Carcinoma of the corpus uteri

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CARCINOMA OF THE CORPUS UTERI

SENIOR THESIS

By

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UNIVERSITY OF NEBRASKA

COLLEGE OF MEDICINE

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INTRODUCTION

The uterus is a muscular organ situated in the female pelvis; normally, anteflexed, antverted, anteposition, in the midline, and the tip of the cervix at the level of the ischial spines. The uterus is an organ of menstruation, in pregnancy acts as reception, retention and nutrition to the fertilized ovum, and at full term pregnancy is the main expelling force in the expulsion of the fetus. No organ probably undergoes as many changes throughout the life of the individual as that of the uterus.

The uterus is still probably the most frequent seat of disease of women. According to recent writers about twenty percent of the uterine cancers affect the corpus. Most of the early literature treats carcinoma of the cervix and the body of the uterus together. Carcinoma of the corpus uteri differs so widely from carcinoma of the cervix, especially in regard to diagnosis, prognosis and treatment, that these differences deserve particular emphasis. Although carcinoma of the corpus is less frequent than carcinoma of the cervix, it gives a better prognosis, gives symptoms early, does not tend to invade the underlying structures until the symptoms are well established, and does not give rise to metastasis, as a rule, until late in its course. It is for these reasons, that I wish to treat carcinoma of the corpus uteri as a separate clinical entity.
HISTORICAL

Hippocrates and other writers of his time were quite familiar with cancer of superficial organs. They introduced the terms karkinos and karkinosa, carcinos apparently signifying a non-healing ulcer. It thus appears that Hippocrates (B.C. 460-375) was responsible for the use of the term carcinoma as applied to malignant tumors showing progressive growth. Nevertheless the condition now spoken of as cancer was well-known and treated by excision and by caustic ointments a thousand years before the time of Hippocrates (20). In the diseases of women scirrhoue induration of the cervix of the uterus is mentioned, and lumps are described in the breast. The phymata of the ancients, mentioned as far back as Archilochus (719-633 B.C.), apparently included abscesses and tubercles as well as what we now consider true tumors (71).

Cancer is mentioned in the Papyrus Ebers (B.C. 1500) and in the oldest remnants of the literature of India and Persia (12). The Papyrus Ebers contain short sections on malignant and other tumors, from which it may be inferred that the cardinal features of these maladies were then well recognized.

Aetuis of Amida in Mesopotamia (B.C. 502-575) was physician to the Emperor Justinian (71). His work is largely compiled from writings of Rufus of Ephesus, Leonides of Alexandria, Soranus and Archigens. He gave an excellent description of carcinoma of the uterus, distinguishing ulcerated from non-ulcerated forms.

Archigens of Opameia, a great surgeon, who is usually considered a representative of the pneumatic school, seems to have known a good deal about cancer of the breast and uterus. Paul of Aegina (B.C. 625-690)
stated that cancer occurred in every part of the body, for it takes place in the eyes and the uterus (12).

The work of Quigley (56) states that the Ancients spoke of cancer as the "Stinking Death". The term is descriptive and it contains elements of truth, especially in the advanced stages, and as far as the Ancients were concerned, it practically always meant death.

Ewing (12) states that in the Byzantine Period (470-1500) considerable progress was made in the description of various tumors. Paulus of Aegina (625-690) separated chronic metritis from uterine tumors. During the Twelfth to the Fifteenth Centuries, the Church forbade the dissection of the human body. It was about this time that the Church also dictated what books should be used in the colleges, such as the Universities at Paris (1110), Salerno (1150), Montpellier (1150), and Prag (1348). The study of all medical branches was held back even retrograded.

The Renaissance (1500-1700) bringing the discovery of the printing press and the circulation of blood, (Harvey 1628), Malpighi, Leawenhock, and others greatly facilitated the spread of knowledge and aided the diagnosis and treatment of cancer. It was due to these discoveries that the humoral theory (71) of cancer was overturned and the blood was regarded as the true source of the disease. Andreas Vesal (1514-1564) began the attack on many of the concepts of Galen, identifying deep seated cancer with ulceration. Fabricius (1537-1619) warned against incomplete removal of cancer, he extirpated the uterus and experimented with internal remedies. Paracelsus (1413-1541) was really the first opponent to Galen's theory of atra bilis as the cause of cancer. This led to the demoralization in the treatment of cancer,
and even permitted the faith cure career of Queen Elizabeth (1602). Olen's (1652) discovery of the lymph vessels and Malpighi's (1661) discovery of the red blood cells also aided in the demolishing of Galen's doctrine. LeDran (1685-1770) conceived that if a drop of cancer lymph passed the adjacent lymph nodes it contaminated the entire system. This led to the lymph theory as the causation of cancer.

Quoted from Quigley (56), Morgagni was contemporaneous with LeDran, and in his work on cancer - probably through his study of pathological specimens and autopsies - he distinguished between syphilitic gumma, tubercular swellings, inflammatory exostosis, fatty tumors, and cancer. He did not agree with LeDran on the so-called lymph theory. Peyrlilhe (1735-1804) submitted an article on cancer to the Academy of Lyons, giving the first systematic investigation of the whole subject, and dealt with the cancer toxin, the nature of the disease, the manner of growth and the treatment. His conception of the toxin coming from the degeneration of the primary mass and causing cachexia, is the same as that of today.

In 1802, The Society for Investigating the Nature and Cause of Cancer was formed in London, and formulated the problems of the disease as they stand today. The Society was dissolved in 1806 (12).

Since the construction of the achromatic microscope in 1824 in Paris, the recognition and study of the cellular structure of the malignant tumors has been possible (20). From this time on many theories on the causation of carcinoma have been brought out. During the second half of the Nineteenth Century the efforts of the clinicians and research workers in the medical science were devoted largely to problems of etiology and diagnosis, while in the Twentieth Century
this knowledge is being turned into weapons for the treatment and prevention of disease, hence we are living in a Medical Era of prophylaxes and therapeutics (20).
ETIOLOGY

INCIDENCE

Findley (15) states that one woman in eight, thirty-five years of age and over, dies of cancer, and that approximately one-third of all cancers in women are located primarily in the uterus. Hoffman, as chairman of the committee on cancer statistics, reports 80,000 deaths annually from cancer, and estimates that the annual increase is two and one-half percent. In a population of 100,000,000 this means 2500 additional deaths annually from cancer, even with the improved methods in diagnosis and treatment.

The work of Ewing (12) states that Welch collected (from the literature) over 31,000 cases of cancer of which twenty-nine and one-half percent involved the uterus. The British statistics of Williams (71) gave thirty-eight percent in 1868, thirty-one and one-half percent in 1888, and twenty-two and one-half percent in 1900. This showed a drop of the incidence of cancer of the uterus to other organs from 1868 to 1900.

I will try to show the frequency of carcinoma of the body of the uterus as compared with that of the cervix uteri. The known frequency of carcinoma of the corpus has increased considerably during the last half century. Wilson (72) in 1904 reported only 5.6% of uterine cancer began in the corpus. Palmer (51) recites that Arnolt in 1870 and Schotz in 1876 found only two percent in 57 cases, and four percent in 80 cases respectively. Gebhard, in 1899, found six percent of the cancers were primary in the corpus. Buben (4) and Ewing (12) both reported that ten percent of all pelvic cancer originates in the corpus.
The reason for this low percentage of uterine cancer originating in the corpus during the past may be accounted for, in that the majority of cases were seen in advanced stages. In a later report by Wilson (72) the following table will show an increase:

**TABLE I**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Percentages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma of Body</td>
<td>205</td>
</tr>
<tr>
<td>Carcinoma of Cervix</td>
<td>506</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>711</strong></td>
</tr>
</tbody>
</table>

Mahle (38) reviewing 186 cases in 1923, found that carcinoma of the corpus occurs in 30 percent of all uterine cancer. Whereas Norris and Vogt (44) in 1924, reviewing 115 cases places the incidence at 25 percent. Palmer (51) in 1928, reported 26.65 percent of primary corporeal carcinoma.

