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Staff Meeting Bulletin
Hospitals of the » » »
University of Minnesota

**Adenocarcinoma of the
Body of the Uterus**

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William A. O'Brien, M.D.

I. LAST WEEK

Date: January 8, 1943
Place: Recreation Room - Powell Hall
Time: 12:15 - 1:15 p.m.
Program: "Plasma and Serum Transfusion Reactions
Milton Levine and David State
Read by William A. O'Brien.

Discussion
Paul Dwan
Ralph Ellis
Rudolph Koucky - St. Mary's
Hospital, Minneapolis
O. H. Wangenstein
C. J. Watson

Attendance: 123

Gertrude Gunn,
Record Librarian

II. MEETINGS1. ST. PAUL SURGICAL SOCIETY

Thursday, January 14, 1943,
7:30 p.m. at the University Club of St.
Paul, Lounge Room.

(1) Chronic diseases of chest amenable
to surgery: with case reports.
D. Greth Gardiner

(2) Principles of treatment of chest
injuries.

T. J. Kinsella

Charles E. Rea, Secretary

2. PHYSIOLOGY-PHARMACOLOGY SEMINAR

Tuesday, January 19 at 12:30 p.m.
in 214 Millard Hall.

Acclimatization to desert conditions.
Austin F. Henschel.

3. BACTERIOLOGY SEMINAR

Thursday, January 21, 1943
at 4:30 p.m., 214 Millard Hall.

Physical properties of the microbial
cell.

Henry Tsuchiya

4. ANATOMY SEMINAR

Saturday, January 16, 1943
at 11:30 a.m., in room 226, Institute
of Anatomy.

Manchu anatomy of the 17th century.

S. P. Miller.

5. MINNESOTA PATHOLOGICAL SOCIETY

The University of Minnesota
Medical School
Institute of Anatomy

Tuesday, January 19, 1943,
8:00 p.m.

Female pseudohermaphroditism and
adrenocortical insufficiency with
bilateral adrenal hyperplasia.

W. H. Thompson
T. E. Bratrud

Pulmonary diseases with hyperplasia
of the alveolar epithelium.

E. T. Bell

III. ADENOCARCINOMA OF THE BODY OF THE UTERUS

J. L. McKelvey
C. E. McLennan

Adenocarcinoma of the body of the uterus is a disease which is comparatively amenable to study and treatment. It usually develops slowly, tends to be localized and to an exophytic type of growth and can be treated by a type of surgical attack which does not carry too great operative mortality. Diagnosis and treatment can be nicely controlled since tissue is readily available. There is good reason to believe that the possibilities of improvement of results have not been exhausted.

On the other hand, the condition has certain inherent disadvantages. Symptomatology of the early disease is of a minor nature which interferes with the finding of early cases. It occurs in a relatively advanced age group and carries the surgical dangers and constitutional disturbances inherent in these circumstances. The frequency of its occurrence in the excessively fat individual with degenerative cardiovascular lesions and liver pathology adds nothing to the pleasure of working with it. While accurate histological controls are available, it is not possible to assess the position and degree of local extension or the presence or absence of iliac or aortic gland extension unless and until surgery is undertaken. The degree of radiosensitivity of the tumor under various conditions is still not accurately known.

The object of this paper is to examine the evidence which bears upon some of these problems and to critically evaluate the results which have been obtained.

Adenocarcinoma of the body of the uterus is by definition a carcinoma arising from the columnar epithelium of the endometrium of the uterine cavity above the level of the internal cervical os. It is thus of Müllerian origin but is to be sharply distinguished from the adenocarcinoma of the cervix of similar origin

and the occasional squamous cell tumor of the uterine cavity which may be of urogenital sinus origin. In a series of 23,000 carcinomas of the uterus, adenocarcinoma of the body was found to make up 6.3%.

It is important to bear in mind the origin of the tumor from Müllerian epithelium since there is good evidence to believe that the tissue of origin of tumors plays a large role in the natural history and response to therapy of tumors. It is certainly of vastly greater significance than the changing histological characteristics of the tumor cell. There is no similarity between this tumor and the more frequently occurring squamous cell carcinoma of the cervix which is derived from urogenital sinus epithelium.

The tumor occurs at all ages from the second decade of life but the vast majority occur between the ages of 40 and 70. As many occur in the sixth decade of life as in all others together (Hinselman, 199 of 375 cases). This presents an obvious clinical problem.

The literature contains numerous attempts to evaluate possible etiological factors which might play a role in the development of adenocarcinoma of the body of the uterus. Certain of these are worth discussing.

