22.3	25.3	39.3	
Under 10	.07			
10-24	.6			
1-19		.2	.2	
20-24		1.	1.3	
25-34	7.8	7.9	17.7	8.4
35-44	32.6	43.4	62.9	34.7
45-54	71.2	85.7	109.7	75.6
55-64	91.4	109.4	131.6	99.9
65-74	90.8	110.3	131.5	103.2
75 and over	82.2	93.8	145.2	98.

*From Hoffman's statistics.

In the United States Census for 1918, carcinoma of the stomach and liver predominate over carcinoma of the female genital organs. Among males, carcinoma of the stomach and liver is responsible for nearly one half of all deaths, while among females, only one third of the deaths are assigned to this cause. Carcinoma of the female genital organs, however, accounts for 41 per cent of all carcinoma deaths. Hoffman places the cancer mortality rate for female generative organs of all ages in the United States registration area for 1903 to 1912, as 22.3 per 100,000 population, and carcinoma of the stomach and liver as 29 per 100,000 population, while Welch, compiling statistics from various clinics in Europe and America, found that among 31,482 cases of primary carcinoma, 21.4 per cent were from the stomach and 29.5 per cent from the uterus. Williams, quoting mortality statis-

tics of England and Wales, places the uterus first (23.5 per cent) in the localization of malignant disease, and the breast second (15.8 per cent). As regards the frequency with which uterine carcinoma affects the corpus, Ewing, quoting Koblanck places it at 10 per cent. He further mentions Backer and Blumenfeld who found corpus carcinoma at autopsy below 3 per cent. Cullen, over a period of six years (May, 1893 to April, 1899) collected 182 cases of carcinoma of the uterus of which 128 were squamous cell carcinoma of the cervix, nineteen were adenocarcinoma of the cervix and thirty-five were adeno-carcinomas of the body.

Among 9,777 women, dying from carcinoma, Bland found 3,172 in the uterus, 2,139 in the stomach, and 1,776 in the breast. He reports fifty-nine cases of uterine carcinoma which were proportioned as follows: vaginal cervix 63 per cent, cervical canal 18.5 per cent, body 15 per cent and vagina 35 per cent. Kaufmann gives the proportion of the corpus carcinoma as 10 to 12 per cent of all uterine carcinomas.

In the period between January 1, 1910 and January 1, 1919, there were 855 carcinomas of the uterus in this Clinic, of which 70.3 per cent were located in the cervix and 29.7 per cent in the fundus.

The uterus is roughly divided into two main portions--the body (corpus uteri) and the cervix,--by a transverse constriction, the isthmus. The corpus uteri in women who have borne children is larger than the cervical portion, comprising about two thirds of the organ, and is, when normal, slightly antiflexed upon the lower third,--the cervix.

The peritoneum covers the upper half of the anterior surface of the uterus, the fundus, and almost the entire posterior surface. Between this fold of peritoneum, which, extending laterally, forms the broad ligaments, lie the arteries, veins, lymphatics and nerves. The two main arteries, supplying the uterus, arise from the anterior division of the internal iliac, pass through the folds of the broad ligaments to the cervix. They then ascend along the lateral border

of the uterus, giving off branches to the anterior and posterior surfaces and anastomose freely with the uterine branch of the ovarian arteries. The veins follow the course of the arteries.

The lymphatics which cover the entire surface of the uterus arise from three capillary plexuses,--a mucous, a muscular, and a peritoneal. The collecting vessels of the body of the uterus are divided into three sets. From the fundus one set runs laterally in the suspensory ligament of the ovary and follows the ovarian vessels to the lumbar and the pre-aortic lymph nodes. Some smaller vessels of the fundus follow the round ligament of the uterus and terminate in the inguinal nodes. A third set passes laterally with the uterine vessels and terminates in the iliac nodes. The collecting vessels from the cervix form a large plexus after leaving the cervix and from this plexus one set of vessels runs along the uterine artery in front of the ureter and terminates in the iliac nodes. Another set passes behind the ureter and ends in a node in the hypogastric group. A third set from the posterior surface runs downward over the vagina, backward and upward, to terminate in the lateral sacral node and the node of the promontory of the sacrum.

Histologically, there is some slight difference between the endometrium of the fundus and that of the cervical canal. The cells of the former are not as high but are thicker and take a deeper stain. The nuclei are somewhat larger, more prominent and more centrally placed. The nuclei of the epithelial cells of the cervical canal are more peripherally placed, and the cytoplasm is faint and clear-staining.

It has been stated that malignant neoplasia is not a definite entity. The carcinoma of one tissue differs from that of other tissues throughout the body. Carcinoma of one individual differs from carcinoma of another even though they be in similar tissues. The pathological literature contains many terms describing these differences, such as carcinoma simplex, medullary carcinoma,

scirrhous and colloid carcinoma and many others. To many pathologists these terms denote only differences of histological structure; while to others they also express varying degrees of malignancy of the neoplasm.

Hippocrates (460-375 B. C.) described many of the facts relative to the progress of malignant tumors. We know, from clinical experience, that certain carcinomas are relatively highly malignant and the outlook grave, while others grow more slowly and metastasize late, if at all. Even malignant tumors arising from different structures and in different locations of the same organ vary as to their degree of malignancy. While lymph drainage, the relation of a part to other organs, the rapidity of growth and the mode of invasion are cited as factors in determining the mortality from a definite type of carcinoma, still the pathologist is able in many instances to estimate the relative degree of malignancy of a given neoplasm by its gross and microscopic characteristics.

In this series of 186 cases of carcinoma of the corpus uteri attention has been especially directed to the study of the degree of malignancy based upon the degree of cellular differentiation. The series includes only those cases of carcinoma of the fundus uteri between January 27, 1905 and January 21, 1919, which were available for study and could be accurately determined, grossly and microscopically, as true carcinomas. This, therefore, does not include all hysterectomies for carcinoma of the fundus during this period.