Smith and Grinnell (63) found that the ratio of carcinoma of the corpus to carcinoma of the cervix at the Free Hospital for Women, in a period of 51 years was 1:4.41, while, the ratio in the private practice of the staff members over a period of 25 years was 1:1.11 or 108 cases of the cervix and 97 cases of the body. Other later authors report corresponding percentages of primary corporeal carcinoma. The increase in the frequency of carcinoma of the corpus with the last few years has been noted by various writers. The same factors which have played a part, at least, in the increase in cancer in general during the last decade may apply to the increase in the number of cases of carcinoma of the corpus uteri, namely: the increase in life expectancy, bringing a greater number to the cancer age; the increase in knowledge among the laity of early symptoms of carcinoma of the corpus; the more frequent examination of the pelvis and the more accurate diagnosis made by the family physician.
AGE

From the review of the literature, most writers agree that carcinoma occurs later in life than carcinoma of the cervix. Carcinoma of the corpus occurs usually after the menopause or thereabouts, most frequently during the fifth decade but may occur from the second to the eighth decade. The youngest case that I found reported was that of a girl eleven years old and the oldest was in the eighties. The case of the eleven year old girl was reported by Gilbert (18). He was able to find only five other authentic cases of carcinoma of the corpus in girls under fifteen years of age in the literature. I found several cases reported occurring in young women around the age of nineteen.

Beattie (2) in 1933, reported fifty cases treated at the St. Bartholomew's Hospital during the last ten years. He found that the average age at which cancer of the corpus gave rise to symptoms was 57 years. Table II shows the age incidence.

<table>
<thead>
<tr>
<th>DECADE</th>
<th>CASES</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 - 40</td>
<td>1</td>
<td>2%</td>
</tr>
<tr>
<td>50 - 60</td>
<td>26</td>
<td>52%</td>
</tr>
<tr>
<td>60 - 70</td>
<td>11</td>
<td>22%</td>
</tr>
<tr>
<td>70 - 80</td>
<td>5</td>
<td>10%</td>
</tr>
<tr>
<td>80 - 90</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>

Mahle (38) states that the average age was 55 years, the youngest was 21 years and the oldest 75 years. Smith and Grinnell (63) gave the average age as 54 years. Suben (4) states that, in nulliparae, cancer of the corpus is more common than cancer of the cervix; and that most of his patients with carcinoma of the corpus have passed the menopause.
Table III consists of 205 cases operated on at the London Hospital between 1909 and 1927 inclusive.

<table>
<thead>
<tr>
<th>DECADE</th>
<th>CASES</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-20</td>
<td>1</td>
<td>0.48</td>
</tr>
<tr>
<td>20-30</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>30-40</td>
<td>4</td>
<td>1.95</td>
</tr>
<tr>
<td>40-50</td>
<td>43</td>
<td>20.97</td>
</tr>
<tr>
<td>50-60</td>
<td>110</td>
<td>53.65</td>
</tr>
<tr>
<td>60-70</td>
<td>41</td>
<td>20.0</td>
</tr>
<tr>
<td>70-80</td>
<td>8</td>
<td>2.96</td>
</tr>
</tbody>
</table>

Table IV Palmer (51) shows the comparison of a few groups giving the earliest cases, the latest cases, and the decade with the highest incidence as follows.

<table>
<thead>
<tr>
<th>GROUPS</th>
<th>EARLY CASES</th>
<th>LATE CASES</th>
<th>DECADES</th>
<th>PERCENTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilson</td>
<td>47</td>
<td>76</td>
<td>50-60</td>
<td>64.2</td>
</tr>
<tr>
<td>Gilliat</td>
<td>39</td>
<td>69</td>
<td>60-70</td>
<td>57.1</td>
</tr>
<tr>
<td>Combined group</td>
<td></td>
<td></td>
<td>50-60</td>
<td>52.4</td>
</tr>
<tr>
<td>of 205 cases</td>
<td></td>
<td></td>
<td></td>
<td>64.5</td>
</tr>
</tbody>
</table>

The Table confirms the older view that carcinoma of the body most commonly occurs between 50 and 60 years (52.4%) and that the second period of greatest frequency is between 60 and 70 years (22.4%).

Gilbert (18) states that in recent study of cancer of the uterus by Lane-Claypon, the age incidence is recorded from five countries supplying the most reliable statistical data. One and two-
tenths percent of the total number of patients were under thirty years of age. The mean average age of all patients was fifty-three and three-tenths years. Stacy (64) reported three hundred and thirty-three cases at the Mayo Clinic, operated between 1907 to 1923. He found that ten and one-half percent of the patients were less than forty-five years of age, the youngest being nineteen years. He emphasized that carcinoma of the fundus of the uterus occurs in a fairly large number of women under fifty years of age; and that recent studies show a greater incidence in younger persons than was shown in earlier reports. Peterson (53) states that of his patients 73.2 percent were between fifty-five and sixty-five years of age. This series apparently shows the highest percentage of carcinoma of the fundus in this age incidence than any reviewed. The largest percentage was during the fifth decade. Cullen (10) and Wilson (71) both showed that fifty percent of carcinoma of the fundus occurred in the fifth decade.

RACE

I found very few statistics as to the incidence of carcinoma of the uterus in the different races. It apparently occurs in all races. Statistics from the Johns Hopkins Hospital confirm the opinion that carcinoma occurs more frequently in the colored race (35). Horwitz (27) collected some data from the Mayo Clinic showing the incidence of carcinoma of the uterus among the Jewish women. In his series, primary carcinoma of the uterus from 1920 to 1925 inclusive, 1,227 cases were among the Gentile women and only 10 cases among the Jewish women or 6 times as frequent in Gentile women as in the Jewish women. This list ratio is approximated in other countries.

THEORIES

As yet, the etiology of cancer is not known. This accounts
for the host of theories relating to this condition. Some are based on clinical observations, others on careful experimental work, and many are purely philosophical conjecture. At the present time the study of cancer has been carried on by chemical and biological investigation both of the neoplasm and of the general body metabolism of the host. Since the memorable discoveries of Pasteur, scientists have been divided into two quite different groups according to their conception of the origin of cancer: Some believe it to be due to intrinsic causes, hereditary or acquired, of cellular evolution; Others holding exogenous, living, specific agent to be responsible (59). I will briefly mention a few of the theories but it would be impossible, in a paper of this kind, to dwell on details.

The theory of Cohnheim (12) (35) is an old theory, that cancer develops by the proliferation in an atypical manner of embryonic inclusion of epithelial elements, which have remained dormant for a long period of time. This has not received any support from histological studies. The parasitic theory is the oldest hypothesis of the origin of cancer. It appealed to the Ancients and reached the height of its popularity as a scientific theory about 1895 (12). It has been advocated by a number of investigators who show that there are more points of similarity between cancer and infection than seems evident on casual reflection as the former runs a definite clinical course, becomes disseminated, and leads to constitutional disturbances, just as infection does. This theory, sometimes spoken of as the infectious theory has been strengthened by Peyton Rous work (59).

The Hereditary theory was emphasized highly in the past, but in recent years it has been minimized, since it has not been found in
a very large percent of cases. This may be due partly to poor history
taking and also to the lack of the American people to be able to trace
their family tree. It seems that in the last few years more stress is
being put on the taking of a good family history. Maude Slye in her
discussion of Rousey's paper (53) states that hereditability of resistance
to cancer is a very encouraging fact. It may be that instead of everyone
being susceptible, large numbers of people are wholly immune to cancer.

Rousey (53) describes the regard for the recent theories:

1. The recent Bacterial Theories

(a) Theory A. Cancer is caused by a living organism
exactly as are infectious diseases. A large number
of bacteria, parasites and fungi have been described
as the specific etiologic agent but the research in
this has not stood the test.

(b) Theory B. Cancer is due to the combined action
of a filtrable virus and a chemical agent. Gye
and Barnard developed an interesting hypothesis,
but made a mistake of generalizing too much in
regard to its significance. Up to the present
time both early and recent workers have failed to
prove the specificity of the organisms they have
isolated.