Pregnancy has long been suspected of playing some role in both squamous cell carcinoma of the cervix and adenocarcinoma of the body of the uterus. Approximately 10% of females in the countries which supply accurate census data remain unmarried and a further 10% marry but do not reproduce. Twenty per cent of females then may be considered as nulliparas. About 25% of adenocarcinomas of the body of the uterus occur in nulliparous women (Hinselman, 134 of 318 cases; other authors report 25%, 20%, 24%, 21%, and 10%). In view of the fact that a very large proportion of adenocarcinomas of the body of the uterus occur after the age of 40 years, the chance is very great that those who are going to become pregnant have already done so. There is, however, no convinc-

ing evidence that the uterus which will develop adenocarcinoma tends to be sterile or that pregnancy tends to remove some etiological factor. Perhaps this would be more generally accepted were it not for the fact that only 5% of squamous cell carcinoma of the cervix occurs in the nullipara. This deviation in different directions from the expected incidence has kept interest alive.

A somewhat analogous situation is present with the uterine myoma. About 25% of adenocarcinomas of the body of the uterus occur in association with myomata. The expected incidence of myomata at some time during life is 20% for white women and 30% for black. There is only a tiny incidence of adenocarcinoma of the body of the uterus in the surgically treated myoma group. This would appear to be of no significance since many myomata require no treatment at all, since bleeding is a common indication for surgical treatment of the myoma and since adenocarcinoma bleeding will then load the treated myoma group with an unnatural incidence of adenocarcinoma. One can only say that there is no evidence that the myoma plays a significant role in the etiology of adenocarcinoma of the body of the uterus.

The literature dealing with the question of the etiological role of endometrial hyperplasia must be interpreted with caution. It is clear that the two conditions may be expected to occasionally co-exist since endometrial hyperplasia is of frequent occurrence. Undoubted examples of this are recognized. On the other hand the histological details of hyperplasia are often not as accurately interpreted as they might be. Tissue at the margin of an active carcinoma commonly shows evidence of proliferation. The endometrium at the margin and even over a large part of the endometrium often shows hyperplastic changes which on occasion have been interpreted as endometrial hyperplasia when in reality they are a characteristic early form of diffuse carcinoma. Actually, it appears that adenocarcinoma of the body as well as squamous cell carcinoma of the cervix occur with less than the expected frequency in association with endometrial hyperplasia.

There is no evidence of an etiological relationship of this condition to inflammatory lesions. The proliferative effect of acute inflammation which occurs just before cell destruction has been mistakenly diagnosed as adenocarcinoma. The proliferative form of tuberculosis may also be confusing.

Endometrial polyps present a vexing problem and diverse evidence of an etiological role has been presented. By and large, polyps and all new tissue in the female generative tract does not become malignant. This applies as well to squamous cell carcinoma of the cervix although in this condition carcinoma commonly begins from the old epithelium at the margin of the erosion. Adenocarcinoma may be polypoid and may invade polyps but evidence is lacking to support the concept that the polyp gives rise to the carcinoma.

Most adenocarcinoma of the body of the uterus is diffuse and involves relatively large areas of the endometrium. At least for relatively long periods of time, the majority of these tumors involve only the endometrium and do not invade the musculature. The terms endophytic and exophytic have been applied to this tumor and are only correct in expressing a relationship to the uterine muscle. The tumor invades the surrounding stroma to produce labyrinthine forms and later produces solid masses of tumor so that it is not, strictly speaking, exophytic. It is characteristic of this tumor that invasion of the musculature occurs late. There is reason to believe that this is the result of mechanical factors. As do many other tumors, this one tends to grow along lines of least resistance. The uterine muscle is peculiarly resistant to invasion by endometrium and usually some trauma such as inflammation seems to be necessary before invasion can occur. The same resistance seems to be presented to the carcinoma. It spreads superficially and polypoid forms may be produced. Indeed, the tumor may involve only the functionalis or may be even more superficial to produce what Ruge described as the Zuckerguss or cake-icing form of surface extension. The adenocarcinoma of the

cervix also derived from Müllerian epithelium characteristically does the reverse and invades. This appears to be due to the fact that the cervical glands lie in the depth of the musculature and simple surface extension is interfered with. In adenocarcinoma of the body of the uterus, the lack of resistance in the endometrial stroma and the uterine cavity, together with the resistance of the musculature to invasion all seem to determine the peculiarly fortunate type of extension of the tumor.

The upper part of the uterine cavity is the site of pre-dilection and spread occurs from here. For some unknown reason, the tumor tends to remain in the cavity of the uterus and only seldom extends to the cervical canal and portio or to the tube lumen.

