

THE VARIOUS TYPES OF CARCINOMA CERVICIS UTERI: THE CHANGES THEY UNDERGO WITH THE PROGRESS OF THE DISEASE AND THEIR CLINICAL SIGNIFICANCE

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Experience has taught us that the clinical course of cancer of the uterine cervix is usually rapid; the patients rarely live over three years, about three-quarters of them die within two years, and one-third within one year, after the first manifestation of the disease. Bleeding in some form is usually the first evidence of this condition; this is sometimes not present until late in the course of the disease, but if absent, usually some other symptoms such as a watery or foul discharge should call attention to the growth. In a small percentage of the cases all symptoms referable to the growth are absent until after it has extended beyond all possibilities of a cure. Bleeding or a blood-tinged discharge was present in about ninety-three per cent of 412 cases of cervical cancer admitted to Dr. Kelly's clinic at the Johns Hopkins Hospital, and in over sixty per cent of these cases there was a history of neglected uterine bleeding for over six months. When we bear in mind the usual rapid course of the disease, we can readily understand why hysterectomy so seldom cures this condition, why it is important to make an early diagnosis and also why the patient should be operated upon as soon as possible after making this diagnosis.

We know that only a small percentage of all cases have been "operable," and we also have learned that a small percentage of those operated upon can be cured, but believe that all could be cured if the entire diseased condition could be removed and implantation avoided. The importance of an early diagnosis is very urgent, and fortunately it is possible in a large percentage of the cases if women only realized the curability of this condition in its early stages and we, the physicians, would ascertain without delay, in every instance, the cause of uterine bleeding or of any other symptom referable to the uterus.

Two things then are very essential; first, the education of women along these lines, and second, our own education in order that we may better understand the pathological changes caused by this disease and their clinical manifestations.

All women should fully realize that any uterine bleeding or other symptoms referable to the pelvic organs may be indicative of some slight trouble, which may not need any attention or can be easily remedied if it does, or on the other hand, that it may be the first manifestation of cancer which, if operated upon in its incipiency, should be cured in a large percentage of the cases. This bleeding may be slight, "only a show" appearing at irregular intervals as on exertion, or after coitus, or after using a douche or straining at stool. In

other cases the bleeding may be slight but constant, the patient noticing that her clothes are slightly soiled on taking them off at night. Sometimes the bleeding is more profuse, so that it may appear like a prolonged menstruation, an irregular menstruation or a return of the flow after the menopause. In still other cases there may be severe hæmorrhages.

All physicians should bear in mind that there are various types of the growth which may alter the clinical picture of the disease, and the various stages of each type may also present different clinical features.

It seems appropriate to study these various types and the changes they undergo during the progress of the disease, in order that we may understand the clinical manifestations of the disease, its diagnosis and the indications for its treatment.

While Resident Gynecologist at the Johns Hopkins Hospital, I began a careful study of twenty-seven specimens removed by the more radical abdominal operations and also one autopsy specimen from a patient with cervical cancer, dying from cerebral embolism due to an acute endocarditis. Fortunately only a few of these cases had been curetted and an excellent opportunity presented itself to study the various types and the changes they undergo as the disease progresses. A drawing, to measure, was made of each specimen removed and also one of the vaginal portion of the cervix and in several instances plaster casts of the latter were made. The specimens were hardened in 4 per cent formalin and, after hardening, a sagittal slice about 2 mm. in thickness was removed, thus dividing the specimen into two halves. This slice (either as a whole or else divided if too large) was imbedded in celloidin, cut and stained as a microscopical section, thus giving a stained sagittal section of the entire uterus, demonstrating the relation of the disease to the cervix and its method of extension through the tissues of the cervix, and in a few instances into the fundus. Cross sections were then made of each half of the specimen and by this incomplete series the invasion of the parametrium was studied. From the sagittal sections and the series (incomplete) of cross sections, the growth was reconstructed thus demonstrating its relation to the parts involved. Cancer was either found or its existence excluded from the pelvic lymph nodes removed.

Here I wish to thank Dr. Kelly for the use of this material from his Clinic and also for the use of the eight drawings bearing Mr. Broedel's name, which were made for the second edition of Dr. Kelly's Operative Gynecology. I also wish to

thank Mr. Broedel for the aid he kindly gave me which enabled me to make the other illustrations.

CLASSIFICATION OF CANCER OF THE UTERINE CERVIX.

I. *Histological*.—The vaginal portion of the cervix is normally covered by stratified epithelium which is directly continuous with that of the vagina and usually ends at the external os but may extend up into the cervical canal for varying distances, which is especially true as women grow older. The cervical canal, on the other hand, is lined by high cylindrical cells which generally meet the stratified epithelium at the external os, but may extend over the vaginal portion of the cervix. Cancer arising from the stratified epithelium, no matter the place of origin, whether from the vaginal portion or within the cervical canal, is known as *squamous cell carcinoma*. Likewise cancer arising from the cylindrical epithelium or glands of the cervix, no matter its place of origin, is known as *cylindrical cell* or *adeno-carcinoma*.

II. *Topographical*.—As we may group all forms of uterine cancer according to whether they arise in the body or in the cervix, in like manner we may classify cervical cancer according to its origin whether in the *vaginal portion* of the cervix, or within the *cervical canal*.

III. *Morphological*.—Irrespective of the situation of the growth or its histological structure, we may group it according to its morphology. We do not know why, in one case, the growth seems to "evert" giving rise to a papillary or cauliflower mass, or in another, apparently the same type of growth may "invert" forming a nodule or mass of cancerous tissue in the cervix with but very little evidence of the disease on the surface. The malignant process may be circumscribed in one instance, and apparently the same type of growth may be diffusely scattered throughout the cervical tissue in another. Intermediate forms and sometimes both processes are present in the same specimen. Apparently in the progress of the disease the growth may sometimes pass from one morphological type into the other. We can, however, frequently make the following classification:

1. Everting or vegetative (synonyms—cauliflower, papillary and proliferating);
2. Inverting or infiltrative (synonyms—nodular, ulcerative and parenchymatous).

In some cases the cancer cells predominate and the stroma forms a very small part of the tumor, as a result the tumor may feel soft, hence the term *medullary*, and it may early become necrotic and portions of it slough away. The process less frequently invades the cervical tissue in a diffuse manner forming a growth in which the stroma predominates, the so-called "scirrhous" cancer, which may retain its form for a long period of time. Specimens are encountered which cannot be included in the above classification and which should be looked upon as "exceptions" or isolated cases until we learn more about them and either discover, on further study, that they belong in one of the above groups, or that it may be necessary to form new groups for them.

The following groups of cases will be considered:

I. Squamous cell carcinoma; (1) Vaginal portion of the cervix; (a) everting, (b) inverting; (2) Cervical canal; (a) everting, (b) inverting.

II. Cylindrical or adeno-carcinoma. Sub-classification as above.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Everting or Vegetative.

This type of growth apparently begins as a proliferation of the epithelium of the vaginal portion of the cervix and, associated with this, there is a reaction of the deeper cervical tissue giving rise to a papillary outgrowth into the vagina, which consists of a central core of vascular connective tissue covered by the proliferated epithelial cells. This outgrowth may arise from any portion of the vaginal portion of the cervix and may form either a pedunculated or a sessile tumor. As the disease progresses the tumor increases in size, either spreading over the surface of the vaginal portion of the cervix, or over the vaginal walls or up the cervical canal, and it may partially or completely fill the vagina. At the same time the deeper tissues are invaded. In one case there may be an enormous mass filling the vagina with but little extension of the disease into the deeper tissue, and in another case the external manifestation of the growth may be small, while its extension into the deeper tissues may be great. Figs. 1 and 2 illustrate one of these growths which has involved the posterior cervical lip and is gradually absorbing the deeper tissues, spreading over the vagina posteriorly and invading the cervical canal by replacing its mucosa. It has extended about one-third the way up the canal and in places has occluded the openings of the cervical glands, thus causing retention cysts. Figs. 3 and 4 illustrate another case where the entire vaginal portion of the cervix is involved and the growth is beginning to invade the deeper tissues at the junction of the vagina and posterior cervical lip. This is probably the least malignant of the various forms of cervical cancer. The external evidence of the disease may suggest a very advanced case and there may in reality be but very little extension of the disease. One would infer that bleeding would occur early in the course of the disease in this group of cases and probably this is true. Both cases, represented here, had been bleeding for over five months before the operation. The situation of the growth on the vaginal portion of the cervix and its morphology renders its detection, on palpation or inspection, comparatively easy. Unfortunately this group probably occurs less frequently than the following group which is more malignant and difficult to diagnose.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Inverting or Infiltrating.