2. The Cellular Theories

(a) Theory A. Cancer is due to a specific principle,
elaborated by the cell itself. This theory was
greatly supported by Alexis Carrel's method of
tissue cultures in vitro and by the work done
on the biology of the cell.
(b) Theory B. Cancer is caused by an abnormality of the cellular glycolysis, supported by Warburg.

It seems, that the problem of the origin of cancer is bound up with the question of its contagious and hereditary transmission, the former would support the infectious theory, and the latter the cellular theory and perhaps an inherited disease.

PREDISPOSING CAUSES

In the uterine body, a section more or less secluded and relatively immune to trauma and irritation, the disease probably owes its origin to cell metaplasia and other factors related in some mysterious and inexplicable way to the menopause. Norris and Vogt (44) state that child birth plays little part in the etiology of carcinoma of the corpus uteri. Most workers seem to take the same stand. Quigley (56) says that it is a disease of single women rather than married women. It is much more common in women who have not born children than in child bearing women. Twenty-six percent of Norris's series were spinsters. Beattie (2) in his fifty cases, showed twenty-five were multipara and twenty-five were never pregnant.

Table V Beattie shows the least number of cases with the increasing number of pregnancies.

<table>
<thead>
<tr>
<th>Number of Pregnancies</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
</tr>
</tbody>
</table>
Table VI The Incidence of Carcinoma with Miscarriages.

<table>
<thead>
<tr>
<th>Number of Pregnancies</th>
<th>Number of Miscarriages</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

Although only fifty percent of the patients were nulliparae, it will be seen that the incidence of endometrial carcinoma was very low in women who had more than two pregnancies, and surprisingly high in those who had been pregnant one or two occasions. Hence, it can hardly be said that trauma plays any part as the causation of carcinoma of the fundus of the uterus. Likewise the occurrence of carcinoma of the body of the uterus with pregnancy is rare. Schumann (60) in 1927 reports one case after several pathologists examined the specimen. Usually neoplasm in the fundus acts much more as an inhibition of conception than does the cervical form. The histologic diagnosis of the nature of this tissue also presents great difficulty. Adenocarcinoma of the pregnant uterus may easily be mistaken for chorioepithelioma, especially the form discussed by Ewing as choriocarcinoma.

In the woman who has borne children the uterus has performed its physiological function, and if infection occurs drainage is likely to be good, as compared with the single woman whose uterus has never performed its physiological function, where the cervix is narrow and hard, therefore, drainage is not good. In the spinster, we have no trauma, no thermal irritation, none of the usual predisposing conditions leading to the development of cancer, except chronic, low grade
infection, and as a result of this, a small amount of acid discharge. It is understood that cancer always grows in the presence of acid. The interior of the healthy uterus is always alkaline.

Quigley states that in carcinoma of the body of the uterus we have a very insidious, very slow, very low-grade infection, gradually, in the course of years, changing the uterine reaction to acid, and eventually exciting the growth of new cells or cancer cells. Norris (43) states that acute endometritis is a common condition following abortion or labor, it rarely, however, becomes chronic, differing in this respect from the cervicitis, which engrafts itself upon the lacerated cervix. Lynch (35) states, that there is no definite knowledge concerning the part played by previous inflammation as predisposing causes for carcinoma of the uterine body. He says, that Cullens was not able to find that an endometritis antedated the growth in any of the sixteen reported cases with carcinoma. Genital tuberculosis has been observed in association with carcinoma of the corpus in many instances, as is shown by Coblents, yet as Cullen suggests, this relation may well have been accidental (35).

Findley (16) states that in endometritis the glands of the endometrium can pass from the normal to the so-called inflammatory stages and from the inflammatory stage to the malignant. The proliferation of these glands, their great increase in size and number, their close proximity one to another, their great irregularity in shape, and finally the proliferation of the epithelial lining of these glands, all speak for the transition of the benign to the malignant. Øwing (12) relates the local hyperemia, chronic endometritis and ulceration of the mucosa are frequent concomitants of myoma which favor the development
of carcinoma, which, localized or diffuse, present peculiar anatomical and clinical features which usually permit of their identification.

From what has been said about infection of the endometrium, one can hardly conclude that it is a direct predisposing factor of carcinoma, yet, it may be indirect as a causation for factors that are fore-runners of carcinoma and may be said to aid the development of carcinoma.

Taylor (68) speaks of the etiologic relationship of endometrial hyperplasia to carcinoma giving the following evidence: Morphologic similarity; Biologic similarity and transformation of hyperplasia into carcinoma, as indicated by change in the character of the tissue obtained in successive curettings in the same patient. Also the association of diffuse endometrial hyperplasia and carcinoma in the same uterus. There is a clinical relationship as well. In Patients of the menopause age and older the symptoms may be identical. It is thought by Gardner and Finola (17) and others that the hyperplasia of the endometrium may be due to the continued overstimulation of the anterior lobe of the pituitary gland. This was assumed because the growth and development of the endometrium is concluded largely by the anterior lobe of the pituitary body.

Norsworthy (47) thinks women of the working class that have large families are more prone to develop carcinoma of the cervix while those of the richer class with few children are more apt to develop carcinoma of the body of the uterus. It is a well established fact that carcinoma of the body of the uterus occurs oftener in nullipara and women of few children. After my outcall service I agree that the poor class of people have their quota of children.

It is generally conceded that myoma of the uterus occurs in
from ten to twelve percent of all white women more than thirty-five years of age. Stacy (64) assumes that uterine myoma and polypi, acting as chronic irritation, may be an etiologic factor. Thirty-seven and thirty-three one-hundredths percent of the cases in his series presented myoma. He also thinks that polypi of the fundus, like those of the rectum, are prone to become malignant in contradistinction to the polypi of the cervical mucosa which rarely undergo carcinomatous changes. In his series the carcinoma of the corpus was on a polypus in twenty-five cases. Macfarlane (37) speaks of carcinoma developing in a myomatous uterus after the xray menopause. She was able to find only twenty-nine such cases reported. The downgrowth of the epithelium of a uterine polypi into the glands is atypical enough to create the impression of a developing malignant growth. In carcinoma of the body of the uterus, Ewing (12) believes that myomata are the first causative factor, or an opinion apparently borne out by Mayo Clinics, reporting that of forty cases of corpus carcinoma there were ten associated with myomas. This clinic also states that the chronic irritation of the uterine tumors is a causative factor in a large percentage of cases. The frequent association of adenocarcinoma of the body of the uterus with fibroids has been emphasized by Lynch (35), and it is possible that the changes in the endometrium induced by the fibroids may occasionally be responsible for the malignant condition.

Burnam (5) and others think that sterility may play a part as a predisposing factor in corporeal carcinoma. Yet others think that anemia following the menopause is supposed to favor the formation of uterine carcinoma.
PATHOLOGY AND CLASSIFICATION

Carcinoma of the body of the uterus is, in the beginning, essentially a local process, growing rather slowly and tends to metastasize quite late in its course. Infiltration of the growth into the uterine muscles occurs early but remains localized for a long period of time. Carcinoma in this site, like all other neoplasms have been classified differently by different men. Lynch (35) grouped them from three different standpoints, according to the site of the original growth, according to histology and morphology.

1. The squamous cell carcinoma of the corpus.
   (a) Evert ing Type. (b) Inverting Type.

2. The glandular carcinoma of the corpus.
   (a) Evert ing Type. (b) Inverting Type.

The evert ing type gives rise to a papillar y, cauliflower-like mass. This type is more frequent and the common site of origin is the upper half of the endometrial cavity, often in one of the cornua, or it may spring from any part of the endometrium. Both types may be present in the same specimen. The inverting type may form a nodule mass of cancerous tissue, which tends to infiltrate the neighboring structures. This type is synonymous with contracting, infiltrating, nodular, ulcerating and parenchymatous (35).

Ewing (12) classifies carcinoma of the body of the uterus as circumscribed and diffuse, the latter in most cases being a late result of the former, but is occasionally seen as a primary type.