Invasion is usually local but may be diffuse. A recently obtained specimen showed the whole uterus to be replaced by tumor which was covered only by a few layers of muscle and the serosa. Direct spread may extend to involve broad ligaments, tubes, ovaries and diffusely throughout the pelvis. Under circumstances of extensive spread it may be clinically difficult to accurately determine the primary site as uterine, ovarian or tubal. Study of the operative specimen will almost always settle this point. The radiologist, however, may be faced with an impossible differential diagnosis when only curettage material is available.

The outstanding feature in regard to metastasis is that it tends to occur late. When it does occur, the part of the lymphatic system involved seems to be dependent in part at least upon the site of the tumor. Since this is usually in the fundus, the lymphatics which surround the uterine vessels are commonly involved. Most of the lymphatic drainage from the uterus follows the uterine vessels and it is surprising that parametrial involvement is as rare as it is. Occasionally, the tumor follows the round ligament to the inguinal glands. The strange feature of the metastasis is the surprising frequency of spread of an embolic character to the vagina. This is

of great clinical importance. These vaginal metastases are surprisingly radiosensitive and it is not unusual to find a complete and apparently permanent response to adequate radiation therapy here, irrespective of the course of the disease elsewhere.

All forms of metastases tend to occur relatively late in the course of the disease although there are exceptions to this rule. One patient has been curetted and an unquestioned diagnosis made. No treatment was accepted and thirteen years later, the tumor was treated surgically without the production of evidence of spread beyond the uterus. This fact is of importance in at least two directions. Poor operative or radiological risks may be treated palliatively with local radium with a fair prognosis as to time of survival. It is also of significance as pointing to caution in concluding that cures have been produced by some non-surgical procedure, even after long observation and the absence of symptoms.

This tendency to localization and late metastasis and the simplicity of the surgical attack have made treatment highly satisfactory when this is compared to the results of treatment of many other types of malignant disease. It is only in recent years that active study has been given to the possibility of making further essential improvement.

The problems of histological diagnosis in this condition will not be considered in detail. Reference is made to the volume on the uterus by Dr. Robert Meyer in the Henke-Lubarsch Handbook. But here, as in all other malignancies, early and accurate diagnosis is of decisive importance. The symptomatology of early brownish watery vaginal discharge, followed by blood spotting with later frank vaginal bleeding, is common to a number of other gynecological conditions, particularly in this age group. Pain is absent so that the patient is apt to present herself late. Myomas with bleeding are much more common than adenocarcinoma of the body of the uterus. Where these require treatment, subtotal hysterectomy is the usual choice. When adenocarcinoma of the body of the uterus is also present,

this type of surgical attack may be disastrous. For this reason this department has set down the clinic rule that all bleeding uteri must be subjected to curettage and a histological diagnosis obtained before surgery is undertaken. All curettages where ever the possibility of malignancy is present are now done in such a way as to yield separate specimens from portio, cervical canal and fundus. This satisfies a number of requirements but among others, it allows the accurate recognition of the anatomical source and the extent of an adenocarcinoma. It cannot be too much stressed that it is impossible to make an accurate diagnosis from gross material and that all curettings must be subjected to histological investigation. The further clinic rule that all surgical specimens must be opened and carefully examined as soon as they are removed will allow avoidance of occasional diagnostic error.

Under some circumstances, repetition of the curettage after an interval of a few weeks may yield reassuring confirmation of a technically difficult diagnosis. This may be desirable where an original curettage has yielded little or no tissue, where very active hyperplasia is present or where an overwhelming inflammatory process obscures the basic tissue and cellular changes. In one such patient in our series, a diagnosis of the body was made elsewhere but was changed to acute endometritis here on the original slides. Curettage then weeks later hielded an unquestioned diagnosis of endometrial hyperplasia and so confirmed the diagnosis of the benign lesion.

The problem of therapy is still somewhat confused. The standard handling of adenocarcinoma of the body of the uterus is still pan-hysterectomy and bilateral salpingo-oophorectomy for operable cases and x-ray and local radium irradiation for inoperable tumors and for patients who present a too serious surgical risk. It is quite possible that this will change in the future with a demonstration of better results by other methods. Pre-operative radiation, postoperative radiation and radiation alone are at present

being tested in various clinics. To this, Heyman of the Stockholm Radiumhemmet adds and recommends a fifth possibility which is radiation to be followed by surgical interference when and if failure of the radiation is demonstrated.