The inverting or infiltrating type also apparently begins as a proliferation of the epithelium of the vaginal portion of the cervix, and here the papillary formation is absent or plays a minor part. The growth seems to invert itself into the

tissues of the cervix and usually gives rise to a more or less circumscribed mass of cancerous tissue. Usually the stroma plays a small part in the structure of the tumor and the epithelial cells predominate, the so-called medullary cancer; less frequently, however, the disease process invades the cervical tissue in a diffuse manner forming a growth in which the stroma predominates, the so-called scirrhus cancer. The starting place of the new growth varies in different cases. In the one shown in Figs. 5 and 6, it apparently started in the centre of the anterior lip near the junction of the squamous and cylindrical epithelium, while in the case shown in Figs. 7 and 8, it apparently started in a similar place of the posterior lip. On the other hand, in the case shown in Figs. 9 and 10 there is possible a double focus, *i. e.*, the simultaneous appearance of the growth in each angle of the external os.

As the disease progresses it invades the deeper tissues of the cervix, extending directly in and usually avoiding the cervical canal. Sometimes a large mass of cancerous tissue will be found, hence the name "nodular cancer." In the specimen shown in Figs. 5 and 6 the entire anterior wall of the cervix had apparently become involved before ulceration had taken place. More often, however, the processes of invasion, necrosis and ulceration go on together as shown in Figs. 7, 8, 9, 10, 11, and 12, hence the term "ulcerative" cancer. As the disease progresses further and replaces the tissues of the cervix, the central core including the cervical canal frequently sloughs away and the cervix is converted into a crater-like cavity lined by necrotic cancerous tissue as shown in Figs. 13 and 14. The clinical manifestations of this type depend on the amount of necrosis and ulceration. A growth which becomes necrotic early in its course would give rise to symptoms sooner than one which did not. In the patient shown in Figs. 5 and 6, where there was an extensive cancerous mass with but very little necrosis, bleeding had been noticed but seven weeks before the operation, while in the one shown in Figs. 9 and 10 bleeding had been present for over eight months. Yet in the latter case the growth was small and without metastases, while in the former, the growth was large and metastases had occurred. We must infer, that in the patient with a small growth and symptoms for eight months either the disease progressed very slowly or the symptoms appeared very early, and in the other with a large growth and bleeding for only seven weeks, either the cancer grew very rapidly or else the symptoms did not appear until late. The patient, whose uterus is shown in Figs. 7 and 8 had known of the ulcerated condition of the cervix for six months and yet one sees that the primary growth was very small; on the other hand, metastases to the pelvic lymphatics had already occurred. In the case shown in Figs. 11 and 12 the diagnosis was made on examining the patient for symptoms arising from a pelvic inflammatory disease which was associated with the cancer, but independent of it, and symptoms referable to the cancer had been of but ten days' duration. The disease had metastasized at the time of the operation and the patient

later died from recurrence due to some of the cancerous pelvic lymph nodes which had not been removed at the operation. On the other hand, the uterus shown in Figs. 13 and 14 had been bleeding for over six months before the operation.

It can readily be seen in this type of cancer, that if the growth is rapid or necrosis is delayed the disease may easily pass beyond the curative stage before it is detected. On the other hand, if the growth is slow and especially if necrosis occurs early, the diagnosis may be made while the disease is still local. *Unfortunately there is no relation between the extent of the diseased process and the duration of the symptoms, i. e.*, the disease may be extensive and the symptoms of short duration and also the disease may be early and it may have manifested itself, clinically, for a long time.

In the further progress of the disease the bladder may be involved anteriorly as shown in Fig. 15 and later a vesico-vaginal fistula may appear. In the posterior extension of the disease the cul-de-sac may become obliterated and the rectum become invaded as shown in Fig. 16 or the rectum may become invaded through the posterior vaginal wall. As a result of the posterior extension of the disease a recto-vaginal fistula may appear. In the lateral extension of the disease the ureters soon become surrounded and compressed, or if it extends both posteriorly and laterally, the sciatic nerves may become invaded and cause excruciating pain. Fortunate indeed is the woman when the ureters become compressed before the formation of the above mentioned fistula or invasion of sensitive nerves, for the resulting renal insufficiency benumbs the sensibilities and favors a terminal infection.

It can be seen that the inverting or infiltrating variety is more malignant than the everting type and is also of more frequent occurrence. Unfortunately it may not give rise to any symptoms until after it has extended beyond the uterus. Its detection by inspection or palpation, unless ulceration is present, is also more difficult than in the everting type.

Squamous Cell Carcinoma—Vaginal Portion of Cervix—Both Everting and Inverting.

As has been previously stated, both types of growth may be present in the same specimen and in fact usually are, for the one name or the other is given to the prevailing type. We have papillary projections from the floor of the ulcer or sides of the craterous cavity and every everting type eventually has an infiltrating base. So the classification is somewhat artificial, but is of importance as a help in understanding the various forms of growth. In the case shown in Figs. 17 and 18, which probably belongs in the last group mentioned, the disease apparently began as an infiltrating form but burst its outer shell and assumed the everting type. This patient had been bleeding for three months. Notice that the growth apparently began in the posterior lip, invaded the deeper tissue and through it encircled the cervical canal.

Squamous Cell Carcinoma—Cervical Canal—Everting.

Squamous cell carcinoma arising within the cervical canal

may also be grouped into the everting and inverting forms; the everting form may fill the canal or even protrude through the external os into the vagina. In Figs. 19 and 20 is shown the shrunken and retracted cervix so characteristic of the growths developing in the cervical canal and in addition a portion of the growth is protruding from the external os as a papillary outgrowth. The sagittal sections show that a pyometra had resulted from the occlusion of the cervical canal by the growth. This is the only instance in the twenty-eight cases where there was any resemblance to an everting type of growth arising from the cervical canal. A history of three months' bleeding was present and the growth had invaded the parametrium, and metastases were found in the pelvic lymph nodes.

Squamous Cell Carcinoma—Cervical Canal—Inverting.

The same changes occur in the inverting type of growth starting in the cervical canal as in the similar type of growth arising from the vaginal portion of the cervix. However there is this difference. This form of growth, arising from the vaginal portion of the cervix, nearly always extends by invading the deeper tissue of the cervix rather than spreading over the mucous membrane and up the cervical canal; as a result the cervical canal may be entirely surrounded by cancer and yet remain intact until late in the course of the disease, and finally the central core including the canal may slough away. On the other hand, in cancer arising within this canal the mucosa of the canal is the first tissue attacked. From the mucosa, the cancer spreads on all sides into the cervical tissue. We nevertheless see the changes caused by infiltration and ulceration, and finally the cervix is converted into a thin shell lined by cancerous tissue just as in the other type. In the advanced stages the picture may be such that it is impossible to state whether the disease started within the canal or from the vaginal portion of the cervix. Frequently, however, the vaginal portion of the cervix may not be invaded—even in cases of extensive cancer developing within the canal (see Figs. 25 and 26). In Figs. 21 and 22 is shown a very early case in which the disease had started within the external os and after spreading over the surface of the cervical canal, had invaded the deeper structures on all sides, and yet there has been but little change in the vaginal portion of the cervix. A little puckering of the anterior lip, caused by the lower edge of the growth just within the external os, was present. In the specimen shown in Figs. 23 and 24 the disease is further advanced, more of the cervical tissue has been invaded and also the tissue beneath the mucosa of the vaginal portion of the cervix, thus causing a retraction and puckering of the latter. The specimen shown in Figs. 25 and 26 represents a still further stage of the disease where the entire central portion of the cervix had sloughed away. Note, however, that there has been but very little involvement of the vaginal portion of the cervix, the latter being retracted, shrunken, and puckered, but its mucosa, for the most part, is intact.