There are various pathological classifications of carcinoma of the corpus. Kaufmann divides them into those which arise from the surface epithelium, and the more common type, those arising from the glandular epithelium. Under the latter type he classifies first, the so-called "adenoma malignum", found most frequently in the corpus but which may appear in the cervix. These are characterized by little stroma and a predominance of glandular tissue, the cells of which lie in close apposition and are highly differentiated. The second type, the usual form of adeno-carcinoma of the fundus, is characterized by areas of apparent

re-duplication of the glands which one finds in normal endometrium, while in other areas the true carcinomatous nature of the tumor is evident. The cells in these latter areas have all the morphological characteristics of carcinoma cells and are arranged in a typical gland formation. There is a moderate amount of stroma between the carcinoma cells. The third group is the papillary adenocarcinoma and in it the connective tissue stroma, like in the "adenoma malignum", is very sparse and the glandular tissue rests upon thin connective tissue trabeculae. In a fourth group he places the "adeno-carcinoma solidum" where one sees only few areas with glandular arrangement and large numbers of closely packed undifferentiated cells. The last group comprises adeno-carcinomas showing in the midst of the cylindrical cell masses, cornified cells and even epithelial pearls, not unlike those found in squamous cell carcinoma of the cervix.

The carcinomas arising from the surface epithelium show marked variation, are very rare, and are found in older persons. The most interesting type is that which covers the entire mucosa as a squamous cell carcinoma without glandular formation, which may or may not be cornified. The underlying tissues may be infiltrated with small celled, carcinomatous projections, and the surface may be papillary.

Ewing divides carcinoma of the corpus anatomically into a circumscribed and a diffuse group, stating that the diffuse are most probably the advanced stages of the circumscribed. Histologically, he follows a very similar classification to that of Kaufmann.

Under the histological types of corpus carcinoma, Aschoff describes the "adenoma malignum", adeno-carcinoma, solid or medullary carcinoma, and the squamous cell carcinoma, adding that in the same carcinoma one or even all types may be present.

Carcinoma of the fundus is not divided by Cullen into any definite groups. He states that while all cases may be classed under one main heading,

the gland grouping varies greatly in individual cases. He is of the opinion that where the papillary arrangement is the most marked the origin of the tumor is from the surface epithelium, whereas when the gland-like arrangement predominates, the process has started first in the glands.

In the study of our cases no special attempt has been made to classify anatomically other than note the general shape, extent of involvement of uterine cavity and invasion of the myometrium in relation to the histological type. From the histological appearance, an attempt has been made to prognose the relative degree of malignancy or mortality of a group of cases taking as a basis the cellular changes. That there are other factors cannot be denied; as the rate and extent of growth manifest in the amount of uterine cavity involved, the degree of invasion of the myometrium, and the late involvement of lymph nodes, to say nothing of that uncertain factor, personal resistance to carcinoma. Many of these factors cannot be directly proven from the following data. Cellular differentiation alone does not explain the high mortality of certain carcinomas whose cells were well differentiated, nor the long duration of post-operative life of other patients whose carcinomas were histologically highly malignant. Taken as a whole, however, cellular differentiation appears to be the most important factor.

Each case was studied separately. As a standard to judge cellular differentiation, the scheme of MacCarty was followed. According to him, cells arranged as to the general direction of adult tissue--or with normal polarity,--with normal appearance of cytoplasm and nucleoplasm, and with normal function, i. e., completely differentiated, are classed as showing tertiary differentiation, expressed for reasons of convenience by the Arabic figure 3. The second stage, (secondary differentiation expressed by figure 2) consists of the establishment of tissue polarity but morphological undifferentiation of cells (see Figs. 7, 8, 9). Primary differentiation (expressed by figure 1) consists of morphological

undifferentiation of cells but alignment according to the general direction of adult tissue (see Figs. 10, 11). Thus cells showing no differentiation (expressed by 0) have neither morphological differentiation nor alignment (see Figs. 12, 13, 15).

Appreciating that the degree of malignancy is dependent upon the phenomenon of cellular differentiation, the foregoing types were also incorporated into different grades of malignancy expressed by the Roman numerals I, II, III, IV, similar to Broders' classification of squamous cell epitheliomas (see Figs. 7 - 15). Grade IV corresponds to those cases which were highly malignant and whose cells show 0 differentiation throughout practically the entire tumor though occasional areas may show some primary differentiation (see Fig. 15). Grade III includes those carcinomas showing largely 0 differentiation, some primary differentiation and occasional areas may show secondary differentiation (see Fig. 11). Grade II carcinomas show a predominance of secondary differentiation throughout, though occasional areas of primary differentiation (see Fig. 9). Grade I comprises early cases, where the carcinoma is extremely small and the cells show high differentiation, secondary throughout (see Figs. 7, 8).

Of the 186 cases the average age was 55.01 years, the oldest seventy-three years and the youngest twenty-one years (see Table I). This bears out the statistics quoted on page two as regards the insignificant mortality from carcinoma of the female genitals before the age of twenty-five years. Occasional cases of carcinoma of the uterus are cited in the literature in persons younger than twenty years of age, but the majority are severely questioned as to their authenticity. Ganghofner reports a case of cancer of the portio in a girl of eight years. This case, according to Williams, is not a true carcinoma but a cauliflower excrescence of epithelial hyperplasia. However, Chiari examined the tumor histologically, which should establish its authenticity. Cragin reports a case of carcinoma of the uterus in a girl of eighteen years and upon whom a

radical abdominal hysterectomy was performed, and no recurrence had taken place during a period of five months. In the series of adeno-carcinomas of the corpus collected by Cullen the two youngest patients were thirty years of age.