1. Malignant adenoma, as the most frequent type, presents greatly enlarged and elongated alveoli, giant reproductions of uterine
glands, lined by several compact layers of cuboidal and cylindrical cells. The cell bodies are usually paler than the normal lining cells, but the large hyperchromatic nuclei give a dark staining character to the gland linings. The stroma is greatly reduced and adjacent alveoli become contiguous, and may fuse.

2. Papillary adenocarcinoma usually exhibit a certain papillary tendency in their superficial portions. They arise from superficial cells and are usually diffuse and compact. It is this group in the early stage that show special interest because, while the curettings show carcinoma, the extirpated uterus retains no trace of the disease. It is probably attached to the endometrium by a narrow pedicle and is completely removed by the curet (16) (34) (33) (58).

3. Alveolar carcinoma is rare in the uterus. Extremely small, numerous and indistinct alveoli may form but it usually shows masses of cells forming alveoli and small cell groups infiltrating spaces and vessels.

4. Squamous cell may predominate the element in adenocarcinoma and produce a true adenoacanthoma.

The German histological differentiation of the carcinoma cells are: (23)

1. Reife corresponding to the adenoma malignum of Ewing.
2. Mittleruf or adenocarcinoma.
3. Unreif, corresponding to the alveolar or solid carcinoma.

For descriptive purpose, Beattie (2) gives the following classification:

1. Simple glandular adenocarcinoma, is made up of enlarged and elongated cells, which are like giant reproduction of the normal
endometrial glands, but they are very numerous and apparently exist at the expense of the stroma, which is correspondingly limited in amount. The cells stain more deeply than normal cells, the nuclei contain more chromatin and mitosis takes place more frequently than in the normal, yet very little evidence of irregular cell and nuclear division.

2. Compound adenocarcinoma.

(a) Glandular type have cells or glands in normal shape, lying in any direction in the stroma. Many of these glands contain red blood cells in their lumen with some epithelial debris, but little or no secretion. There is a large amount of mitotic activity. This variety is the most frequent of all.

(b) Papillary type is thought to develop from the surface of the endometrium, and is usually seen in the type of carcinoma of the body of the uterus, which fills the cavity of the body forming a proliferative mass which breaks down early and becomes necrotic. The histology is the same as that of the glandular type, but they are disposed in a pond-like manner, consisting of a delicate central core of connective tissue containing blood capillaries, and from which delicate processes, lined by carcinoma cells, branch out on all sides.

Mahle's (38) classification has been accepted by a number of writers, Healy (22), Stacy (65) and others. He classifies carcinoma of the body of the uterus into histological types according to the degree of differentiation of the carcinoma cells and therefore divides them into Grades 1, 2, 3, and 4.

Grade I. Papillary malignum is entirely papillary and may be superficial but as a rule does not tend to infiltrate the myometrium. It resembles adenomatoid endometritis and the cells show very little change from the normal.
Grade II. Adenoma malignum which is the largest group and the same as that described by Ewing. I may add that any tendency on the part of the cells to break through into the stroma and to form solid masses takes the tumor out of this group and places it in group three.

Grade III. Adenocarcinoma the next in frequency and the same as described by Beattie and Ewing. Histologically the cases in this group are characterized by greater malignancy, the cells are more atypical, there is more evidence of anaplasia than in the former groups. This tumor while still retaining its glandular arrangement, nevertheless infiltrates the stroma and forms solid masses of tumor cells. It is this evidence of infiltration that distinguishes it from grade two.

Grade IV. Cellular adenocarcinoma is characterized histologically by diffuse growth of small round and polyhedral cells often entirely lacking in glandular arrangements. The cells may be closely packed together, stroma scanty, mitotic figures numerous and marked evidence of anaplasia is seen.

Adenocanthoma is a rather infrequent but distinct histologic variety of corpus carcinoma presenting a combination of glandular and squamous structure (12) (2) (23). This tumor of the uterus may have many squamous cells and even present pearls; yet in many cases neither spine cells nor keratohyalin granules are demonstrable. In a true adenocanthoma the squamous cells must predominate over the glandular structure.

Squamous cell carcinoma of the uterine body is still debated by some. The rarity of this type is well shown by the fact that Cullen at the time of the publication of his book on carcinoma of the uterus was able to find but three authentic cases of this condition, and had himself never seen one (62). The squamous or keratoid changes may take place
in the epithelium of the body of the uterus, such changes occurring independently of a new growth. Leukoplakia uteri is a term often applied to this epidermization of the endometrium. It may occur after curettage, especially when the uterus has been treated with escharotics. It seems reasonable to assume that malignancy developing in such an endometrium would have the characteristics of an epithelioma. Grossly it may give an opaque, warty appearance and lead to infiltration of the mucosa (62) (31).

If the growth is large it usually has a dirty grey color or a pale yellow appearance. The surface is roughened with small lobulations and with papillary surface. The tumor mass may completely fill the uterine cavity or it may be real small attached to a small area of the endometrium, depending mostly on the stage of its development. Whether or not the carcinoma originates from the surface or glandular epithelium, it soon exhibits infiltrating characteristics, and in the later stages the surface becomes necrotic and ulcers develop. Until the late stages, the mass is usually well walled off by the uterine muscle. On section the neoplasm presents a grayish-white or pinkish appearance, and is smooth, homogeneous, semi-translucent, soft, friable, and vascular. Small areas, or even larger masses of degenerated carcinomatous tissue, are often present, these may be yellow, brown, white or black in color. The underlying musculature is usually thinned and it may or may not be invaded (43) (47). It is possible that an entirely distinct cancer of the body of the uterus may develop, precede, follow or co-exist with cancer of the cervix (28).

If the etiology of cancer should be discovered, naturally a definite classification will follow. For a working basis adenocarcinoma and malignum adenoma are of most importance and constitute the greater
percentage of carcinoma of the corpus uteri.

From a pathologist's point of view a classification of carcinoma of the corpus uteri must be a complicated one. In any individual specimen more than one type of growth may be present, so that the type which is preponderant must be found and then transitional varieties described. This is less important for the clinician.
COURSE AND METASTASIS

The corporeal carcinoma is a local process in the beginning, it is of a chronic nature, and runs a slow course, but fatal in the end unless definite steps are taken to dispose of this condition. The tumor extends slowly into the muscular coat, usually in an irregular fashion, and does not reach the peritoneal covering until late in the disease, and only after the entire uterine cavity has been replaced by cancerous tissue. It is invariably chronic and there is always present either induration or ulceration (35). From the nature of the initial symptoms of carcinoma it is obvious that the disease must exist for some time before it attracts attention, and the rate of progress varies considerably. The growth may extend down to, and through the internal os, in advanced stages, producing dilatation of the cervical canal with protrusion of a polyhedral portion of the growth at the level of the external os (23). In some of the far advanced cases, that are less malignant, the protruding portion may fill part of the vaginal vault, making it difficult to diagnose from carcinoma of the cervix. Late in the course of the disease the bladder, rectum and vagina may be involved in a solid carcinomatous mass (30).

Adenocarcinoma may be an extensive papillomatous mass involving practically the entire uterine cavity. The most frequent type encountered, however, is a more or less localized polypoid thickening of the lining mucosa. It may present itself as firm nodules beneath the serosa. In case the underlying musculature becomes too thin the tumor mass may extend through it into the peritoneum, this occurs rather infrequently (47). Judd (30) states that carcinoma of the
Corpus has a tendency to be confined to the endometrium and does not invade the muscular wall of the uterus or extend to the peritoneum for a considerable time. He explains this by the fact that the lesions are usually not of the active type as classified according to Mahle and Border's index of malignancy. Commonly they are of Grade I and II.