In the specimen shown in Figs. 27 and 28 the growth had invaded the cervical tissues in a diffuse manner, the so-called scirrhus type, and had undermined the mucosa covering the vaginal portion of the cervix causing the former to slough away from the greater portion of the cervix, there still being an irregular border of intact mucosa about its outer margin. The growth had also invaded the deeper tissues of the vagina on all sides of the cervix without involving its mucosa.

The symptomatology varies in these cases and there is no definite relation between the duration of the symptoms and the extent of the disease. In the very early case shown in Figs. 21 and 22 a thin watery discharge had been present for three years, and bleeding was first noticed only a few days before the patient came to the hospital. The patient represented in Figs. 23 and 24 had been bleeding for seven months, and the one represented in Figs. 25 and 26 had been bleeding for eighteen months, but here a uterine polyp was found which may have also caused bleeding. Bleeding had been present for two and a half years in the patient represented in Figs. 27 and 28.

The diagnosis of this type presents all the difficulties of the preceding one, with the additional feature that the disease starts within the cervical canal. The disease seems, rarely or only very late, to appear on the vaginal surface of the cervix. However, there is one very important feature which aids in the diagnosis and that is the alterations in the vaginal portion of the cervix caused by the disease invading its deeper tissues. The vaginal portion of the cervix becomes indurated, and with necrosis, the cervix becomes retracted, puckered, and the vaginal mucosa covering it, is thrown into folds. This induration, retraction, and puckering of the vaginal portion of the cervix is as characteristic of this form of cancer, as is the retraction of the skin or the nipple characteristic of the mammary cancer lying beneath. The prognosis in these cases is probably about the same as in the similar type arising from the vaginal portion of the cervix.

Squamous Cell Carcinoma—Inverting—Starting Place Undetermined.

In very advanced cases it may be impossible to determine the origin of the growth. In the two specimens shown in Figs. 15 and 16 the disease apparently started from the vaginal portion of the cervix and not from within the canal, still this cannot be definitely stated. As previously emphasized, it is remarkable how extensive the disease may be in a growth starting within the canal and the vaginal portion of the cervix may not yet have been destroyed. In the specimen shown in Figs. 29 and 30 it is impossible to definitely state the origin of the growth (classified under inverting type arising from the vaginal portion of the cervix), whether from the vaginal portion of the cervix, the vagina, or just within the external os. There was a marked reaction on the part of the surrounding tissue causing an infiltration of eosinophiles, so marked as to greatly obscure the malignant growth. As shown, the cervix and vagina are both involved; in addition

the parametrium was invaded by direct extension and by metastases, and metastases were present in the pelvic lymph nodes. The bleeding was of six months' duration.

Adeno-Carcinoma—Uterine Cervix.

This, as we know, may arise from the vaginal portion of the cervix or from within the cervical canal and may be everting or inverting. The specimen shown in Figs. 31 and 32 now appears as an infiltrating type starting within the cervical canal. There was a history of bleeding for seventeen months, and seven months before her admission to the hospital a tumor was removed from the cervix. This suggests that there was probably present, at that time, a fungating growth protruding from the external os, *i. e.*, it originally manifested itself as an everting type arising from the cervical canal. In Figs. 33 and 34 is shown a specimen of adeno-carcinoma obtained at autopsy, the patient died of cerebral embolism from acute endocarditis. Metastases were found in the lungs, liver, and in the thoracic, abdominal, and pelvic lymphatics. There was a history of bleeding for six months. The growth is apparently of the inverting type starting from the deep cervical glands, as the mucosa lining the canal was normal in places. It may have originated in the left corner of the vaginal portion of the cervix, but this does not seem probable. In Figs. 35 and 36 is represented a third case of adeno-carcinoma of the inverting type starting within the cervical canal and causing occlusion of the canal, with a resulting pyometra. The retracted puckered cervix is well shown, and this is covered by epithelium having the histological appearance of squamous cell carcinoma, thus suggesting the presence of both adeno-carcinoma and squamous cell carcinoma in the same specimen. There was a history of bleeding for seven months.

Figs. 37 and 38 represent a specimen of apparent adeno-carcinoma starting within the cervical canal and suggest a double focus. The growth was apparently very early, symptoms of bleeding having been manifest for only three weeks. It, however, recurred in a few months after the operation and soon filled the pelvis. The recurrence manifested itself first in the vaginal vault and suggested that an implantation of cancer cells had taken place during the operation.

THE CLINICAL SIGNIFICANCE OF THE VARIOUS TYPES OF GROWTHS.

The following classification of cancer of the uterine cervix has been made:

I. Histological: (1) Squamous cell carcinoma. (2) Cylindrical cell or adeno-carcinoma.

II. Topographical: (1) Those arising in the vaginal portion of the cervix. (2) Those arising in the cervical canal.

III. Morphological: (1) Everting or vegetative (synonyms—cauliflower, papillary, and proliferating). (2) Inverting or infiltrating (synonyms—nodular, ulcerative, and parenchymatous).

In the majority of the cases we can employ the above classi-

fication. The histological picture is usually definite, but at times the diagnosis may be in doubt; in the case shown in Figs. 35 and 36 both adeno-carcinoma and the squamous cell variety are present. A difference of opinion has been expressed by different pathologists as to the diagnosis in Figs. 37 and 38. The topographical diagnosis is not always evident. It is remarkable how extensive a growth, arising from the vaginal portion of the cervix and invading the deeper tissues of the cervix, may be, and yet the cervical canal may be intact or very little involved, as shown by the sagittal sections in Fig. 12. Likewise one may have a very advanced growth arising within the cervical canal and the vaginal portion of the cervix may be intact, or slightly involved, or else invaded only from the deeper cervical tissues (see Figs. 14 and 16). However, in many of the very advanced cases it is impossible to state where the growth arose and the same is true of a few of the early or operable ones. In considering the morphology of the growth some are definitely everting, as shown in Figs. 1, 2, 3, and 4, and others are just as definitely inverting as shown in Figs. 5, 6, 7, and 8, but in others both processes may be present in the same specimen and also, in the progress of the disease, the growth may pass from one type to another.

The Clinical Significance of Squamous Cell Carcinoma—Vaginal Portion—Everting.

Four of the twenty-eight specimens were of this variety and possibly one or two others included in the next group. In only one of the four cases was the parametrium involved by cancer and in two of the cases, in which the pelvic lymph nodes were studied, cancer was not found. In one of the four cases there was a history of neglected uterine bleeding for over six months and in the other three for over five.

The above suggests that this is one of the most favorable types of growth, invading the surrounding tissue slowly and soon giving rise to symptoms. It is so situated and of such an appearance and structure that it may be easily diagnosed on inspection or palpation.

The Clinical Significance of Squamous Cell Carcinoma—Vaginal Portion—Inverting.

This is apparently the most frequent type of the squamous cell variety, occurring fifteen times in the nineteen cases of cancer arising from the vaginal portion of the cervix. It is apparently as malignant or even more malignant than the same variety arising within the canal, for it spreads by directly invading the deep tissues of the cervix rather than by extending over the surface, as up the cervical canal or over the vagina. It also soon reaches the parametrium, and metastases may occur even before the latter has become invaded by the tumor. The parametrium was involved, either by direct extension or metastases, in eleven of the fifteen cases. Some of the lymph nodes were studied in fourteen cases and were found involved in six, and in two of these six cases no evidence of cancer was found in the parametrium. In seven of



FIG. 1.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix, Everting or Vegetative (Gyn. Path. No. 7601).