A decision will ultimately be made as to the most effective type of treatment on the basis of results. The same difficulties arise in reaching this decision as have arisen in many of the standard "surgery vs. radiation" arguments. No two clinics have necessarily comparable material. Years of observation are required to accurately assess results. In this case, the standard surgical attack has long been in use while the radiation techniques are comparatively new. It is only recently that maximum x-ray dosages have been used and accurate control of these is too often startlingly deficient. The adequate distribution of radium irradiation within the uterine cavity is a recent acquisition. Histological controls of the effects of radiation therapy to this tumor are still not available in sufficient numbers to be conclusive. The radiologist has been subjected to an unnatural loading with advanced tumors and patients in advanced age and with complicating disease while the early tumors which are good surgical risks gravitate toward the gynecological surgeon. This selection may not appear in the reports of either since it is in large measure determined by the referring physician. Since hysterectomy on the good surgical risk is a simple operation, the large reporting clinics will tend to have referred to them an excessive proportion of advanced tumors while those with a good prognosis are handled at home. This seems to be true of the University Hospitals material.

There are several features which are inherent in the characteristics of this tumor itself and which have interfered with an easy decision as to type of treatment. A slowly growing tumor such as adenocarcinoma of the body of the uterus lends itself but poorly to an expression of results in terms of five year observation. Longer periods of elapsed time

postpone a decision to a point where expected mortalities from other diseases begin to seriously interfere with the significance of results.

It might be asked whether repeat curettage might not yield early information as to the effectiveness of preliminary radiation. It is true that this might be used with benefit perhaps more than it has by those who are using irradiation as a main method of treatment. This will not however supply a completely accurate answer. For four years in the department here and for a previous four years elsewhere, it has been the policy to remove these uteri surgically about four weeks after preliminary irradiation has been complete. In reasonably early tumors it is usual to find in the surgical specimen little or no tumor demonstrable histologically on the surface of the uterine cavity. In a considerable number, tumor which had already invaded the muscular wall has shown little or no effect from the irradiation and appeared to be actively growing. Whether all tumor in the muscularis escapes or not is not known but it is clear that much of it does. Since it lies beneath the surface of the muscularis, curettage will not demonstrate it, and since it has no connection with the surface, no symptomatology will be produced. It is then particularly dangerous tumor and may well have advanced to a hopeless stage before it gives evidence of its presence. Post irradiation curettage will not then give a final answer to the question as to effectiveness of the irradiation or its lack.

The department has focused its attention upon two phases of the problem. An attempt is being made to determine the effect of therapeutic doses of radiation energy upon this adenocarcinoma cell. An adequate series has been collected in which full doses of x-ray (2700 - 3000 tissue roentgens to the uterus over about four weeks) have been followed by full doses (4000 - 5500 mgm. hrs. over 100 hours) of radium adequately distributed to the cavity. These uteri were removed as treatment and for study approximately four weeks after completion of the irradiation. A second series is now being

collected in which full doses of adequately distributed radium irradiation is given and similar surgical removal is carried out. It is too early to report these in detail but certain conclusions appear to be justified. The tumor in the muscular wall frequently escapes radiation effect. The tumor in the uterine cavity is largely removed, bleeding stops and the cervix closes, all of which seems to decrease the danger of infection at operation. There is little to gain in the operable tumor from the use of prolonged and expensive divided dose x-ray irradiation and there are some dangers associated with it. At least one necrosis and rupture of the intestine followed its use. The work is far from complete but it appears that all of the desirable effects of irradiation in the operable case can be obtained by the quicker local radium irradiation. The exceptions to this are the tumor which protrudes past the internal os and the tumor which is infected with the beta-hemolytic streptococcus. These respond more safely to the slower x-ray irradiation. It is necessary to get rid of such infected tumor before surgical removal can be safely carried out.

The second problem which is being studied is the effectiveness of the preliminary irradiation upon the primary operative mortality. Radiation promises to prove of considerable value in accomplishing this end. What information is available in this regard will be presented later in this paper.

Much the best studies as to the effectiveness of radiation therapy alone in the treatment of adenocarcinoma of the body of the uterus have come from the Radiumhemmet and the results have recently been summarized by J. Heyman (*Acta Radiologica*, Vol. 22, Fasc. 1-2, 2:3 P. 14, 1941). His present technique has gradually evolved from previous experiences and has been in use since 1934. The uterine cavity is packed with from 10 to 20 radium containers of three sizes so that a constant dosage can be applied to large, medium and small cavities. 1500 mgm. hrs. of radium irradiation is given twice with an interval of three weeks between applications. Vaginal

irradiation in a long vaginal tube to irradiate the whole vagina is always added at one of these treatments. Depending on the size of the vagina, 2250, 1125 or 900 mgm. hrs. of radium irradiation is used. The purpose of this is to catch the early vaginal metastases. X-ray or teleradium is added "in some special cases" as when there are metastases to the groin, when the uterus is fixed or when there is demonstrable pelvic spread.