Carcinoma of the body of the uterus like all other carcinomas, may metastize by the blood stream, lymphatics, direct extension or implantation. Carcinoma is more prone to choice, the route by the way of the lymphatics in contrast to sarcoma which usually metastasizes through the blood stream. The reason for this is that carcinoma has a relative poor blood supply and arises from epithelium, while sarcoma arises from connective tissue and carries a rich blood supply. Carcinoma of the corpus grows relatively slow and the uterine musculature acts as a barrier. Hence, extension is a slow process. In spite of this the tubes, ovaries, or pelvic peritoneum may be involved relatively early by metastasis through the tubal lumina (63) by the blood stream or by the lymphatics (49). Smith and Grinnell (63) in a series of thirty-nine private cases gave the following report: four metastasis to the peritoneum and omentum; one to the spine, three to the tubes; one to the cervix; one to the vagina; one to the vulva; eight to the ovary and nine to the ovaries and tubes.

Of thirty three necropsies, by Williams (72) for cancer of the corpus uteri, metastasis were met with in fifteen, or in forty-eight percent: the seats of these lesions were - the liver fifteen percent, lungs fifteen percent, intestine twelve percent, spleen, pericardium, pleura, diaphragm, and ribs each three percent. The peritoneum was involved in twenty-seven of these cases.
The lymphatics are apparently the most frequent to be invaded by carcinoma cells from the carcinoma of the body of the uterus (48). The lymphatics of the corpus begin in the mucosa and leave the uterus in four or five trunks which pass beneath the tubes, then through the broad ligaments, anastomosing with the ovarian plexus and around the ovarian artery in the ovarian ligament, to end in the lumbar nodes above the bifurcation of the aorta. From the middle of the corpus, other vessels mingle with those from the cervix, reach the iliac nodes, and some pass along the round ligaments to the inguinal nodes (47) (65). Cullen (11) regularly found the lymph-nodes free. Uterine carcinoma as a whole, cannot be classed among the tumors which invade the lymph-nodes early. Most post-mortem observations suggest the tendency for the tumor to remain localized, either to the uterus, or this organ and its immediate vicinity, including the regional nodes and tissues actually destroyed by the tumor. Ewing (12) in his review of other writers, suggests that from fifty to seventy percent of autopsy cases showed the lymph-nodes free. The rapidity with which metastasis occurs is so variable that one may well wonder what constitutes an early case, for a small initial lesion may have already undergone metastasis, while a large and presumably less favorable one may not (49). Carcinoma metastasis of the tube is often found with that of the ovary. Bilateral distribution so common with ovarian carcinoma suggests a lymphatic source rather than one by implantation. The surface of the ovary is smooth and uninvolved with lymphatic metastasis but not so with direct implantation of carcinoma particles on the surface (49) (50).

Enlargement of the regional glands is very common in the early stage of carcinoma but this enlargement is, as a rule, not due
to carcinoma cells but to the inflammatory hypertrophy that nearly always takes place in the glands draining a region that is subject to severe chronic irritation (9).

By blood stream, some carcinoma cells penetrate into a blood vessel, are caught in the current and carried to distinct organs, where they lodge and grow and form metastatic tumors. There they reproduce the structure of the parent growth. The lungs (9) are most frequently affected, though there are many other organs that are affected occasionally. The brain is involved not as infrequently as was thought to be. Bony metastasis from carcinoma of the uterus are relatively infrequent. Tyler (69) reports a case of primary carcinoma of the corpus with general blood stream metastasis, to spleen, liver, skull, sixth left rib, seventh right rib and right ischium.

The occurrence of metastatic nodules in the vagina is not only an interesting pathology problem but is an important clinical factor. Strachan (67) in his series of thirty cases of corporeal carcinoma found vaginal metastasis in five or better than sixteen percent. Meigs (41) reports twelve percent of all cases of adenocarcinoma of the corpus uteri seen at Collis P. Huntington Memorial Hospital had vaginal metastasis. The route of this metastasis is disputed. Some favor that metastasis probably takes place through the lymphatics or possibly by venous channels (41) (67). Graves (19) claims that transplants are common even before the disease is greatly advanced, and in this respect the cancerous endometrium behaves exactly as does the normal mucosa in forming endometriomata. Metastasis may be superficial along the vaginal wall in these cases and are easily rubbed off, and a diagnosis of carcinoma of the corpus may be made from them. (41) (40)
Direct implantation of cancer cells into healthy tissue of a raw surface takes place principally in operations for cancer, the cells being carried on the knife or scissors or other instruments, or on the fingers or sponges, from the infiltrated area to the healthy tissue exposed in operative work. (19).

In all, carcinoma of the corpus uteri, with very rare exceptions tends to metastasize somewhat more slowly than that of the cervix (5). It is thought by Healy (21) that adenoma malignum is less malignant than adenocarcinoma.
SYMPTOMS

Since entering medical training we have had the importance of early diagnosis of cancer continually preached to us, hence this brings out the importance of early symptoms that bring the patient to the doctor. The early cardinal symptoms are well known as metrorrhagia and brownish, watery and at times irritating vaginal discharge, usually with an odor (3). The later stage of the disease present, anemia, cachexia, pain, and loss of weight, which usually indicate an inopenable and hopeless condition (44). Beattie (2) divides carcinoma of the corpus into three stages, early, medium and late: The early case is one in which the carcinoma is confined to the endometrium over a small area only; the medium case is one which the growth involves only a portion of the endometrium, with a moderate amount of infiltration of considerable degree into the myometrium, and the late case is one in which the carcinoma has filled the cavity of the uterus and has extended down to the level of the internal os, together with infiltration of considerable degree into the myometrium.

Bleeding: The characteristic hemorrhage of carcinoma of the corpus consists of a slight oozing or "spotting" of bright blood, which increases quite rapidly, and tends to follow trauma (44) (3).

Norsworthy (47) states that first there may be an increase or prolongation of the menstrual flow, second, spotting between periods (4), third, severe and alarming hemorrhage, fourth metrorrhagia and irregular bleeding which is more typical than active hemorrhage, especially if after the menopause. Stacy (64) found that 66.66 percent of the cases of carcinoma of the body of the uterus seen at his clinic presented
intermenstrual bleeding. Meigs (40) claims that carcinoma of the corpus before the menopause presents, first, an increase in amount of bleeding, later bleeding between periods and lastly a watery discharge, but carcinoma occurring after the menopause was reversed in that there was a watery discharge first and then bleeding.

It may be stressed that the character of the hemorrhage bears little or no relation to the underlying condition. In both malignant and benign cases, the bleeding may be slight or free in amount; it may have been of short duration or have lasted for weeks or months; it may or may not have been associated with passage of clots. Yet a fairly constant, moderate hemorrhage extending over many weeks is probably, though not necessarily, of malignant origin (14).

As the disease progresses the bleeding becomes more frequent and more prolonged (44).

Discharge: Early the discharge is small in amount, and is often overlooked until hemorrhage develops. This discharge is thin and irritating in nature, and with the advent of necrotic changes in the tumor it becomes malodorous (44). Lynch (35) doesn't believe that this odor is of any special significance, since it depends upon changes in the vagina. Usually the discharge at first is watery and does not attract the attention of the patient until there is a decided disturbance in the menstrual flow or bleeding following the menopause. Later it becomes serosanginous with a foul odor, and is irritating to the skin. Usually bleeding is present before this sort of discharge is present.

In a study of a series of cases, Norris (43)(44) shows that in 81% hemorrhage was a primary symptom, and in the remainder the dis-
charge preceded the bleeding. The patients usually come for consultation because of troublesome vaginal discharge, or because of some irregularity in the menstrual cycle, and that pain is not a feature of the complaint until later in the course of the disease (30).

Beattie (2) states that pain accompanied the first onset of irregular bleeding, but never preceded the latter symptom in 46% of his cases. Nineteen cases had pain in the hypogastrium, two cases had pain in the back and sacrum and one each in the leg and in the left side. In most cases the pain was dull and aching in character and continuous. This is incompatible with the writings and teachings of others in that carcinoma of the corpus uteri is a painless disease until the late stage has been reached.
DIAGNOSIS

It is in the early stage of the disease that the diagnosis is most difficult and it is in this stage that the diagnosis is most important, for efficient treatment in order to save the life of the patient (9). It is important, particularly to the general practitioner, who usually sees the patient first and upon whom rests the responsibility of recognizing malignant disease in its beginning or recognizing the cases in which it may be present and which require special investigation accordingly (8). The detection of early cancer in suspected cases is not a one-man job. It may require the cooperation of the patient, the general practitioner, the specialist and a confident pathologist (49) (3). It may, in some cases, be impossible even then.