Patient 37 years old; 4 children (youngest 9 years). A bloody discharge had been present for five months and a severe hæmorrhage occurred, while straining at stool, three weeks ago. Pain was probably due to adhesions from pelvic inflammatory disease. General condition was excellent.

The movements of the uterus were limited by pelvic adhesions from a previous pelvic inflammatory disease. The parametrium was apparently free.

Vaginal portion of the cervix (natural size) shows that the posterior cervical lip has been replaced by an everting papillary growth which bled on palpation. The growth had begun to spread over the posterior vaginal wall.

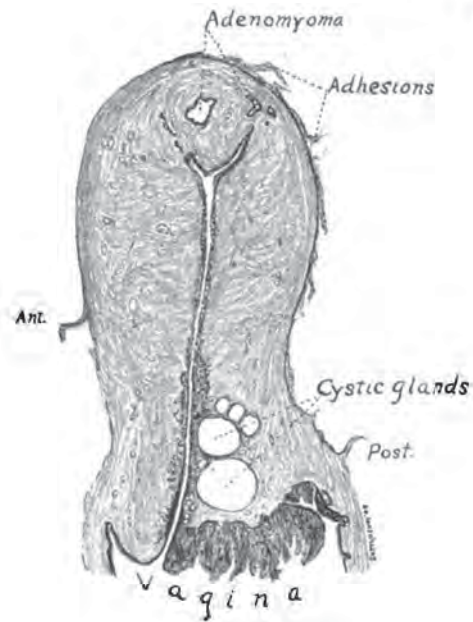
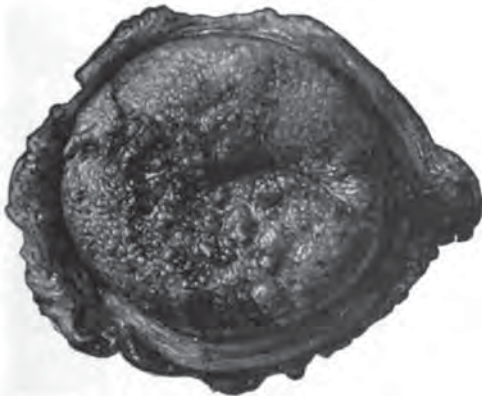


FIG. 2.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 1.

The papillary growth is gradually absorbing the tissue of the posterior cervix lip and is beginning to spread over the posterior vaginal wall and up the cervical canal occluding the openings of some of the cervical glands, and thus causing retention cysts.

The adhesions are shown on the surface of the uterus and an adenomyoma is present in the fundus. Cancer was not found in the parametrium or in the pelvic lymph nodes removed.



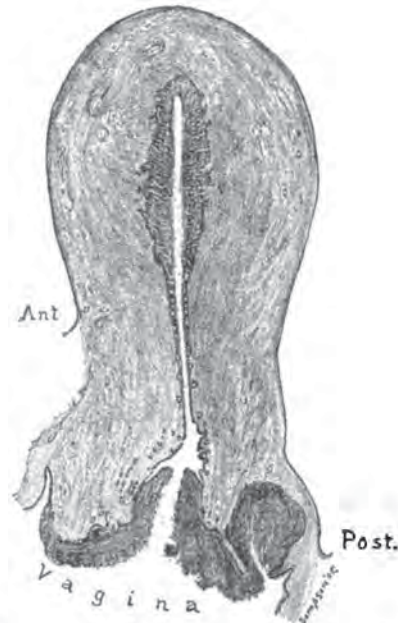
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FIG. 3.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix, Everting or Vegetative (Gyn. Path. No. 8155).

Patient 30 years old; 1 child (15 years). More or less constant bleeding had been present for five months, and was the only symptom. General condition was excellent.

The uterus was freely movable and parametrium was apparently normal.

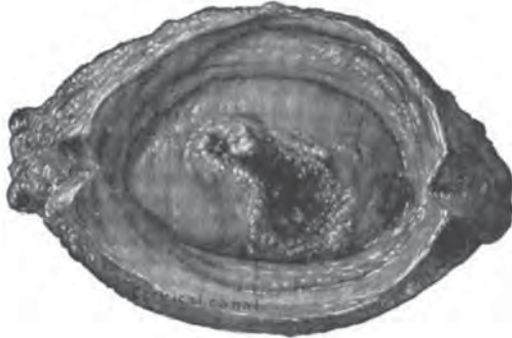
Vaginal portion of the cervix (natural size) shows that both lips have been replaced by an everting papillary growth which bled easily, on palpation.



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FIG. 4.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 3.

The papillary outgrowth has covered the entire vaginal portion of the cervix and has invaded the deeper tissues at the junction of the posterior lip and the vagina. Cancer was not found in the parametrium (the pelvic lymph nodes were not removed).



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FIG. 5.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting or Infiltrating (Gyn. Path. No. 6669). Patient 62 years old; 2 children (45-43 years); menopause nine years ago. Bleeding at irregular intervals had been present for seven weeks, usually when straining at stool and at one time amounting to a severe hæmorrhage. A very profuse watery discharge, not offensive, had been present for four months. Pain was not present. General condition was poor, hæmoglobin 68 per cent.

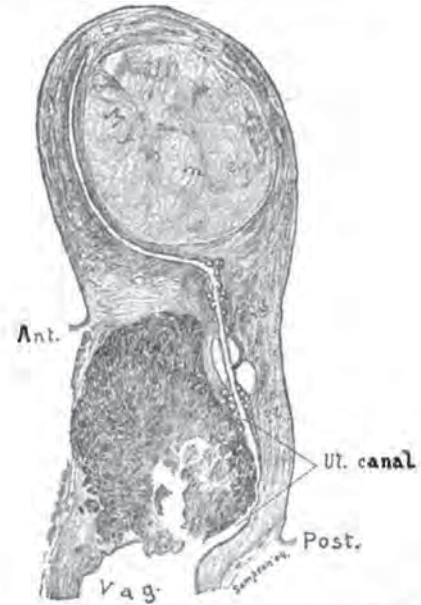
Uterus was freely movable and parametrium apparently normal. Vaginal portion of cervix (natural size) shows a markedly hypertrophied and indurated anterior cervical lip, the center of which has broken down, forming an ulcer lined by friable necrotic tissue, the posterior lip has become atrophied and the canal displaced backwards.



FIG. 7.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting or Infiltration (Gyn. Path. No. —).

Patient 49 years old; 3 children (youngest 21); menopause one and a half years ago. No bleeding, but a profuse discharge requiring the use of a douche had been present for nine months and six months ago her physician recognized "an ulcer" on the cervix, but did not suggest a diagnosis of cancer until two weeks before operation. Pain in the left side (due to metastases) was very severe. General condition was only fairly good.

Uterus was freely movable and parametrium was apparently normal. Vaginal portion of the cervix (natural size and not curetted), shows a superficial ulcer situated in the outer half of posterior lip, edges undermined, and base firm, did not bleed on palpation. Tissue just about the ulcer was indurated.



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FIG. 6.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 5.

The growth has formed a mass of cancerous tissue involving the anterior wall of the cervix and extending as high as the internal os. Note that the cervical canal has just begun to be involved and that it has been displaced backwards and that the fundus, vagina, and posterior wall are free. A submucous myoma is present in the posterior uterine wall.

A metastasis was found in a parametrial lymph node, the pelvic lymph nodes removed were free.

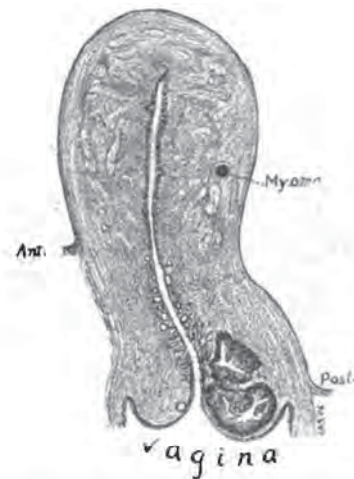


FIG. 8.—Stained Sagittal Section of the Uterus (slightly reduced) shown in Fig. 7.