Heyman's influence on Swedish medical thinking is graphically demonstrated by the change in the type of material presented to him for treatment. Over the years more and more of these tumors appearing at the Radiumhemmet for radiation therapy are operable. Under his influence, fewer cases are being operated and were radiated.

Radiumhemmet Adenocarcinoma
of the Body of the Uterus

Percentage of clinically and
technically operable cases

1914 - 1918	- - - - -	44.4%
1919 - 1923	- - - - -	73.3%
1924 - 1928	- - - - -	82.4%
1929 - 1933	- - - - -	87.6%
1934 - 1938	- - - - -	92.4%

It is difficult to arrive at a real evaluation of Heyman's radiation results. At least some patients who show recurrence of the tumor after radiation are subjected to subsequent operation. If these be included, the result is that of combined treatment and if they be excluded, an indefinite number of certain failures are selectively removed from the group.

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Radiumhemmet Adenocarcinoma
of the Body of the Uterus

Results of radiation therapy,
1914 - 1934

5 year cures

	<u>Operable</u>	<u>Technically operable</u>	<u>Inoperable</u>
Including those operated after failure of radiation	61.5%	41%	22.6%
Excluding those operated after failure of radiation	53.1%	33.5%	19.4%

- - -

These results compare favorably with the results of surgical therapy but are not exactly comparable for the reasons listed above. The most startling results are in the inoperable group and these results persisted to ten years (22.6% to 17.6% and 19.4% to 14.7%). This is a much higher salvage rate than might have been expected from this group.

In 1935, the presently used type of intrauterine radium distribution was begun. A total of 60.9% five year cures is reported for that year's group. This presumably includes those who were sur-

gically treated after failure of radiation therapy. The group is too small to be decisive and it must be remembered that in 92.4% of the cases, the tumor was apparently limited to the uterus. This is a far more favorable material than that of other reporting clinics and the results must be considered in that light. Heyman estimates that this newer technique has in reality improved his own results in the operable cases by 25 to 30% and in the technically operable by 17%. The inoperable group is too small to be of significance.

His five year cure rate for all patients operated because of post radiation recurrence of the tumor is 46%, but it must be remembered that this represents a selected group.

He is not yet prepared to recommend routine replacement of surgical therapy by radiation although he undoubtedly hopes that it will eventually be possible to do this on a proven basis. He suggests that if the patient be a good surgical risk, either surgery or radiation may be chosen. If she is not an ideal surgical risk then radiation should be

given and the patient observed. Operable recurrences should be surgically treated.

This report has been presented in detail since it would seem to represent an important mile-stone in our thinking as to the handling of this tumor. It may well point the way to the future type of therapy.

Before presenting the results obtained in this clinic, the results reported from four large series and treated surgically are given for comparison.

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Adenocarcinoma of the Body of the Uterus

<u>Author</u>	<u>Number</u>	<u>Primary Mortality</u>	<u>Relative 5 year cures</u>
Pfleiderer	163	9.8%	51.5%
Stacy	333	5.4%	55.3%
V. Miculicz	133	17.2%	54.1%
Norris & Dunne	115	4.3%	47.8%

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Carcinoma of the Uterine Corpus

University Hospitals Results

In 15 years, 1928-1942 inclusive, 202 cases of carcinoma of the uterine corpus were seen. Of these, 96 were examined more than five years ago and are suitable for estimations of cure rates. These rates, as well as survival rates for the more recent cases, are shown in Table 1. This includes patients previously treated elsewhere as well as those receiving all of their therapy here.

In Table 2, the 96 patients treated more than five years ago are analyzed in detail. The relative cure rate for the entire group was 46%. It was only 43% for the 69 patients who had not been treated elsewhere. In the latter group, 79% of 19 patients treated with irradiation and total hysterectomy lived five or more years. Only 24% of 41 patients treated with irradiation alone lived more than five years. The remaining nine patients had various forms of therapy or none at all and three of these are living after having had hysterectomies for recurrent carcinoma following irradiation.

In the group of 27 patients receiving preliminary treatment elsewhere, 56% survived five years or more after admission here.