The average age of menopause was 48.8 years showing that catamenia is relatively not altered in patients with carcinoma of the uterus (see Table I). In comparison to the average age, 55.01 years, one is led to believe that a certain factor in etiology exists between decline of functional activity and malignant disease and that the liability to cancer increases as the decline of function progresses. This fact is further emphasized when we compare the active marital lives of these patients as regards number of pregnancies with otherwise normal patients (see Table I).

The longest duration of symptoms occurred in Grades II and III, while the longest average duration of symptoms appeared in the least malignant, Grade I, and the shortest average duration of symptoms in the most malignant, Grade IV (see Table III). This difference when compared with the extent of involvement of uterine cavity and the amount of invasion of myometrium in respect to degree of malignancy and cellular differentiation (as expressed in Tables VI and VII, XII and XIII) illustrates that a tumor of a high degree of malignancy and low cellular differentiation grows larger and invades more extensively in the same period of time, than a carcinoma of a less degree of malignancy, and a high cellular differentiation. The amount of invasion of the myometrium is designated by figures 1 to 4; 1, denoting microscopic involvement of the muscle; 2, invasion of one half of the approximate width of the muscle; 3, invasion to the serosa; 4, invasion of all the muscle layer and also the serosa.

The clinical symptoms, as charted in the table on symptomatology (No. IV) illustrate that vaginal discharge, especially if this be blood tinged, is the most out-standing feature, occurring in 92.46 per cent of all cases. Weight and strength loss taken together occupy the next place of importance,

while odorous discharge except in advanced cases is relatively of little diagnostic value.

The 186 cases of corpus carcinoma divided into grades of malignancy, (I, expressing the least and IV, the highest malignant grade), illustrate that the largest number fall into Grade II (61.29 per cent) with Grade III next (29.03 per cent) (see Table II). In comparison, squamous cell carcinomas of the cervix, graded similarly by Broders are more malignant, and the larger number of his cases fall into Grades III and IV. The number of patients obtaining good post-operative results in Broders' series was 20 per cent, while in our series of carcinoma of the fundus 61.02 per cent of the patients heard from were still living and the percentage of good post-operative results following vaginal and abdominal hysterectomy, was 52.94 per cent and 58.71 per cent respectively. If one considers only the two most malignant grades of corpus carcinoma, III and IV, one sees that only 35.55 per cent of the patients heard from are still living, and good results were obtained in only 32 per cent of the cases operated upon. When one further considers the larger number of cases in Grade IV of the squamous cell carcinomas of the cervix the difference in percentage of good post-operative results in these two types of uterine carcinomas is further equalized. Likewise the relatively late involvement of lymph nodes in carcinomas of the large bowel is consistent with the large number of these carcinomas which show a high type of cellular differentiation and are histologically of low malignancy. In other words, the differences in life expectancy between the two types of uterine carcinoma and in carcinomas found elsewhere, can be explained by their differences in the degree of malignancy based upon the cellular differentiation. Such factors as the lymph drainage, mode and extent of invasion, rapidity of growth appear to be secondary and perhaps to a degree dependent upon cellular differentiation, and in reality of little real importance as regards the potential malignancy of the carcinoma.

Taussig, in a previous personal communication with this clinic, learned that of forty-five cases of carcinoma of the fundus of the uterus, ten (25 per cent) were associated with fibromyomata. In this series our figures are somewhat higher for the reason that they include even the most minute intramural fibromyoma (see Table V). That this is a factor in the etiology of carcinoma can hardly be accepted when compared to the number of fibromyomata found in non-malignant hysterectomies and the overwhelming frequency of fibromyomatous uteri when compared to carcinomatous uteri.

The shapes of the lesions (see Tables VIII and XIV) to a certain extent appear to be dependent upon cellular differentiation. The carcinomas in the least malignant group and those showing the greatest differentiation were largely papillary or polypoid in shape, while the most malignant and those showing the least cellular differentiation were those we have designated as the diffuse or flat type, in distinction from the papillary or polypoid types which are raised above the surface of the uterine mucosa. This fact has likewise been brought out in carcinomas of the bladder by Scholl, that those having a more papillary shape are less malignant than the flat type. However, other factors, such as mechanical pressure play a part in determining shape especially in tumors growing in cavities. Likewise polypoid tumors are surface tumors arising from a local hyperplasia which tends to be non-invasive.

In the general ultimate results according to grades of malignancy, I to IV, (Table XIV) all patients of Grade I (the least malignant) are still living, while those in Grade IV (the most malignant) are dead. Referring to the cause of death of these patients (Table XXI) 75 per cent of Grade IV patients died of carcinoma. In Grade II, 71.76 per cent were still alive while in Grade III, only 38.09 per cent were alive. The cause of death due to carcinoma in these two groups is 62.06 per cent and 74.19 per cent, respectively. One sees that not only does the number of patients dead increase as the degree of malignancy

increases but also the number of deaths due to carcinoma increases.

These facts are likewise verified when considering the ultimate results of the cases, grouped on a basis of cellular differentiation. The highest differentiation, 2, showed the largest percentage of living patients (65.78 per cent) and the smallest number dead (34.21 per cent); while the next group showing primary differentiation as the highest degree of cellular differentiation had the smallest number of living patients (36.36 per cent), and the largest number dead (63.63 per cent) (see Table XX). The average duration of symptoms and the average length of post-operative life is somewhat longer in the group showing the highest cellular differentiation. This fact is likewise emphasized in Table XIX, comparing general ultimate results according to Grades I to IV.

Abdominal hysterectomy was performed upon 136 (73.11 per cent) of the 186 patients while forty-five (24.19 per cent) had vaginal hysterectomies (see Table XVII). Over one half of the patients who were so treated surgically had good results, and are either living today or death has resulted from some cause other than carcinoma. The good results in both vaginal and abdominal hysterectomy decrease in percentage as the degree of malignancy increases. With this decrease in percentage of living patients with good results there is a corresponding increase in operative and carcinoma deaths.