A small primary growth is situated in the tissue of the posterior wall of the cervix (section is taken just mesial to the ulcer in the cervix). This section shows a characteristic feature of this type of growth and that is it extends by the invasion of the deeper cervical tissues and not by spreading, over the surface; also seen in the preceding case.

Cancer was not found in the parametrium, but the pelvic lymph nodes of the left side of the pelvis were extensively diseased.



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FIG. 9.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting, Possibly a Double Focus (Gyn. Path. No. 6848).

Patient 58 years old; 13 children (30-9 years); menopause two and a half years ago. Only symptom had been a slight but constant blood-tinged discharge of eight months' duration following a slight hæmorrhage at the onset. Condition was good, hæmoglobin 90 per cent.

Uterus was freely movable and parametrium was apparently normal.

Vaginal portion of the cervix (natural size and not curetted) shows two small superficial ulcers, situated in each corner of the external os and spreading over the outer surface of the cervix. The bases of these ulcers are covered by friable tissue which bled easily on palpation.

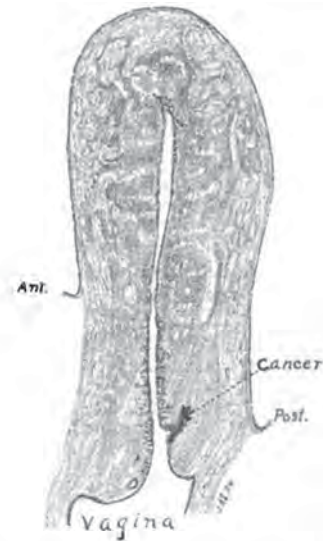
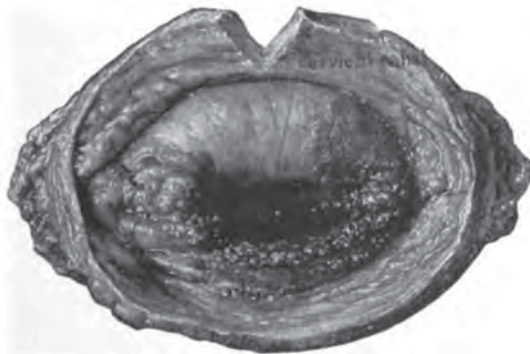


FIG. 10.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 9.

A small cancerous area is present in the posterior lip which as an "isthmus" unites the two areas of cancerous tissue situated on each side. Cancer was not found in either the parametrium or pelvic lymph nodes.

A very early case, but clinically of eight months' duration.



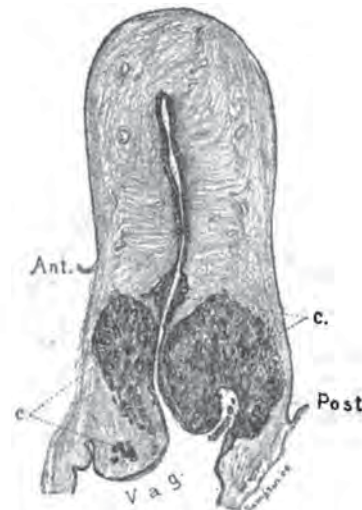
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FIG. 11.—Squamous Cell Carcinoma, Vaginal Portion of Uterine Cervix; Inverting; Extensive (Gyn. Path. No. 7077).

Patient 36 years old; 1 child (age ?). History was unsatisfactory. Bleeding had been present for only a few days, but probably the patient had been curetted a month before her admission. Pain, of seven weeks' duration, was probably due to the extensive pelvic inflammatory disease which was present. General condition was excellent, hæmoglobin 100 per cent.

Movements of the uterus were restricted by pelvic adhesions. Parametrium on left side felt slightly indurated.

Vaginal portion of the cervix (natural size, curetted ? a month ago) shows a necrotic ulcer involving the entire posterior lip and the outer portions of the anterior, which bled easily on palpation.



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FIG. 12. Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 11.

The growth has invaded the tissues of the cervix and has surrounded the cervical canal, in places involving it. The growth stops at the internal os.

The parametrium of the left side was invaded by direct extension and that of the right by metastases. Metastases were also found in the pelvic lymph nodes of the left side.

An extensive growth with a clinical history of short duration.



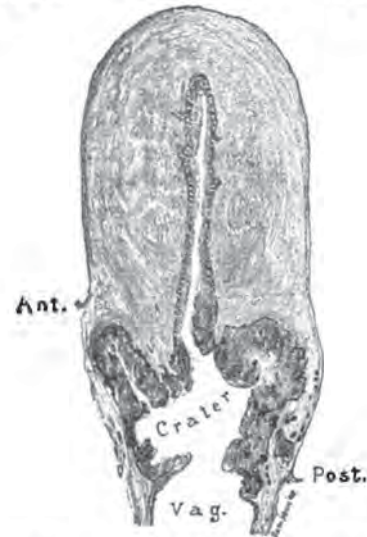
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FIG. 13.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting, with Extensive Necrosis (Gyn. Path. No. 7602).

Patient 40 years old; 3 children (age ?). Uterine bleeding and a foul discharge had been present for eight months, patient had been treated locally with electricity, twice a week, during the last four months. Pain, she had, was probably due to the pelvic inflammatory disease. General condition was fairly good, hæmoglobin 70 per cent.

Movements of the uterus were slightly restricted and the involvement of the left side of the vagina probably accounted for the apparent indurated parametrium of that side.

Vaginal portion of the cervix (natural size and never curreted), shows that the cervix has been converted into a craterous cavity lined by friable cancerous tissue, which has destroyed the greater portion of the vaginal portion of the cervix and has invaded the left side of the vagina.



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FIG. 14.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 13.

The cavity was caused by the necrosis of the cancer and shows how the disease usually stops at the level of the internal os.

Parametrium of both sides were involved by a direct extension of the disease and a metastasis to a parametrial lymph node was found in the left side. Cancer was not found in the pelvic lymph nodes examined.

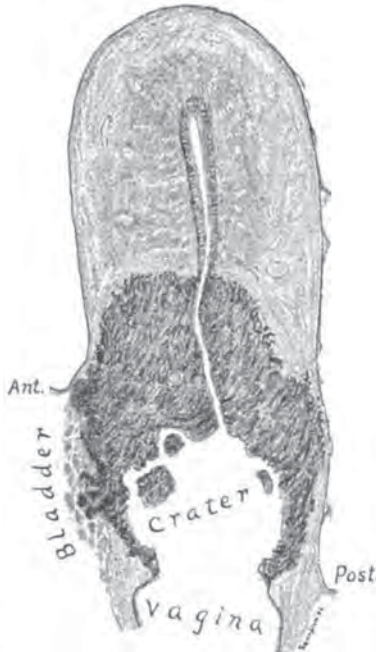


FIG. 15.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting; Extension with Involvement of the Bladder (Gyn. Path. No. 6715).

Patient 36 years old; 7 children (18-5 years). Uterine bleeding, alternating with a foul discharge, had been present for four months. Slight pain in the lower abdomen was probably due to adhesions from the pelvic inflammatory disease. General condition was fairly good.

Movements of the uterus were limited by the pelvic inflammatory disease and extension of the disease into the parametrium.

Stained sagittal section of the uterus demonstrates the invasion of the bladder muscle and the craterous cavity resulting from the necrosis of the cancer. The disease had invaded both parametria and had metastasized to the pelvic lymph nodes. The body of the uterus is beginning to be invaded by the growth.