Table 3 shows the results to date in patients seen from 1938 through 1942. Of 106 such patients, 72 (67%) are alive 0 to 4 years after treatment. In the group of 85 patients having no previous treatment, 52 were given here what may be considered adequate therapy, and 85% of these are living 0 to 4 years later. Only 39% of the remaining 33 are alive now and several of these certainly will die from metastatic tumor in less than a year. It should be noted that 51% of the patients were not given our "routine therapy" (i.e., radium, or radium and x-ray, followed by panhysterectomy). However, 61% of them had acceptable and presumably adequate therapy, including total hysterectomy. The survival rate for the 21 patients treated elsewhere 1938 - 1942 is 71% at the moment (0 to 4 years).

Table 1

Results of Treatment in all Cases of Carcinoma Corpus Uteri 1928 - 1942

Living after -

Year	No. Cases	1 yr.	%	2 yr.	%	3 yr.	%	4 yrs.	%	5 yrs.	%	6 yrs.	%	7 yrs.	%	8 yrs.	%	9 yrs.	%	10 yrs.	%	11 yrs.	%	12 yrs.	%
1928	3	1	33.3	1		1		1		1	33.3	1		1		1		0		0		0		0	
1929	5	4	80.0	4		3		4		3	60.0	3		3		3		3		3		2		2	
1930	3	3	100.0	3		2		2		2	66.7	2		2		2		2		2		2		2	
1931	11	4	36.4	3		2		2		2	18.2	2		2		2		2		2		2		-	
1932	7	5	71.4	4		4		4		4	57.2	3		2		2		2		2		-		-	
1933	12	8	66.7	6		6		5		5	41.7	5		5		5		5		-		-		-	
1934	12	6	50.0	5		5		4		4	33.3	4		4		4		-		-		-		-	
1935	13	10	76.9	9		8		6		6	46.2	6		5		-		-		-		-		-	
1936	13	9	69.2	9		9		8		7	53.8	7		-		-		-		-		-		-	
1937	17	13	76.5	11		8		8		8	47.1	-		-		-		-		-		-		-	
Total	96	63	65.6	55	57.3	48	50.0	43	44.8	42	43.7														
1938	15	8	53.3	8		8		8		-															
1939	25	16	64.0	15		13		-		-															
1940	23	16	69.6	14		-		-		-															
1941	19	14	73.7	-		-		-		-															
1942	24	-																							

Table 2Carcinoma corpus uteri, 1928 - 1937, inclusive.

Total number of patients observed	96
Total number treated by us	92
Living and well 5 years after treatment here . .	42
5-year cure rate for entire group	
Absolute (on basis of total number of patients seen)	43.7%
Relative (on basis of total number of patients treated)	45.7%
* * * * *	
<u>Patients not treated elsewhere</u>	69
Given some form of treatment here	65
Living and well 5 years after treatment	28
Absolute cure rate	40.6%
Relative cure rate	43.1%

Varieties of therapy:

1. Radium, total hysterectomy, postoperative x-ray.	15
Living and well after 5 years	12
5-year cure rate	80.0%
2. Total hysterectomy and postoperative x-ray.	3
Living and well after 5 years	3
5-year cure rate	100.0%
3. Radium, hysterectomy - postoperative death.	1
4. Subtotal hysterectomy, radium and x-ray to cervical stump	1
Died from metastatic tumor within one year.	
5. Radium and x-ray initially; hysterectomy for local recurrences 1½ to 6 years after irradiation	4
Living and well 5 years after radiation (and 3 to 7 years after hysterectomy)	3
5-year cure rate (from date of radiation).	75.0%

6. Radium and x-ray	38
Living and well after 5 years	10
5-year cure rate	26.2%
7. X-ray only	3
Living and well after 5 years	0
8. No treatment	4
Living and well after 5 years	0

Reasons for using only radium and x-ray in 38 cases
(58% of those treated):

Actual or possible extension of tumor beyond uterine body	15
Old age (70 or more)	7
No apparent reason discernible	6
Diabetes mellitus	4
Pelvic inflammatory disease after curettage of radium	2
Corpus tumor mistaken for primary cervical tumor	2
Heart disease	1
Large carbuncle in groin	1

Patients treated to some extent elsewhere 1928-
1937

.	27
Given subsequent treatment here	27
Living and well 5 years <u>after treatment here</u> .	15
5-year cure rate	55.6%

Varieties of therapy elsewhere:

Total hysterectomy	11
Living and well 5 years after irradiation here	4
5-year cure rate	36.3%
Subtotal hysterectomy	7
Living and well 5 years after irradiation here	6
5-year cure rate	85.7%
Radium in uterine cavity	9
Living and well 5 years after irradiation or operation here	5
5-year cure rate	55.6%

Table 3

Carcinoma corpus uteri, 1938 - 1942, inclusive.