While no attempt will be made to discuss the relative value of the two types of operation, it is of interest that in this series vaginal hysterectomy shows a slight increase in the percentage of recurrence both in the number of living patients with recurrence and the percentage of carcinoma deaths (see Tables XXII, XXIII, XXIV, and XXV). Operative deaths are slightly higher in cases having abdominal hysterectomies while the percentage of good post-operative results is somewhat higher than in vaginal hysterectomy.

The classification of cases according to the highest cellular differ-

entiation found throughout the carcinomas, and the grouping according to Grades I to IV show no difference between the total ultimate results. The latter grouping perhaps gives the pathologist a somewhat larger scope which, according to these statistics, is unnecessary. However, the foregoing facts demonstrate that the post-operative prognosis of a group of patients with adeno-carcinoma can be determined by a close study of the cellular differentiation of the carcinoma.

Conclusions

1. The mortality and frequency of carcinoma of the corpus uteri rank within the first two places in carcinoma of the female.
2. Corpus carcinoma is extremely rare before the age of twenty-five years.
3. Carcinoma of the corpus is found in about 30 per cent of all uterine carcinomas.
4. Apparently there exists a definite relation between the decline of functional activity and malignant disease of the corpus uteri.
5. The more active the carcinoma, the shorter are the clinical symptoms.
6. Vaginal discharge, especially if it be blood tinged, is the most out-standing clinical feature of corpus carcinoma.
7. The accepted belief of a relatively favorable outlook for corpus carcinoma in comparison to cervical carcinoma has a pathological basis in that the number of cases which show a high degree of differentiation are in the majority, and the more malignant types rare.
8. From an etiological point, association of fibromyomas with corpus carcinoma does not appear to play an important role.
9. The shape of the lesion appears to be related to the degree of cellular differentiation, for the more malignant the carcinoma the less liable it is to assume a papillary form.

10. A carcinoma of high degree of malignancy grows larger and invades more extensively in a given length of time, than one of a lower degree of malignancy.

11. Lymphocytic reaction appears more marked in groups showing a higher degree of malignancy.

12. The clinical diagnosis of carcinoma of the body, before curettage or hysterectomy, is possible in 40 per cent of all cases.

13. The longest length of life since operation of those patients who are now dead occurred in Grade III, while the shortest length of life since operation of the patients dead occurred in Grade IV.

14. The greatest average length of life following operation of the patients now living occurred in Grade II, and the shortest in Grade III. Grade IV had no patients living.

15. The shortest length of life following operation of those patients who are now dead occurred in Grade IV and the longest length of life in Grade II.

16. The shortest average length of life following operation of patients now dead occurred in Grade IV and the longest in Grade II. Grade I had no patients dead.

17. Grade I contains the largest percentage of living patients and Grade IV none, while Grades II and III contain 71.76 per cent and 38.09 per cent respectively.

18. The largest percentage of deaths from carcinoma occur in Grade IV and a smaller percentage in each preceding group to Grade I, in which there have been no deaths from carcinoma.

19. Abdominal hysterectomy in this series of cases was more frequently performed than vaginal hysterectomy and post-operative good results among living patients is slightly higher among those having abdominal hysterectomy. The percentage of recurrence is slightly higher in vaginal hysterectomy.

20. The sum total of ultimate results shows practically no variation when interpreted from a basis of relative amount of a definite type of cellular differentiation present in the tumor expressed in Grades I to IV, than when the interpretation depends upon the highest type of differentiation present in the tissue.

21. A series of adeno-carcinomas of the uterus can be so classified according to groups, expressing various degrees of malignancy that the ultimate post-operative results obtained will vary in direct proportion to the mortality of each group.

Table I

Adeno-carcinoma of Fundus of Uterus
186 cases from Jan. 27, 1905 to Jan. 1, 1919.

	<u>No.</u>	<u>Per cent</u>
Patients	186	
Age:	<u>Yrs.</u>	
Youngest	21	
Oldest	73	
Average	55.01	
Family history of malignancy	29.	15.59
Single	18.	9.63
Married	168.	90.33
Never pregnant	63.	33.87
Pregnant	123.	66.12
Total pregnancies	412.	
Pregnancies per married patient	2.4	
Patients having had miscarriage	53.	28.49
Total miscarriages	75.	
Miscarriages per married patient43	
Menopause:	<u>Yrs.</u>	
Youngest	35	
Oldest	55	
Average	48.8	

Table II

Grades in 186 Cases on a Basis of I to IV according to
Cellular Differentiation

	<u>No.</u>	<u>Per cent</u>
Grade I	10	5.37
Grade II	114	61.29
Grade III	54	29.03
Grade IV	8	4.30

Table III
Duration of Symptoms

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of all cases</u>
	yrs.	yrs.	yrs.	yrs.	yrs.
Longest	4.	5.	5.	3.	5.
Shortest	.08	.08	2.5	2.5	.08
Average	1.57	1.25	1.42	1.0	1.29

Table IV
Patients' Symptomatology

	<u>No.</u>	<u>Per cent</u>
Vaginal discharge	182	98.38
Bloody vaginal discharge	172	92.46
Odorous vaginal discharge	53	28.49
Tissue passed	2	1.07
Weight loss	44	23.65
Average weight loss in pounds 20.29		
Loss of weight and strength (amount not stated)	64	34.40

Table V
Carcinoma of Body of Uterus (161 cases) with associated
Fibromyomata

Grade I	5(55.55% of 9)
Grade II	30(30.30% of 99)
Grade III	19(42.22% of 45)
Grade IV	3(37.5 % of 8)
Total	57(35.4 % of 161)