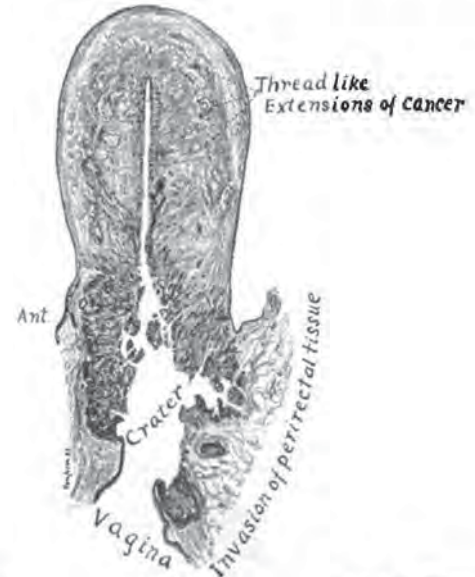


FIG. 16.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; Inverting; Extension with Obliteration of the Cul-de-sac and beginning Involvement of the Rectum (Gyn. Path. No. 7419).

Patient 37 years old; 6 children (14 years to 13 months). Bleeding, of ten months' duration, began three months after her last pregnancy. Condition was fairly good, hæmoglobin 73 per cent.

Movements of the uterus were restricted by the extension of the growth posteriorly and also by the apparent induration of the parametrium.

Stained sagittal section of the uterus shows the craterous cavity resulting from the necrosis of the growth, the extension of the disease into the body of the uterus as thread-like processes and the direct extension of the disease posteriorly obliterating the cul-de-sac and invading the tissue about the rectum.

The parametrium was involved by direct extension and cancer had metastasized to the pelvic lymph nodes.



FIG. 17.—Squamous Cell Carcinoma, Vaginal Portion of the Uterine Cervix; both Inverting and Everting (Gyn. Path. No. 7467).

Patient 50 years old; 3 children (25-20 years); menopause one year ago. Bleeding had been present for three months, first noticed when straining at stool, severe hæmorrhages six weeks ago, and more or less constant offensive watery discharge, but no pain. General condition was good, hæmoglobin 74 per cent.

Movements of uterus were limited by pelvic adhesions, but the parametrium felt normal.

Vaginal portion of the cervix (natural size and not curetted), shows that the entire cervix is indurated and the outer portion of the posterior lip has become "ulcerated" and from the floor of the ulcer has arisen a cauliflower or everting growth. Another cauliflower growth is seen, about to "burst through" the center of the anterior lip.

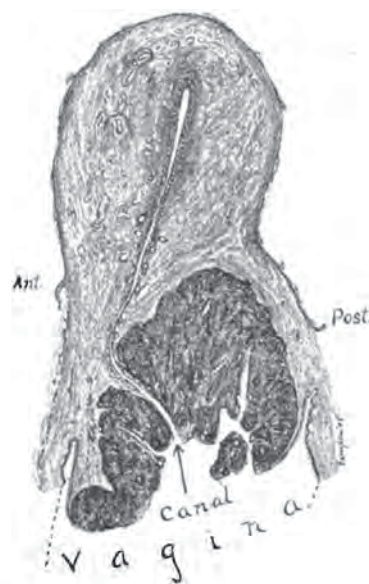


FIG. 18.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 17.

The growth is invading the cervical tissue *en masse* and in the posterior wall has reached the level of the internal cervical os. Notice how it grows through the cervical tissue and not along the cervical canal.

The adhesions on the surface of the uterus are shown. Cancer was not found in either the parametrium or pelvic lymph nodes removed.

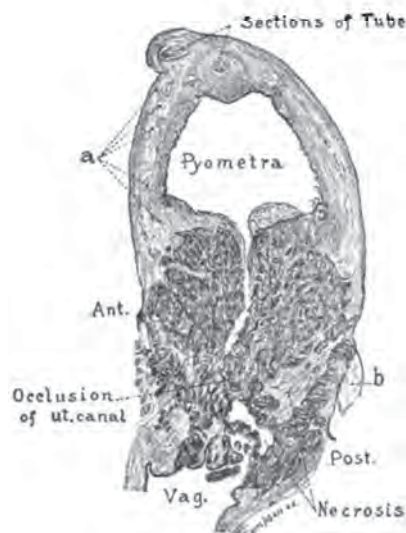


FIG. 19.—Squamous Cell Carcinoma, Cervical Canal; Everting. Causing Occlusion of the Canal and Pyometra (Gyn. Path. No. 7658).

Patient 63 years old; 7 children (youngest 26); menopause sixteen years ago. Bleeding for three months had been the only symptom. General condition was excellent, hæmoglobin 85 per cent.

Movements of the uterus were limited by pelvic adhesions from double pyosalpinx, probably secondary to pyometra. Parametrium on both sides was indurated.

Vaginal portion of the cervix (natural size and not curetted) has become indurated, retracted and puckered and protruding from the external os is a cauliflower or everting growth.



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FIG. 20.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 19.

The canal has been occluded by the growth, causing a pyometra. The fundus has become invaded by thread-like extensions of the growth (a) and the invasion of an adherent epiploic appendage of the sigmoid (b) is shown. The retracted shrunken and puckered vaginal portion of the cervix is also shown.

The parametrium on both sides was invaded by the growth and metastases to the pelvic lymph nodes were found.



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FIG. 21.—Squamous Cell Carcinoma, Cervical Canal; Inverting (Gyn. Path. No. 8153).

Patient 46 ? years old; 9 children (youngest 10 years). History very unsatisfactory, but symptoms apparently of very short duration. Diagnosis was made by curetting a small piece of tissue from within the external os. General condition was excellent.

Uterus was freely movable and parametrium on both sides was apparently normal.

Vaginal portion of the cervix (natural size, had been curetted) showed absence of vaginal epithelium about the external os, probably caused by the curette. The anterior lip was a little retracted about the external os and just within the canal could be seen friable cancerous tissue.



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FIG. 22.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 21.

The growth has started within the canal and has involved the latter as high as the internal os and is invading the cervical tissue on all sides in a diffuse manner. (a) represents the junction of the vaginal mucosa and the growth within the posterior lip.

Cancer was not found in the parametrium. The pelvic lymph nodes had not been removed.



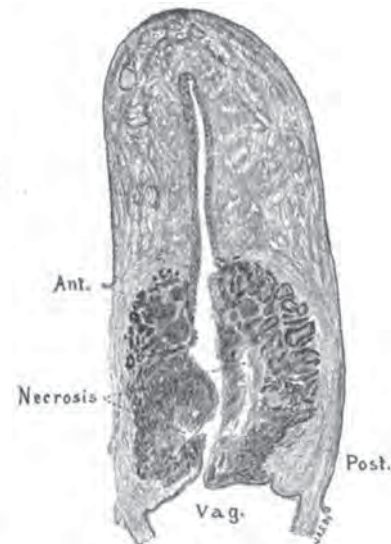
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FIG. 23.—Squamous Cell Carcinoma, Cervical Canal; Inverting. A Later Stage than One Shown in Fig. 21 (Gyn. Path. No. 6074).

Patient 54 years old; 6 children (youngest age ?); menopause eight years ago. Bleeding had been present for eight months, constant but never profuse; no other symptoms. General condition was good, hæmoglobin 75 per cent.

Uterus was movable, parametrium of the right side was apparently normal, that of the left side felt slightly indurated.

Vaginal portion of the cervix (natural size—small piece removed from within the canal for diagnosis) shows very well the indurated, retracted, and puckered vaginal portion of the cervix caused by the invasion of the cervical tissues from above.



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FIG. 24.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 23.

The growth has started within the canal and has involved nearly the entire cervix extending above as high as the internal os. Metastases had occurred to the lymph nodes of both the parametrium and the sides of the pelvis.



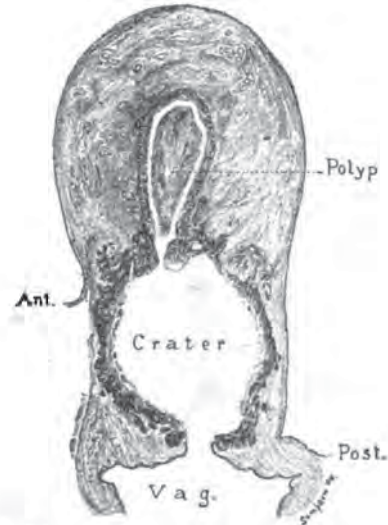
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FIG. 25.—Squamous Cell Carcinoma, Cervical Canal; Inverting. A later stage than the one shown in Figs. 23 and 24 (Gyn. Path. No. 6860).