Total number of patients seen	106
Treated elsewhere to some extent	21
No treatment before coming here	85
Number subjected to "routine therapy"	42
(radium, or x-ray and radium, followed in 4-6 weeks by panhysterectomy)	
Number receiving other varieties of treatment	43
Radium only	12
Radium and x-ray	12
Total hysterectomy only	7
X-ray and total hysterectomy	2
X-ray only	2
Total hysterectomy followed by radium.	1
Incomplete course of x-ray	1
Exploratory laparotomy only	1
Subtotal hysterectomy and x-ray	1
Uterine fundectomy only	1
No treatment	3

* * * * *

Of 42 given "routine" treatment - 39 (93%) are living 0-4 years.
(2 of 3 deaths due to intercurrent disease)

Of 43 given incomplete therapy - 18 (42%) are living 0-4 years.
* * * * *

Of 52 given adequate therapy (hysterectomy with or
without some form of irradiation) -
44 (85%) are living 0-4 years.

Of 33 given irradiation or no therapy -
13 (39%) living 0-4 years.

Varieties of treatment elsewhere, 1938--1942:

Subtotal hysterectomy	10 - 7 living 0-4 years
Radium	6 - 3 "
Total hysterectomy	5 - 5 "

15 out of 21, or 71%, living 0-4 years.

Reasons for employing less than "routine" therapy, 1938-1942:

Obvious metastases when first seen	13
Heart disease, severe	5
Obesity and hypertension	4
Obesity and diabetes mellitus	2
Malignant disease elsewhere (other primary)	2
Death before hysterectomy (after x-ray)	2
Probable extension beyond uterus	1
Uterus perforated during attempt at radium insertion (hysterectomy done)	1
Uremia following irradiation	1
Operation refused	1
All therapy refused	1
Carcinoma not diagnosed by repeated curettage, hysterectomy finally done	1
Myomata uteri	2
Advanced psychoses	2
Unfavorable reaction to x-ray	1
Old age (over 75)	2
Pelvic inflammatory disease	1
No reason discernible in record	1
	<u>43</u>

(10 of these patients had total hysterectomy,
so inadequate therapy given only to 33).

Table 4

Operative mortality in adenocarcinoma corpus uteri

<u>Period</u>	<u>No. of patients operated</u>	<u>No. of post- op. deaths</u>	<u>Mortality rate, per cent</u>
1928 - 1942	84	6	7.1
1928 - 1937	22	1	4.5
1938 - 1942	62	5	8.1

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Summaries of postoperative deaths:

1. , age 63, adm. 7-16-34, died 7-22-34. Given 2400 mgh. radium in corpus 3-23-34. Did not return for hysterectomy until 7-16-34. Hypertensive heart disease, compensated, B.P. 180/105. Operation 7-19-34. On the first postoperative day she became irrational, the following day there was evidence of bronchopneumonia and peritonitis, with temperature up to 105, and she died at 11 A.M. on the third day. Autopsy revealed no evidence of either pneumonia or peritonitis. The heart showed coronary

sclerosis and there was questionable evidence of occlusion of the anterior descending branch of the left coronary artery.

2. , age 41, weight 190#, adm. 4-19-39 for deep x-ray and radium, discharged 6-6-39, readmitted 6-27-39 for hysterectomy, died 8-3-39. Panhysterectomy 6-30-39. Separation of the wound occurred 7-12-39, secondary closure was done. This recurred 7-20-39, at which time there was evidence of bronchopneumonia. She went gradually down hill despite oxygen,

- sulfonamides and blood transfusions. 5. . . . , age 67, weight 159#. Admitted 2-10-42, died 2-27-42. Hysterectomy 2-19-42 without preliminary radiation because of adnexal mass (found to be myoma). Death on the eighth day was tentatively attributed to septicemia, although there is no bacteriologic proof of this. Autopsy was not helpful in establishing the cause of death as examination was limited to the abdomen, which was normal.
3. . . . , age 68, weight 203#. Had received radium and x-ray in 1935 for adenocarcinoma corpus uteri. This therapy was repeated in 1937 when recurrent tumor was found. Admitted 8-9-39 for surgical treatment of recurrent carcinoma. Panhysterectomy on 8-25-39. She developed a pelvic abscess and died on the tenth day. Autopsy was done; this revealed, in addition to the pelvic infection, questionable evidence of pulmonary embolism.
4. . . . age 37, weight 288#. Admitted 11-14-39, with vaginal and vulvar metastases from adenocarcinoma corpus uteri. Laparotomy 11-28-39 showed extension to aortic glands. Only a right salpingo-oophorectomy was done. She expired on the third day with a temperature of 108°F. Autopsy failed to reveal any adequate explanation for the sudden exitus. Death appears to have been due to hepato-renal syndrome.
6. . . . , age 55. Admitted 10-18-42, died 11-10-42. She had pelvic carcinomatosis with vaginal metastases. Laparotomy was done 10-23 to remove as much tumor as possible prior to palliative x-ray. Uterine fundectomy was done along with bilateral salpingo-oophorectomy. Condition was poor postoperatively. On the thirteenth day she developed a right hemiplegia, went into coma, and died five days later. Autopsy was done, but the cerebral findings are not yet available.