Table VI

Extent of Involvement of Uterine Cavity, expressed in fifths

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of all cases</u>
1/5	4(44.44% of 9)	17(17.00% of 100)	4(8.88% of 48)	0	25(15.43% of 162)*
2/5	3(33.33% of 9)	13(13.00% of 100)	4(8.88% of 48)	1(12.50% of 8)	21(12.96% of 162)
3/5	0	12(12.00% of 100)	9(20.00% of 48)	1(12.50% of 8)	22(13.58% of 162)
4/5	2(22.22% of 9)	34(34.00% of 100)	15(33.33% of 48)	1(12.50% of 8)	52(32.09% of 162)
5/5	0	24(24.00% of 100)	13(28.88% of 48)	5(62.50% of 8)	42(25.93% of 162)

Table VII

Invasion of Myometrium, expressed on a basis of 1 to 4

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of all cases</u>
1	6(66.66% of 9)	27(27.27% of 99)	7(15.55% of 45)	1(12.50% of 8)	41(25.46% of 161)*
2	3(33.33% of 9)	36(36.36% of 99)	16(35.55% of 45)	3(37.50% of 8)	56(34.78% of 161)
3	0	23(23.23% of 99)	10(22.22% of 45)	0	35(21.73% of 161)
4	0	13(13.13% of 99)	12(26.66% of 45)	4(50.00% of 8)	29(18.01% of 161)

Table VIII

Shape of Lesion

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of all cases</u>
Papillary	4(44.44% of 9)	78(78.78% of 99)	31(68.88% of 45)	4(50.00% of 8)	118(73.29% of 161)*
Diffuse	1(11.11% of 9)	12(12.12% of 99)	10(22.22% of 45)	2(25.00% of 8)	25(15.52% of 161)
Polypoid	4(44.44% of 9)	9(9.09% of 99)	4(8.88% of 45)	2(25.00% of 8)	18(11.18% of 161)

*Only this number (of 186 cases) were available for this study.

Table IX

Lymphocytic Reaction of 186 Cases grouped according to degree of Malignancy on a Basis of 1 to 4

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of all cases</u>
1	7(70.00% of 10)	45(39.50% of 114)	23(42.59% of 54)	3(37.50% of 8)	78(41.93% of 186)
2	3(30.00% of 10)	47(41.22% of 114)	21(38.88% of 54)	2(25.00% of 8)	73(39.24% of 186)
3	0	20(17.62% of 114)	10(18.51% of 54)	3(37.50% of 8)	33(17.74% of 186)
4	0	2(1.75% of 114)	0	0	2(1.07% of 186)

Table X

The Relation of Cellular Differentiation of 186 Cases, to degree of Malignancy

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of all cases</u>
0	0	0	0	3(37.50% of 8)	3(1.61% of 186)
1	0	1(.83% of 114)	29(53.71% of 54)	5(62.50% of 8)	35(18.81% of 186)
2	10(100% of 10)	113(99.17% of 114)	25(46.29% of 54)	0	148(79.56% of 186)

Table XI

Cellular Differentiation of 186 Cases

Differentiation 0	3(1.61% of 186)
" 1	37(19.89% of 186)
" 2	146(78.49% of 186)

Table XII

Extent of Involvement of Uterine Cavity (expressed in fifths) of 161
Cases grouped as to Differentiation

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Of all cases</u>
1/5	0	2(6.66% of 30)	22(17.18% of 128)	24(14.90% of 161)*
2/5	0	5(16.66% of 30)	17(13.28% of 128)	22(13.66% of 161)
3/5	0	7(23.33% of 30)	16(12.50% of 128)	23(14.28% of 161)
4/5	0	7(23.33% of 30)	45(35.15% of 128)	52(32.29% of 161)
5/5	3(100% of 3)	9(30.00% of 30)	28(21.87% of 128)	40(24.84% of 161)

Table XIII

Invasion of Myometrium (expressed on a basis of 1 to 4) of 161 Cases
grouped as to Differentiation

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Of all cases</u>
1	0	5(16.66% of 30)	36(28.12% of 128)	41(25.46% of 161)*
2	1(33.33% of 3)	11(36.66% of 30)	46(35.93% of 128)	58(36.02% of 161)
3	0	6(20.00% of 30)	27(21.09% of 128)	33(20.49% of 161)
4	2(66.66% of 3)	8(26.66% of 30)	19(14.84% of 128)	29(18.01% of 161)

Table XIV

Shape of Lesion of 161 Cases grouped as to Differentiation

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Of all cases</u>
Papillary	1(33.33% of 3)	16(53.33% of 30)	101(78.90% of 128)	118(73.29% of 161)*
Diffuse	2(66.66% of 3)	8(26.66% of 30)	15(11.71% of 128)	25(15.52% of 161)
Polypoid	0	6(20.00% of 30)	12(9.37% of 128)	18(11.18% of 161)

*Only 161 cases were available for this study.