Patient 48 years old; 8 children (aged ?); still menstruating. Bleeding had been of eighteen months' duration, foul watery discharge of shorter duration, some pain possibly due to the adhesions from a previous pelvic inflammation. Uterine polyp, may have accounted for some of the bleeding. Condition was fairly good, hæmoglobin 80 per cent.

Movements of the uterus were restricted and parametria of both sides felt indurated.

Vaginal portion of the cervix (natural size and never curetted) shows very well how the growth within may be very extensive and yet the vaginal portion of the cervix may be but very little involved. Notice the shrunken, puckered, and retracted vaginal portion of the cervix caused by the necrosis of the growth.



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FIG. 26.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 25.

The "craterous" cavity resulting from the necrosis of the growth is shown and the latter is beginning to invade the body of the uterus. A polyp is present in the fundus.

There was hypertrophy of the connective tissue of the parametrium, but the primary growth was apparently limited to the uterus. Metastases were found in the pelvic lymph nodes of both sides.



FIG. 27.—Squamous Cell Carcinoma, Cervical Canal; Inverting. An Extensive Growth of "Scirrhus" type (Gyn. Path. No. 7468).

Patient 37 year old; 7 children (15-2½ years). Bleeding had been the only symptom; of two years' duration, at first irregular but very profuse; constant the last three months. Patient was anæmic, hæmoglobin 55 per cent.

Parametrium was apparently indurated, growth had involved the deeper tissues of the vagina, all around the cervix.

Vaginal portion of the cervix (natural size, never curetted), shows that both lips present an "eroded" appearance with an irregular "fringe" of vaginal mucosa about the circumference. The eroded portion of the cervix appears "honey-combed" and the vagina about the cervix is indurated as a result of the invasion of its deeper tissues.

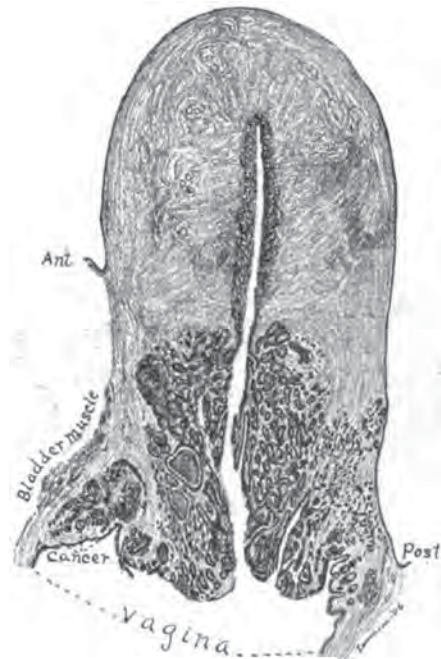


FIG. 28.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 27.

The growth is shown invading the deeper vaginal tissue, and the vaginal mucosa of the vaginal portion has sloughed off from the greater portion of both cervical lips. The disease does not extend above the internal os.

The growth had also extended in the parametrium of both sides, but cancer was not found in the pelvic lymph nodes removed.



FIG. 29.—Squamous Cell Carcinoma; Inverting; Origin ? but probably Vaginal Portion of Cervix (Gyn. Path. No. 7370).

Patient 35 years old; 2 children (ages?). A leucorrhœal discharge had been present for six months, bloody every time she had sexual intercourse or used a douche. Pain, for several years, was due to pelvic adhesions from previous inflammatory trouble. General condition was fair, hæmoglobin 75 per cent.

Uterus was adherent. parametrium on both sides indurated, and posterior vaginal wall involved.

Vaginal portion of the cervix (natural size, never curetted), shows that both lips present an "eroded" appearance, the posterior lip being much larger than the anterior, and on the outer right half of the latter a small area of mucosa is still present. The growth has involved the entire posterior vaginal wall, causing a large ulcer whose floor is composed of friable cancerous tissue.

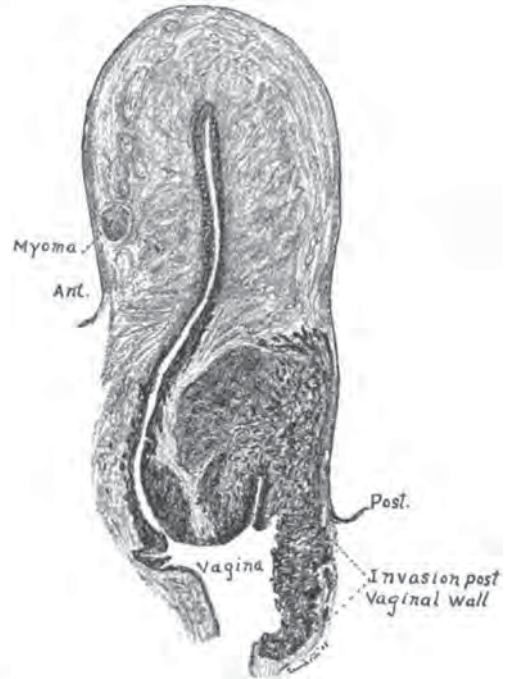


FIG. 30.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 29.

The growth is limited almost entirely to the deeper tissues of the posterior cervical wall and vagina. The cervical canal is involved only about the external os and for a short distance within, the anterior lip is compressed, and involved only about the external os.

Cancer was found in both the parametrium and pelvic lymph nodes.



FIG. 31.—Adenocarcinoma; Cervical Canal—Originally Everting (Gyn. Path. 6603).

Patient 37 years old; 4 children (21-15 years). Bleeding began seventeen months ago, and seven months ago a fungoid growth was removed from the cervix and there has not been any bleeding since, but for the last five months there has been severe pain in lower abdomen and back, requiring morphia. General condition was fairly good, hæmoglobin 60 per cent.

Uterus was movable, parametrium of each side felt normal.

Vaginal portion of the cervix (natural size and from which a fungoid growth had been removed seven months ago) shows that both cervical lips appear normal, but the external os is a little enlarged, edges ragged, and within can be seen and felt friable tissue.



FIG. 32.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 31.

An adenomatous growth has invaded nearly the entire cervix about the external os and is gradually replacing the endometrium of the body of the uterus.

Cancer was present in both the parametrium and pelvic lymph nodes.

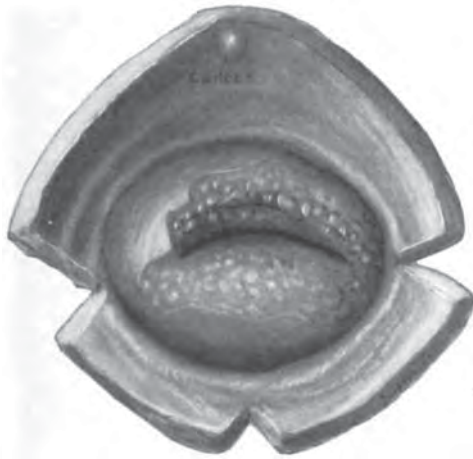


FIG. 33.—Adeno-carcinoma, Probably Starting in the Cervical Canal; Inverting (J. H. H., Path. No. 2377).

Patient 40 years old; 7 children (13-2 years). Bleeding for six months had been the only symptom. Local treatment before entering the hospital (length of time?). General condition was bad.

Uterus was movable, some induration of the left parametrium. Patient died from cerebral embolism, following acute endocarditis. Specimen was obtained at autopsy a few hours after death.

Vaginal portion of the cervix (natural size, local treatment, including curettage for sometime before patient came to hospital), shows that about one-third of the surface is covered by mucosa, while the rest presents an "eroded" appearance, the extreme left side and also the portion of the anterior lip about the external os being composed of friable tissue which bled on palpation. A small cancerous nodule was found in the anterior vaginal wall about 1.5 cm. from the cervix.