The diagnosis is made with greater ease in those cases which develop carcinoma after the menopause has been established. Kanter (32) states that 68.4 percent of the patients in their series with postmenopausal bleeding had conditions of malignancy nature. Hence, all cases of postmenopausal bleeding should be considered as malignancies until proven otherwise. The symptoms of carcinoma of the fundus in the earliest stage are not characteristic, and a positive diagnosis at this time can be made only as the result of a histologic examination. Yet a number of writers (39) (58) (2) (24) believe that the diagnosis of carcinoma of the corpus is tentatively made from the history of metrorrhagia and spotting. Other clinical signs, such as increase in the size of the uterus, foul discharge, and large irregular cavity are uncertain, because small necrotic fibroids, placental rests or purely
hyperfunctional changes alone or in combination, may give quite similar symptoms.

In all suspected cases of carcinoma of the corpus it is well to use the following procedure: (6) (46).

(1) Make a careful pelvic examination. Remember that vigorous bimanual examination may result in slight bleeding if carcinoma is present in the fundus (70).

(2) Employ the Clark Test. The cervix should not be pierced by a tenaculum as this may leave a raw bleeding surface and the test will fail. This test is easily carried out in the office and it does not require any anesthetic or special equipment. This test consists in the passage of a sterile sound into the cavity of the uterus and the absence of bleeding following this goes a great way towards excluding carcinoma of the fundus. The only contraindication of this test would be in younger individuals in which pregnancy is suspected.

(3) The final and most dependable procedure is the curettage and subsequent examination by a skilled pathologist, of the material thus obtained. Most men agree that this procedure constitutes the most certain method of diagnosis, and the one that should be employed routinely in all early cases. There are still a few that consider the exploratory curettage as having the danger of perforation, infection and metastasis, yet think it is often indispensable (70) (34). Few women will object to the curettage, and, if carcinoma is found, they will be richly rewarded (48).

One should consider differential diagnosis before advising radical treatment (47). Myomata and diffuse adenomyoma both cause about the same symptoms as carcinoma except they usually cause painful menstruation.
Fibroids usually occur earlier and cause a slow progressive increase in the size of the uterus. Hyperplasia may occur any time during menstrual life, more common at puberty and at the menopause. They bleed frequently and the periods often overlap. This condition usually extends over a long period of time and may cause a severe secondary anemia. If this condition does not clear up after the usual treatment, it is probably carcinoma. Polypi produce the same symptoms as does carcinoma, but curettage and microscopic examination will differentiate the two.

It is important to impress upon the practitioner of scientific medicine, and indirectly upon the public, the fact that carcinoma is curable by the use of well-known and established methods of treatment if the diagnosis is made early (39) (8).
TREATMENT

The question of the treatment of carcinoma of the corpus uteri by irradiation or by surgery is passing through the same stages as has been noted in that of cancers of the uterine cervix. If Doctor Sharp's Cure for Cancer or Money Back Guarantee, published in the Boston Gazette 1720, had been a reality, the research for cancer cure would be quite unnecessary (61). The cancer problem will be solved only when the nature and etiology of the disease are discovered, and the research work that is being carried out with that end in view, gives us hope and encouragement that this most important problem will eventually be solved (2). Until the cause of cancer is known, the cure of this disease must depend on early recognition, and early and complete removal or destruction of the tumor while it is still a local process (64).

The operative treatment of uterine cancer has made slow, but on the whole, continuous progress since surgery was made safe by the work of Lister and Pasteur. One-half century ago surgical intervention was practically limited to cancer of the cervix, and the operation was done with the actual or galvanic cautery. In 1882 Pawlik reported 136 intravaginal amputations of the cervix with the galvanic current (72).

The earliest vaginal hysterectomy with detail procedure was reported by Ma渭air (38). This historic operation was performed by Blendell on February 19, 1828, in the presence of Bransby, Cooper, Astor, Key and John Morgan. The patient survived the operation and died one year later. The specimen is stored at the Royal College of Physicians. The time of the operation was one hour and fifteen minutes, and the anesthetic used was gin.
The vaginal hysterectomy was first performed on regular anatomical lines by Ezermy, and in the later Eighties began to displace the supravaginal amputation in England. The first important discussion on the subject took place at the Obstetrical Society in 1885, when Duncan introduced two tables of collected cases. One table showing 139 cases of abdominal hysterectomy with an immediate mortality of 72 percent. The other table represented 276 cases of vaginal hysterectomy with 28.6 percent immediate mortality. Schuchardt (1901) did the extended operation performed with the help of a vaginoperineal incision, by means of which the parametrium could be widely removed. He claimed a cure in 24 percent (72).

By the use of the extended vaginal operation, Schouta until 1911, obtained a five-year absolute curability of 16.6 percent on 211 operations. In this country this operation was used by Sinclair and after his death it has fallen entirely into disuse. Abdominal hysterectomy was once more attempted in 1895, and at this time Clark and Rumpf first dissected the ureters in order to remove as much of the parametrium as possible, and Reis proposed the removal of pelvic lymphatic glands. In 1898 Wertheim in Vienna began his operation, which is known by his name in all parts of the civilized world. This was an exceptionally radical operation with the extensive removal of the gland-bearing fascia. This leaves large surfaces of denuded peri- toneum, and is a potential cause of postoperative obstruction. Doctor Kelly added the introduction of bougies in the ureters to prevent the great danger of cutting or ligating the ureters in the part. He also removed a larger portion of the vagina (72).

Since the return of the abdominal hysterectomy in 1895, it is practically the routine method of today, but with modifications.
The Wertheim operation has been discarded by many (65) (41) (45) (54), and replaced by pan-hysterectomy and salpingo-oophorectomy without the dissection of the glands. The primary mortality of the Wertheim operation was from 8 - 42 percent even in skilled hands (55).

Percy (52), in 1917, advocated the continuous use of heat as a method of treatment for carcinoma of the body of the uterus. He says heat, not fire, will destroy cancer. Of course his great problem was the application of it.

Since the discovery of X-ray by Roentgen in 1896, and of Radium by Madame Curie in 1898, the treatment of cancer has progressed. The radium therapy, which is only emerging from its infancy, has already passed surgery in the frequency of its use. Irradiation was first used in the treatment of external and superficial cancerous conditions. The unique property on the part of radiation from radium gives us, following its use, exceedingly smooth, pliable, elastic scars, which are entirely different from scars following any other kind of treatment. The difference between the neoplastic cells and the normal cells in regard to the reaction of radium is so clear-cut and well defined that the tissues in the neighborhood are not sickened (56).

The present-day trend of thought is away from the old concept that cancer of the body of the uterus is not susceptible to radiation therapy and that operative removal is the only acceptable treatment. There is a continuous increase in the number of Gynecologists, who use radiation therapy for corporeal carcinoma. Early writers are especially pessimistic (10) (40) (7). Many encouraging reports have appeared by careful workers (1) (3) (13) (25) (42) (24). In considering the present status of radiotherapy in carcinoma of the body of the
uteros its limitation as well as its benefits must be evaluated (3). Most men agree that the difficulty in radium treatment is to place the radium on the local lesion in the uterus without effecting the surrounding tissue and getting all of the cancerous tissue. It is also thought that when the amount of radium is sufficient to destroy the cancer, it produces marked irritation of the bladder and rectum.

Novak (48) states that it is not the method of treatment, which determines the fate of the patient nearly so much as the factor of the stage of the disease at which the treatment is instituted. That it is best to increase our proportion of early cases, by educating the laity and by thorough examination of every woman who presents herself with suspicious symptoms.