Table XV

Lymphocytic Reaction (expressed on a basis of 1 to 4)
of 186 Cases grouped as to differentiation

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Of all cases</u>
1	1(33.33% of 3)	14(37.83% of 37)	63(43.15% of 146)	78(41.93% of 186)
2	1(33.33% of 3)	14(37.83% of 37)	58(39.72% of 146)	73(39.24% of 186)
3	1(33.33% of 3)	8(21.62% of 37)	24(16.43% of 146)	33(17.74% of 186)
4	0	1(2.70% of 37)	1(.68% of 146)	2(1.07% of 186)

Table XVI

Clinical Diagnoses of 186 Cases of Carcinoma of Body of Uterus

Definite diagnosis of carcinoma of body of uterus	75(40.32% of 186)
Questionable diagnosis of carcinoma of body of uterus	36(19.35% of 186)
Diagnosed other than carcinoma of uterus	68(36.55% of 186)
Diagnosis not recorded	7(3.76% of 186)

Table XVII

Surgical Treatment of 186 Cases of Carcinoma of Body of Uterus

Total abdominal hysterectomy with removal of tubes and ovaries	128(68.81% of 186)
Subtotal abdominal hysterectomy with removal of tubes and ovaries	8(4.30% of 186)
Vaginal hysterectomy with removal of tubes and ovaries	7(3.76% of 186)
Vaginal hysterectomy	38(20.43% of 186)
Curettage only	4(2.14% of 186)
Cautery only	1(.53% of 186)

Table XVIII

Cause of Death of Patients who died at Clinic

Peritonitis	5(2.68% of 186)
Myocardial degeneration	2(1.07% of 186)
*Pneumonia	1(.53% of 186)
Intestinal obstruction	2(1.07% of 186)
Pulmonary embolism	1(.53% of 186)
Operative mortality	11(5.91% of 186)

*One death from pneumonia followed thyroidectomy one year after hysterectomy for carcinoma of uterus.

Table XIX

General Ultimate Results according to Degree of Malignancy

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Of total traced</u>
Patients traced	136(73.11% of 186)				
Patients living	6(100% of 6) yrs.	61(71.76% of 85) yrs.	16(38.09% of 42) yrs.	none yrs.	83(61.02% of 136) yrs.
Longest P.O. life	2.18	15.63	14.39		15.63
Shortest P.O. life	3.51	3.005	3.35		3.005
Average P. O. life	7.24	7.27	7.05		7.23
Deaths (excluding operative deaths)	none yrs.	24(28.23% of 85) yrs.	26(61.90% of 42) yrs.	3(100% of 3) yrs.	53(38.97% of 136) yrs.
Longest P.O. life		10.76	13.66	1.23	13.66
Shortest P.O. life		.33	.106	.082	.082
Average P.O. life		2.96	1.91	.759	2.29

Table XX

General Ultimate Results according to Cellular Differentiation

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Of total traced</u>
Patients living	none	8(36.36% of 22) yrs.	75(65.78% of 114) yrs.	83(61.02% of 136) yrs.
Longest P.O. life		11.51	15.66	15.66
Shortest P.O. life		4.35	3.005	3.005
Average P.O. life		6.51	7.30	7.23
Deaths (excluding operative deaths)	none	14(63.63% of 22) yrs.	39(34.21% of 114) yrs.	53(38.97% of 136) yrs.
Longest P.O. life		13.66	10.76	13.66
Shortest P.O. life		.106	.106	.106
Average P.O. life		.027	2.36	2.27

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Table XXI

Causes of Death*

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Total Dead</u>
Carcinoma		18(62.06% of 29)	23(74.19% of 31)	3(75% of 4)	44(67.69% of 65)
Carcinoma (?)		1(3.44% of 29)	1(3.22% of 31)	0	2(3.07% of 65)
Operation**	1(100% of 1)	4(13.79% of 29)	5(16.12% of 31)	1(25% of 4)	11(16.91% of 65)
Unknown	0	2(6.89% of 29)	1(3.22% of 31)	0	3(4.61% of 65)
Other than carcinoma	0	4(13.79% of 29)	1(3.22% of 31)	0	5(7.69% of 65)
Total deaths	65(43.91% of 148)			

*Information received from relative, home physician, or other reliable source.

**See Table XIX

Table XXII

Patients Having Abdominal Hysterectomy (according to Grades)

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Total</u>
Living					
Good results	3(75% of 4)	46(67.64% of 68)	12(35.29% of 34)	0	61(55.96% of 109)
Recurrence	0	1(1.47% of 68)	0	0	1(.91% of 109)
Dead					
Operative death	1(25% of 4)	3(4.41% of 68)	4(11.76% of 34)	1(33.33% of 3)	9(8.25% of 109)
Other causes (operative results good)	0	3(4.41% of 68)	0	0	3(2.75% of 109)
Carcinoma	0	13(19.11% of 68)	16(47.05% of 34)	2(66.66% of 3)	31(28.44% of 109)
Unknown	0	2(2.94% of 68)	2(5.88% of 34)	0	4(3.66% of 109)
Information received		109(80.14% of 136)		
No information received		27(19.85% of 136)		
Total number of patients having abdominal hysterectomy		136		

Table XXIII

Patients Having Vaginal Hysterectomy (according to Grades).

	<u>Grade I</u>	<u>Grade II</u>	<u>Grade III</u>	<u>Grade IV</u>	<u>Total</u>
Living					
Good result	1(100% of 1)	13(65% of 20)	3(25.00% of 12)	0	17(50.00% of 34)
Recurrence	0	1(5% of 20)	0	0	1(2.94% of 34)
Dead					
Operative death	0	1(5% of 20)	1(8.33% of 12)	0	2(5.88% of 34)
Other cause (operative re- sult good)	0	0	1(8.33% of 12)	0	1(2.94% of 34)
Carcinoma	0	4(20% of 20)	7(58.33% of 12)	1(100% of 1)	12(35.29% of 34)
Unknown	0	1(5% of 20)	0	0	1(2.94% of 34)
Information received			34(75.56% of 45)		
No information received			11(24.44% of 45)		
Total number of patients having vaginal hysterectomy					45

Table XXIV

Patients Having Abdominal Hysterectomy (according to Differentiation)