Cases 3, 4, and 6 were virtually hopeless when surgery was undertaken. Had they not been operated upon, the immediate mortality from surgical treatment would have been:

3 deaths in 81 operations, or 3.7%.

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IV. GOSSIP

The room was crowded with fathers, mothers, and teachers in anticipation of the special town message on the school curriculum. The lady song leader had urged us on and on to bigger and louder efforts. The business of the last meeting was duly recorded in the books. The correspondence was read, the soloists had done their bit, and then the main speaker of the evening came on. One of the members of our professorial staff in education started out bravely to tell us of the differences between children in the sixth grade. He complimented us as parents and had praised our teaching staff. Apparently the effort was too much for him, for at this stage he fainted. Yours truly did a little first aid, correcting the attempts of those near at hand to put the luckless fellow in the opposite position. While our speaker was recovering we had more songs and more business. Then he told his story. It seems that children vary in every conceivable way from individual to individual and within themselves in their various traits and accomplishments. If you pass the good ones and retard the poor ones this makes the matter worse, so it is better to pass them all. Special teachers for each subject fail because it is more important to have an exact knowledge of the student than it is to have an exact knowledge of the subject. The ideal method would be to start the children in the first grade with one teacher and keep them together until they had completed the school program. I could hardly believe my ears for this sounds like our one-room ungraded school in the country. Grades we learned were introduced into our schools by visitors who went abroad in the early school days of Illinois-Indiana, and Michigan...On the train to Fargo to give speeches. The road is rough and the frozen swamp lands throw the passengers up and down in their berths. Large blocks of ice fall from the train and are struck by the on-coming wheels. This sounds as if three children had fallen out of bed at the same time and fathers anxiously spring to attention until they realize that they are far from home and loved ones. There are plenty of blankets and few curves. North of Brainerd the

combination is to throw individuals up and down and to both sides at the same time. We park in a desolate part of the yards. I wonder why trainmen seem so anxious to get rid of their passengers at the appointed time. If the car is to be in all day why not let those who care to do so sleep longer. To my meetings and I heard of a splendid personnel scheme engineered by Sister St. Thomas of St. John's Hospital. She needed help here and there for various jobs. Remembering the days of large families when boys were given certain jobs to do she hired a group from the high school. The first day they were assigned sissy jobs, washing dishes, dusting, sweeping, etc. They were paid at the end of the day in order to show them that there was an immediate return for their labor. She fixed their salaries at \$5.00 a week. The pay is as follows: Monday, \$.50, Tuesday, \$.50, Wednesday, free, Thursday, \$.50, Friday, \$.50, Saturday, \$1.50 and Sunday, \$1.50. No overtime pay can be collected without a regular week's performance. The boys are doing a fine job and have already earned a place for themselves in the organization. The extra pay over the week-end seriously interferes with recreation but there will be better times ahead. Saw Obstetrician-and-Gynecologist Hanna who delivered the quads, Internist John Bond, who remembers his days at Minnesota with great pleasure, Radiologist and part-time Pathologist, Nash, of our hospital, and many others at the splendid medical center...Another one leaves for New Orleans--Allan Hill this time to add to the growing number of Minnesotans in pediatrics at Tulane and L.S.U. (Ralph V. Platou, Chester A. Stewart, and Wallace Sako). Bjarne Pearson, formerly connected with our hospital department of pathology is now in the pathologic department at Tulane (was connected with L.S.U.). Bert Dippel and his fine family accompanied by Emil G. Holmstrom leave today for Salt Lake City to open the new department of obstetrics and gynecology in the medical school there. We are glad to see them get this opportunity but it is difficult to give them up. Both have played an active part in our group and leave a host of friends here. We know they will be successful in their new spot, representing as they do, the first branch of the old oak tree. Good luck and best wishes.....