The next essential is the extensive correlation of the experience in individual observers to establish the correct basis of judgment as to the relative merits of surgery, radium and of Xray in the treatment of carcinoma of the corpus uteri (8). Most writers of today agree that the use of the semi-radical hysterectomy combined with careful applied radiotherapeutic measures assures the best results. Of course, each has his method of combining the two. It appears that the malignancy of the uterus, if not extensive, or if the operation is not otherwise contraindicated, should have an early hysterectomy. Radium is to be considered before or after hysterectomy, in addition to massive xray (29) (40). Even in some extensive fundus cases, remarkable results have followed the use of radium (29). Some think that radium should be employed at the same time of "D & C", if the microscopic report is positive for carcinoma, while others believe in a radical hysterectomy at the same sitting of "D & C" (48).
Heyman (25) advises against radium alone in the treatment of cancer of the corpus unless the uterine cavity is narrow and of regular contour, so that the radium container can be placed uniformly in close contact with the uterine wall. He always uses radium in the vagina either before or after the operation on account of possible vaginal metastasis. The radium should extend from the top of the fundus to the cervix and the applicators are constructed to take the shape of the uterine cavity.

Bailey (1) applies radium in the cavity of the uterus, in a tandem in each capsule of which there are 100 millimeters and irradiation should be for 2,500 to 3,000 milli-curies hours depending on the filter. The best filter being 1 millimeter of platinum for the larger dose and 0.5 millimeter of platinum or gold for the smaller dose. Neill (42) applies radiation in the form of radon, contained in a glass bulb, surrounded by 1 millimeter of brass and 2 millimeters of rubber so that only the gamma rays are emitted. From 1 to 2 curies, contained in from 4 to 6 tubes, are employed. A single dose given should be from 2,000 to 3,000 milli-curie hours. This he follows with roentgen irradiation to the iliac glands and pelvic wall. This should be given with exactness, for there is a definite danger of injury to the intestines when combined with heavy intra-uterine exposure.

If radium is used before the operation, there is some dispute as to the elapse of time between them. Bailey (1) does abdominal hysterectomy within five days after the radium treatment. He follows this in two weeks with a series of x-ray given about the pelvic girdle. He gives four doses of fifteen minutes each with 5 millimeters of aluminum as a filter, and at a focal distance of twelve inches. The spark gap being ten inches, and the K.V. to 110 with 5 milliamperes. One week following this
he applies radium in the vault of the vagina. Other writers believe in waiting from 5 to 8 weeks following radium treatment before hysterectomy should be performed.

Healy (24) says, that you will get 20 to 22 percent total absolute salvage, according to the literature and their personal experience, whether you are treating these cases by roentgen irradiation plus radium, or by roentgen irradiation plus radium plus hysterectomy, or by radical surgery alone. The advantage of the radiation therapy over surgical treatment is the lessened primary mortality. In those cases of poor surgical risk in which surgery is contraindicated, it is better to use radium. These cases may live from one to three years.

Radium may be expected to reduce some inoperable cases to operable ones, and may even cure some cases that appear hopeless to all other methods of treatment (40). In metastatic carcinoma, radiation can be a valuable palliative remedy relieving pain, hemorrhage, and probably prolonging life.

The operative mortality as found in the literature, is suggestive of the probability that irradiation in time may become the method of choice for carcinoma of the corpus uteri, as it did for carcinoma of the cervix uteri. Surgical and radiation combined appear to be the choice of treatment of corporeal carcinoma and have stood the test.
RESULTS

Several factors evidently determine the prognosis following hysterectomy for carcinoma; the grade of malignancy, the age of the patient, the duration of the symptoms before operation, and the personal resistance to malignancy, a term used for the unknown factor of carcinoma (66).

It would seem that the best results obtained, regardless of the type of treatment used, depends mainly on an early recognition of the disease. Carcinoma of the body of the uterus is the most benign form of cancer encountered in the female genital tract. Many cases, if operated on at an early stage, remain cured after simple vaginal hysterectomy. Beattie (2) found a direct relation between the duration of symptoms and the spread of the growth, this factor may have a direct bearing upon the prognosis. Norris (43) gives the following table.

Table VII The Relationship of the Duration of Symptoms to Prognosis

<table>
<thead>
<tr>
<th>Duration of Symptoms</th>
<th>Number of Cases</th>
<th>Percentage of 3-Year Cures</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months of less</td>
<td>24</td>
<td>57.0</td>
</tr>
<tr>
<td>7 to 12 months</td>
<td>32</td>
<td>31.2</td>
</tr>
<tr>
<td>More than 12 months</td>
<td>28</td>
<td>17.8</td>
</tr>
</tbody>
</table>

Table VIII Three-year results in cases upon whom hysterectomy was performed (43).

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL NUMBER</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>PERCENTAGE ALIVE</td>
<td>37.5</td>
<td></td>
</tr>
<tr>
<td>PERCENTAGE ALIVE NO RECURRENCE</td>
<td>30.5</td>
<td></td>
</tr>
<tr>
<td>PERCENTAGE ALIVE PROBABLE RECURRENCE</td>
<td>7.</td>
<td></td>
</tr>
<tr>
<td>PERCENTAGE DEAD, ALL CAUSES</td>
<td>62.5</td>
<td></td>
</tr>
</tbody>
</table>

I could find very little definite data as to the percentage
of five-year cures in carcinoma of the body of the uterus. Heymen (25) reports fifty-eight percent in 323 operations and fifty percent cures in 52 cases treated by radium alone.

Quoted from Gardner and Finola (17). Voltz, a German writer, obtained a five-year cure in 45.8% of 107 patients treated by radiation alone. The primary mortality was only 0.3 percent as contrasted with the primary mortality of 10 percent usually estimated for operative treatment.

Bowing (3) treated 87 patients by radium, surgery and roentgen-ray. Twenty-two lived less than three years, twenty-three lived more than five years, and with an average life of 22.32 months. In a summary of 189 cases referred to the department of therapeutic radiology from 1916-1929 inclusive, he gave the following report: Primary mortality rate of 2.11 percent, of 172 cases traced 80 were still alive and 92 have died.

Cullen (11) checked up on his cases in 1921 and found only 26 percent of his patients operated upon for carcinoma of the corpus were alive at the end of five years. Healy (24) in 1930 after the review of the literature and in his own experiences concluded that an absolute cure was around 20 - 22 percent. This is contrary to a later report.

Martin (39) observed the following at the Hospital of the University of Pennsylvania. Table IX Results secured by various methods of treatment.

| TABLE IX |
|------------------|------------------|------------------|------------------|
| TREATMENT        | Number of Patients | 5-Year Cure Absolute Cure | Relative Cure |
| Irradiation (radium) | 28 | 15 | 55.5 | 55.5 |
| Operation        | 5  | 3  | 60  | 60  |
| Operation plus radium | 15 | 10 | 68.6 | 68.6 |

Healy (21) in February 1934, stated that the hospitals under direction and encouragement of the American College of Surgeons,
established follow-up records of all surgical cases. Hence it was discovered that hysterectomy was yielding less than 50 percent of the five-year cures. The combining of radiation therapy and surgery may increase the percentage of five-year cures. Neill (42) took 109 treated cases from the clinic and found that 76 have died and 33 are living, making a total of 33 percent of the five-year cure. The following table was recorded by Norris and Vogt (44). Table X gives the number of three year cures as to the method of surgery used.

<table>
<thead>
<tr>
<th>TREATMENT</th>
<th>NUMBER OF CASES</th>
<th>PERCENTAGE OF 3-YEAR CURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hysterectomy</td>
<td>57</td>
<td>37.8</td>
</tr>
<tr>
<td>Pan-hysterectomy</td>
<td>40</td>
<td>43.3</td>
</tr>
<tr>
<td>Supra-vaginal hysterectomy</td>
<td>17</td>
<td>24.2</td>
</tr>
</tbody>
</table>

Stacy (65) reported 288 cases with 63 percent of five-year cures. The treatment was pan-hysterectomy in most of the cases and irradiation only for those patients who were poor surgical risks, the latter method gave poor results.