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Total</u>
Living				
Good result	0	5(25.00% of 20)	56(63.63% of 88)	61(55.96% of 109)
Recurrence	0	0	1(1.13% of 88)	1(.91% of 109)
Dead				
Operative death	1(100% of 1)	4(20.00% of 20)	4(4.54% of 88)	9(8.25% of 109)
Other causes (operative good result)	0	0	3(3.40% of 88)	3(2.75% of 109)
Carcinoma	0	9(45.00% of 20)	22(25.00% of 88)	31(28.44% of 109)
Unknown	0	2(10.00% of 20)	2(2.27% of 88)	4(3.66% of 109)
Information received				109(80.14% of 136)
No information received				27(19.85% of 136)
Total number of patients having abdominal hysterectomy				136

Table XXV

Patients Having Vaginal Hysterectomy (according to Differentiation)

	<u>0</u>	<u>1</u>	<u>2</u>	<u>Total</u>
Living				
Good result	0	2(33.33% of 6)	15(53.57% of 28)	17(50.00% of 34)
Recurrence	0	0	1(3.57% of 28)	1(2.94% of 34)
Dead				
Operative death	0	1(16.66% of 6)	1(3.57% of 28)	2(5.88% of 34)
Other causes (operative good result)	0	1(16.66% of 6)	0	1(2.94% of 34)
Carcinoma	0	2(33.33% of 6)	10(35.71% of 28)	12(35.29% of 34)
Unknown	0	0	1(3.57% of 28)	1(2.94% of 34)
Information received			34(75.56% of 45)	
No information received			11(24.44% of 45)	
Total number of patients having vaginal hysterectomy				45

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Figure 1. (146326). Papillary type of adeno-carcinoma of corpus uteri associated with fibromyomata.



Figure 2. (91620). Papillary type of adeno-carcinoma of corpus uteri cut in sagittal section, showing extensive invasion of the myometrium.



Figure 3. (63423). Polypoid type of adeno-carcinoma of corpus uteri.



Figure 4. (341145). Polypoid type of adenocarcinoma of corpus uteri originating in right horn.



Figure 5. (335600). Diffuse type of adenocarcinoma of corpus uteri associated with multiple fibromyomata.



Figure 6. (145653). Polypoid type of adenocarcinoma of corpus uteri of high degree of malignancy. (See Fig. 12).

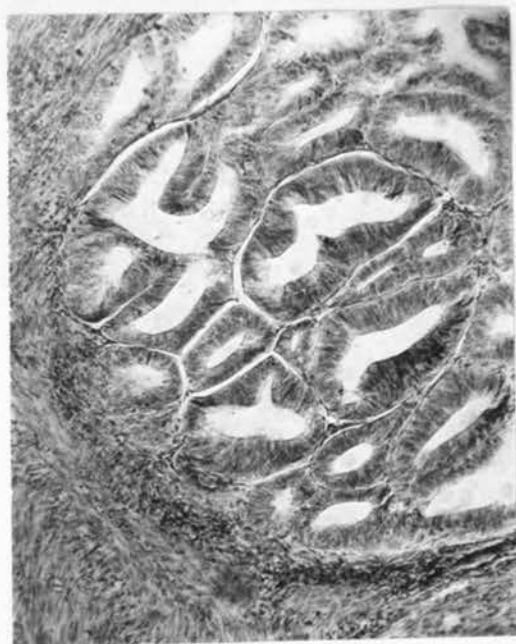


Figure 7. (146326). Photomicrograph of adeno-carcinoma, Grade I, showing secondary cellular differentiation.

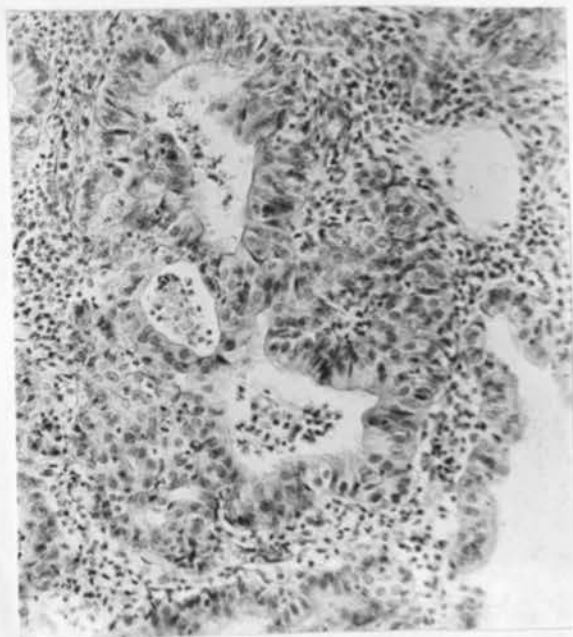


Figure 8. (8570). Adeno-carcinoma showing a high cellular differentiation. The area of carcinoma in this section came within one low-power field.

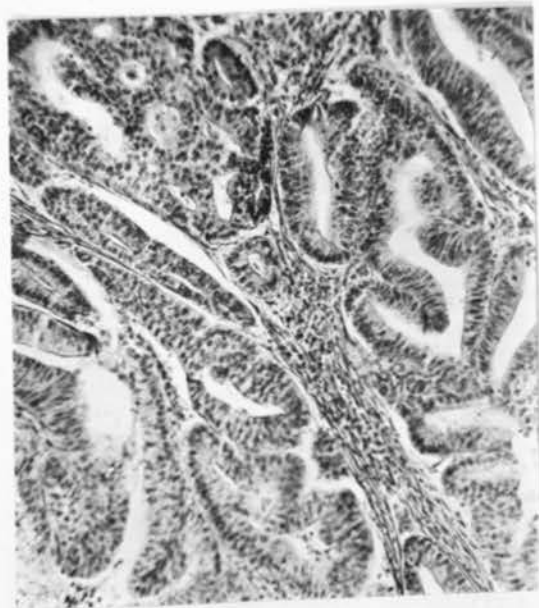


Figure 9. (59495). Area of an adeno-carcinoma showing secondary cellular differentiation.