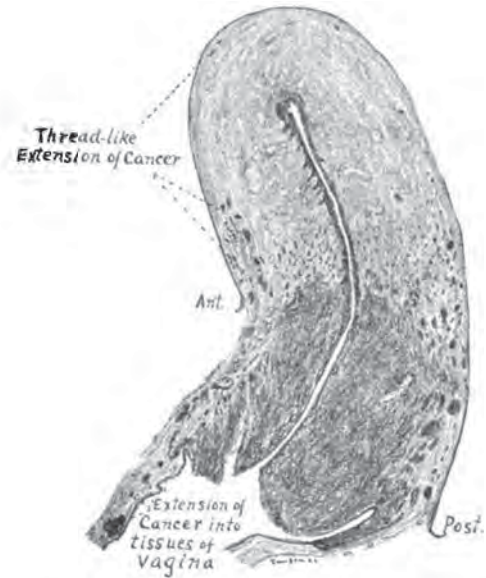


FIG. 34.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 33.

The growth apparently started from the deep cervical glands, the superficial cervical mucosa being for the most part intact. The growth has invaded the body of the uterus and the deep tissues of the vagina.

Cancer was found in the parametrium of both sides, liver, diaphragm, lungs and thoracic, abdominal and pelvic lymphatics.



FIG. 35.—Adeno-carcinoma; Cervical Canal, with Possibly Squamous Cell Carcinoma of Vaginal Portion of Cervix (Gyn. Path. No. 8154).

Patient 62 years old; 4 children (41-35 years); menopause seventeen years ago. Constant bloody discharge had been present for seven months, and at times bearing-down pains in the uterus. Condition was fairly good.

Movements of the uterus were restricted by adhesions from previous pelvic inflammation. Parametrium on the left side felt indurated.

Vaginal portion of the cervix (natural size and never curetted) shows the shrunken, puckered, and retracted cervix, so characteristic of the advanced cases of cancer developing within the canal. Just within the external os, friable tissue which bled easily could be palpated.

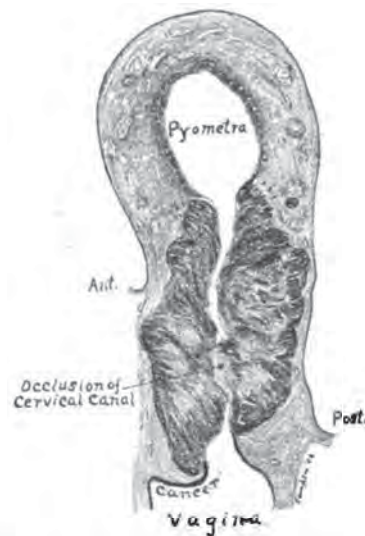


FIG. 36.—Stained Sagittal Section of Uterus (slightly reduced), shown in Fig. 35.

The growth has occluded the cervical canal causing pyometra. It is also beginning to invade the body of the uterus. The vaginal portion of the uterus is apparently covered by a thin layer of cancerous tissue of the squamous cell type which, to the naked eye, looks like the normal mucosa.



FIG. 37.—Adeno-carcinoma ?; Cervical Canal; Inverting. Very Malignant (Gyn. Path. No. 6763).

Patient 41 years old; 1 child (9 years). Only symptom was bleeding, of three weeks' duration. General condition was excellent, hæmoglobin 85 per cent.

Uterus was freely movable; apparently a very early growth.

Vaginal portion of the cervix (natural size, a small piece had been removed from within the external os for diagnosis) is apparently normal for a parous woman, except for a small nodule of tissue seen just within the external os and apparently arising from the anterior cervical wall.



FIG. 38.—Stained Sagittal Section of the Uterus (slightly reduced), shown in Fig. 37.

A growth has arisen from within the cervical canal, apparently an adenocarcinoma. It has spread over the posterior surface of the cervical canal and is invading the deeper tissues. The anterior surface of the canal is involved just within the external os; a second cancerous nodule or part of the primary growth is seen just posterior to the other. It was impossible to determine its exact relation to the first one. Cancer was not found in the parametrium. The growth recurred soon after operation.

the fifteen cases, there was a history of neglected uterine bleeding for six months or more, but in two cases with metastases to the pelvic lymph nodes this was of less than two months' duration. As the disease invades the cervical tissue, necrosis usually occurs with a resulting ulcer. Occasionally the tumor may increase greatly in size with but very little necrosis, but usually the one closely follows the other. As the cervical tissue becomes invaded by the growth necrosis usually occurs, later the cervical canal becomes surrounded, then invaded and the central core of the cervix may slough away, and thus convert the cervix into a crater lined with cancerous tissue.

In the seven cases of bleeding for six months or over, the cervix had been converted into a crater in four of the cases. While a long duration usually indicates an extensive growth it does not necessarily follow as shown in Fig. 9, nor does one of apparently short duration indicate an early one, see Fig. 11.

This type of growth is a very unfavorable one, usually soon invading the surrounding tissues and even metastasizing before the latter becomes involved. The symptoms may appear early or late, depending on how soon necrosis appears and its extent. We are unable to make a definite prognosis from the history of the case, or the results of clinical or pathological examinations unless it be that if metastases are present the prognosis is very unfavorable. A history of long duration may reveal an early growth, one of short duration an extensive one, and a small primary growth may give rise to metastases and an extensive one may still be local.

Squamous Cell Carcinoma—Cervical Canal.

This occurred in five instances, in four cases inverting and in one everting. In the latter case, pyometra was present. The inverting type of growth undergoes the same changes as the inverting type arising from the vaginal portion of the cervix. It, however, offers the additional clinical disadvantage that it is situated within the cervical canal and this renders its diagnosis by inspection or palpation more difficult. It is remarkable how far advanced the growth may be and yet the mucosa of the vaginal portion of the cervix may be intact or but little involved, as shown in the illustrations. There is one very important clinical feature to be emphasized and that is the induration, retraction, and puckering of the vaginal

portion of the cervix caused by the growth invading it from above, analagous to a similar condition of the skin or nipple of the breast usually seen in cancer of that organ.

The Clinical Significance of Adeno-carcinoma of the Cervix.

There were but four instances of this type of growth, and all arose in the cervical canal. One was probably of the everting type but the everting part had been removed before I saw the patient. In all specimens the growth had extended beyond the uterus, and all four patients are dead. One died from cerebral embolism due to acute endocarditis, another died on the fifteenth day after hysterectomy, and the two others died from recurrences within a year and a half after hysterectomy. All four cases could not have been cured at the time of the operation. Bleeding as a symptom was present in these four cases; in one three weeks, in the three others six, seven, and seventeen months, respectively.

These four cases support the view that this is the most malignant form of uterine cancer.

CONCLUSIONS.

From a study of these cases, some of the types of cervical cancer may be seen and the changes they undergo as the disease progresses, and from this study we are able to understand the clinical manifestations of the disease. One very important feature must be emphasized and that is the importance of an early diagnosis, for the parametrium was involved in seventeen of the twenty-seven operable cases and the pelvic lymph nodes were involved in nine out of nineteen cases where they were removed and studied. In three of the nine cases in which the pelvic lymph nodes were involved, the parametrium was free, thus demonstrating that, in at least twenty of the twenty-seven cases, the growth had extended beyond the uterus.

One hopeful sign, however, was present and that is there was a history of neglected uterine bleeding for six months or more in over half of the cases. Put back the growth where it was six or even two months before the cases were operated upon and probably it would have been local in the majority of them. What we need is a *prophylaxis* of the incurable stage, and that can come only by the education of both physician and patient, the former first; and to him this contribution is offered.

STUDIES IN GENITO-URINARY SURGERY

THE JOHNS HOPKINS HOSPITAL REPORTS, Volumes XIII and XIV, will be issued in January, 1907, Volume XIII will consist of about 605 pages with 201 figures in the text, six plates and one colored chart.

Volume XIV will consist of about 632 pages, and have 97 figures in the text.

The price of each volume will be five dollars (\$5.00), bound in paper, and five dollars and fifty cents (\$5.50), bound in cloth.

Remittances and orders will now be received.

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