Most of the data as to results is rather unsatisfactory. Either the series are too small or the report does not distinguish between the methods of treatment used. Until the last decade surgery was the main treatment while now the treatment of choice is radiation and surgery combined, apparently this combination treatment has not been used long enough for thorough study of results.
CASE REPORTS

I will report a variety of cases, to show that carcinoma of the uterine body may occur in practically any age and of more than one variety.

CASE I. This case of a girl, age eleven, was reported by Gilbert (18) in 1932.

J. C., aged eleven, student, admitted to the hospital March 27, 1928, referred by Doctor MacTaggart, with chief complaints of vaginal bleeding, pelvic tumor, and slight abdominal discomfort. In September 1927 she had vaginal bleeding for three days. The following three months the patient had regular vaginal bleeding, lasting from three to four days. In January and February no bleeding occurred. At the time of admission there was vaginal bleeding but no pain. The mass in the pelvis was increasing in size. Physical examination was negative except for pelvic condition. On palpation of the lower abdomen, a mass could be made out in the bladder region, approximately twelve centimeters in diameter. This mass was hard, immovable and not attached to the skin. Vaginal bleeding was determined by pelvic examination. The cervix was normal.

Operation was fundal hysterectomy and right salpingo-oophorectomy. Left tube and ovary were normal and left in situ. Operation was followed by x-ray treatment.

Laboratory report by Ellis Hospital revealed a tumor mass that was irregular, nodular, and measured 12 x 6 x 9 centimeters.

Microscopic: Undifferentiated tumor cells separated by thick fibrous strands, distinct resemblance to epithelium, cells varied greatly in
size and mitotic figures rare. Ewing's report was also carcinoma of the body of the uterus Grade IV, radio sensitive.

Six months after operation, chest plates were taken showing extensive metastasis throughout the chest. Patient died in December 1928.

This case was extremely interesting to me from the age standpoint.

CASE II. This case was reported by Palmer (51) in 1928.

A girl nineteen years of age, bled continuously for six months, no other complaint. On examination a soft dark bleeding nodule protruded from the external os. On removal it was found to be a polyp arising from the endometrium just above the internal os. It was removed flush with the endometrium, and found on section to contain near the distal portion an area of solid trabecular, tubular polygonal celled carcinoma. In view of the patient's age, it was decided not to perform a hysterectomy. The patient was still alive and in good health at the time of Palmer's report, five and one-half years later.

This case not only showed the possibility of carcinoma at an early age, but the removal of the entire lesion by the curet and that an early diagnosis can be made.

CASE III. A case of squamous-cell carcinoma of the body of the uterus reported by Sinton (62) in 1927.

Mrs. M. S., age fifty-seven, a white multiparous, gives the following history: Menstrual periods started at age of fourteen, every twenty-eight days, flowing profusely for one week, always associated with dysmenorrhea. Menopause occurred at the age of forty-eight. After this there was several periods at irregular intervals with a scanty flow. Previous to her menopause a "D & C" was done, it being stated that she had catarrh of the womb.
Some time after the menopause she had profuse and constant bleeding from the vagina. At this time she was given a series of treatment by radiation.

Three months later she started bleeding profusely and the vaginal discharge had a terrible odor. On examination the fundus was slightly enlarged, was anterior and freely movable. Adnexal region was clear. Biopsy report sarcoma of the body of the uterus. She was treated by pan-hysterectomy.

Laboratory report. When uterus was cut open, it contained a large fungoid yellow and red mass adherent to the upper posterior wall. Also a smaller mass adherent to the upper wall near the left corner. Microscopic examination revealed a typical squamous cell epithelioma with some pearly bodies and in general the cellular arrangement was that so often seen in epithelioma of the cervix. Section of the endometrium lower down was normal. Tentative diagnosis of sarcoma was replaced by squamous cell carcinoma.

No comment was made of a follow up on this case.

CASE IV. This case was reported by Stacy (65) in 1925. It is interesting due to its long duration, recurrence and the standpoint of treatment.

A girl of nineteen, with a history of irregular and profuse menstruation continued for a period of four years during which time she had a curettage with temporary relief from symptoms. Later she was given an intrauterine radium treatment of 150 milligram hours with fifteen months control of the bleeding, then six months of irregular bleeding with a watery discharge and enlargement of the uterus. An abdominal hysterectomy was done and extensive adenocarcinoma was reported.
Three years later a left inguinal node appeared which was treated with radium. There has been no evidence of recurrence at the time of Stacy's report, and the girl was well at that time, or six years and three months after the operation.

It appears that there is no means whereby the area of early carcinoma of the fundus, may have radium applied to the affected area alone.

CASE V. This case was reported by Horsley (26) and apparently cured by curetting and radium application.

F. V. S., white, aged 47, housewife, complained of bleeding from the womb. She had eight children. Birth of the last child was seventeen years ago and she had worn a pessary for the past twelve years. She had a large cystocele. For the past twelve years she had a tired dragging sensation in the small of her back. Her last menstrual period was five years ago. She has had a moderate whitish vaginal discharge since her last menses. Three weeks before she came to the doctor she had a slight burning sensation in the left side of the abdomen followed by bleeding from the vagina. She bled a small amount on the two successive days.

Pelvic examination revealed a marked cystocele and rectocele, and the cervix was enlarged and congested. "D & C" was done, cervix amputated and the rectocele and cystocele were repaired.

She returned three weeks later with vaginal bleeding. "D & C" was done and microscopic examination was negative for carcinoma. Three months later she returned with the same story and the same routine was done. This time the pathology report was Grade I adenocarcinoma. She was treated with twenty-five milligrams of radium for twenty-four
hours. Three months later a "D & C" was done with negative pathology report. This was followed by fifty-seven milligrams of radium for twenty-four hours. Another similar radium treatment was given three months later. After this she was apparently cured.

CASE VI. This case was reported by Judd (30) with an absolute cure by hysterectomy.

A woman, aged 58 years, had passed through the menopause at the age of 52 years. One year later she had noticed a very slight bleeding from the uterus. For the next five years spotting or slight staining had occurred about once in two weeks. For one month before she came for consultation, bleeding had been constant. There was pain on micturation and she thought that she had passed some blood in the urine.

January 29, 1909, a pan-hysterectomy was performed with the removal of both fallopian tubes and ovaries. The pathologists reported that the lesion was a carcinoma of the corpus uteri. Examination recently of the preserved specimen disclosed that the malignancy was an adenocarcinoma Grade I. The patient had gallstones at the time of her operation.

Seven years later a cholecystectomy was performed. More than twenty-five years has elapsed since the operation for the carcinoma of the uterus. She was in good health at the time of this report.
CONCLUSION

1. The etiology of carcinoma of the body of the uterus is unknown. It occurs most frequently during the tenth decade, and usually is in nulliparas or in women that have had one or two children. About 20 to 30 percent of all cancers of the uterus occur in the corpus.

2. The cardinal symptoms are well-known as metrorrhagia and a brownish, watery, and at times irritating vaginal discharge, usually with an odor. Pain is usually a late symptom and when it occurs the disease is too far advanced for curability. This profuse bleeding that is supposed to occur at the change of life is not normal, and should always, without fail, be carefully looked into. Every case of post-menopausal bleeding should be considered malignancies until proven otherwise.

3. The diagnosis can be assured only after curettage and the microscopic examination of the specimen by a skilled pathologist.

4. The only forms of treatment that have stood the test of time are those dependent upon surgical removal of the lesion with a knife and treatment with radium and x-ray.

5. The operative mortality as found in the literature, is suggestive of the probability that irradiation may become the method of choice for malignancy of the corpus, as it did for carcinoma of the cervix. Even in operable cases radiation alone appears to be a method of treatment far better than we before realized. In far advanced cases radium can be a valuable palliative remedy.

6. The results obtained depends on an early diagnosis, the physical condition of the patient, the type of malignancy, the degree of
metastasis, and the treatment should be thorough and as early as possible.
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