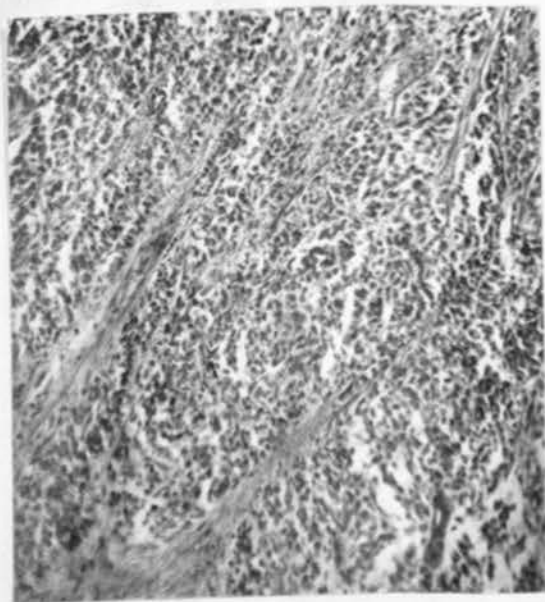


Figure 10. (41057). Area of an adeno-carcinoma showing primary cellular differentiation.

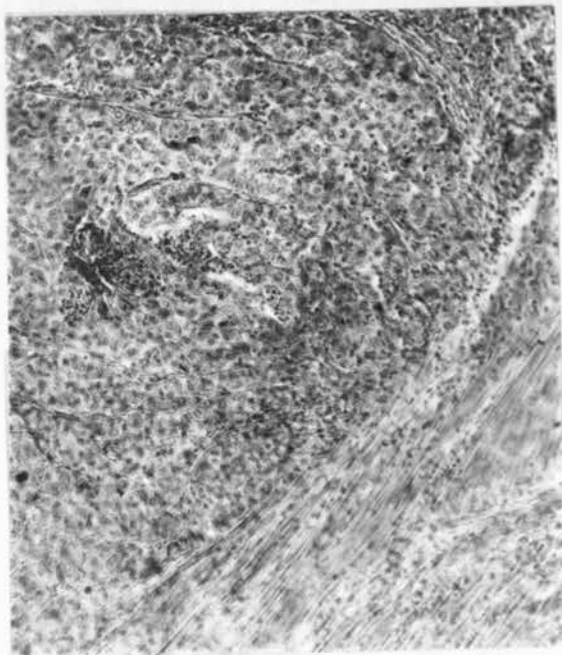


Figure 11. (124544). Photomicrograph showing primary cellular differentiation predominating.

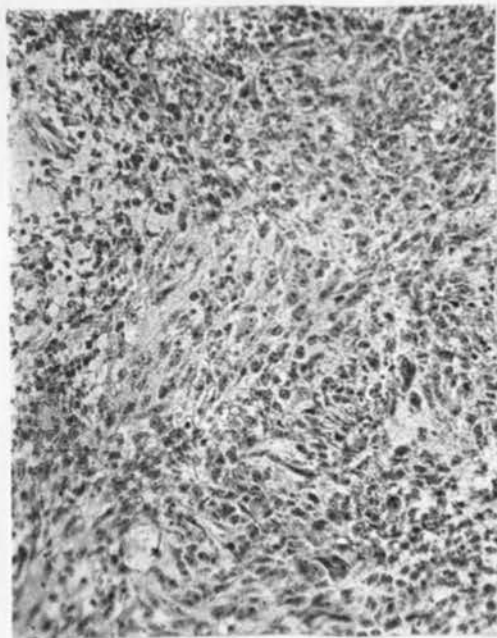


Figure 12. (145653). Photomicrograph of adeno-carcinoma, Fig. 6, showing an area in which there is no cellular differentiation.

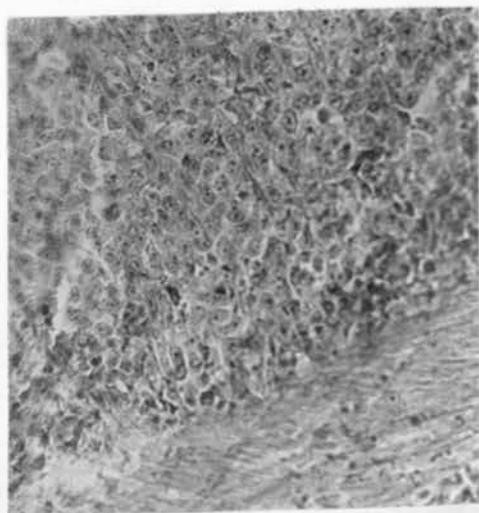


Figure 13. (190227). Photomicrograph of an adeno-carcinoma, Grade IV.

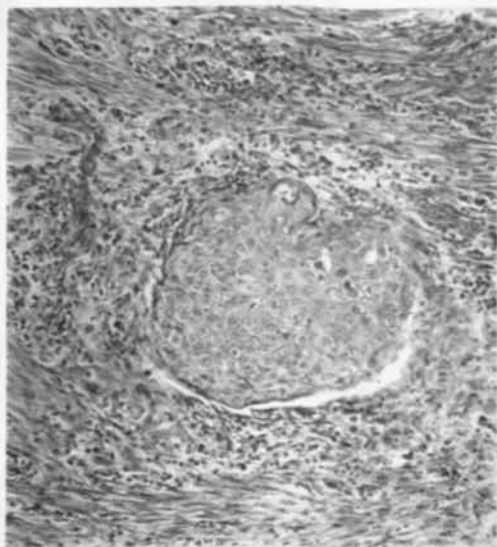


Figure 14. (248037). Photomicrograph showing lymph sinus filled with carcinoma undergoing metaplasia.



Figure 15. (274979). Photomicrograph of an adenocarcinoma whose cells, having no differentiation, completely surround a normal uterine gland.