

**EVERYONE'S GUIDE FOR CANCER THERAPY**  
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4<sup>th</sup> Edition, 2001

**Vagina**

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Carcinoma of the vagina is a relatively uncommon disease, affecting only about 2,000 women in the United States each year. It accounts for only 1 to 2 percent of all gynecologic malignancies. Cancer arising in another organ that spreads to the vagina is much more common.

**Types** The most common type of vaginal cancer (85 percent) develops in the surface (squamous) cells lining the vagina (squamous cell tumors). About 5 percent develop in glandular tissues (adenocarcinoma). Other cell types include melanoma (3 percent), sarcomas (3 percent) and endodermal sinus tumor (1 percent).

Squamous cell carcinomas, leiomyosarcomas and melanomas generally arise in older women. Adenocarcinomas and rhabdomyosarcomas usually occur during adolescence. The very rare sarcoma botryoides and endodermal sinus tumors most frequently occur in infants.

**How It Spreads** Squamous cell carcinomas that originate in the skin that lines the vagina can remain confined to the lining for some time. At this stage it is known as vaginal intraepithelial neoplasia (VAIN), dysplasia, or more recently as vaginal squamous intraepithelial lesion (SIL).

Eventually it will invade the vaginal wall. With time, the tumor can extend directly to the tissue surrounding the vagina, the pelvic walls, the bladder or rectum.

Lymphatic invasion and metastases is another avenue of spread. Carcinomas arising in the upper vagina can spread to the pelvic and aortic lymph nodes, and those in the lower vagina to the lymph nodes in the groin.

Adenocarcinomas spread in a similar fashion, but they may have a higher incidence of metastases to the lymph nodes (*see "Cervix"*).

**What Causes It** The human papilloma virus (HPV), a sexually transmitted virus responsible for genital warts, is believed to cause vaginal intraepithelial neoplasia and invasive squamous cell carcinoma of the vagina. The time from infection to the development of an invasive cancer is thought to be from 5 to 10 years.

Most cases of adenocarcinoma of the vagina used to be associated with exposure to diethylstilbestrol (DES) in embryonic life. DES was given in the 1950s to women who were thought to be at risk for miscarriage. The incidence of DES-related adenocarcinoma is highest for those women who were exposed during the first three months of their mother's pregnancy. The peak incidence is between age 17 and 21. The incidence of this disease peaked in the early 1970s and is now rare, since DES use during pregnancy fell out of favor during the 1960s and was banned in the early 1970s.

What causes other vaginal tumors is not clear.

### **RISK FACTORS**

Squamous cell carcinoma of the vagina is associated with a previous history of genital warts or of intraepithelial or invasive carcinoma of the cervix or vulva. In 10 to 20 percent of women with squamous cell carcinoma of the vagina, there is a history of vaginal radiation therapy, usually for a cervical cancer.

### **SCREENING**

Screening for malignancies of the vagina is similar to screening for cervical cancer. A careful annual pelvic examination and Pap smear is recommended. Women who have been exposed to DES are followed more carefully with twice-yearly pelvic examinations, Pap smears of the cervix and vaginal wall and colposcopic (magnification) examination of the vagina.

### **COMMON SIGNS AND SYMPTOMS**

The most common symptoms are abnormal vaginal bleeding and a foul-smelling vaginal discharge. There may be pain in the pelvis, back or legs, as well as leg swelling (edema).

### **DIAGNOSIS**

#### ***Physical Examination***

- A careful gynecologic, pelvic and rectal examination is performed to assess the local spread of the cancer.
- Women with vaginal SIL are evaluated with a colposcope.

- Examination of the lymph nodes in the groin and neck and an abdominal examination are important to detect masses.

### ***Blood and Other Tests***

- Complete blood count (CBC).
- Serum carcinoembryonic antigen (CEA) and serum squamous cell carcinoma antigen.
- Serum alpha-fetoprotein (for an endodermal sinus tumor).
- Serum kidney and liver function tests.

### ***Imaging***

- Chest x-ray.
- CT scan of the pelvis and abdomen (for advanced cases).
- MRI of the pelvis (on occasion).

### ***Endoscopy and biopsy***

- Cystourethroscopy for advanced cases.
- Proctosigmoidoscopy for advanced cases.
- The cancer is confirmed by a vaginal biopsy.

## **STAGING**

Vaginal carcinoma is staged by either the FIGO system (International Federation of Gynecologists and Obstetricians) or the TNM classification. IN the TNM system, N1 indicates

pelvic lymph node metastases when the upper two-thirds of the vagina is involved or groin node metastases on one side when the lower two-thirds of the vagina is involved. N2 indicates groin node metastases on both sides.

### **TREATMENT OVERVIEW**

Several factors are considered in choosing the most appropriate way to manage vaginal cancer, including the cell type, stage, size, location of the lesion, presence or absence of the uterus and whether the woman has had previous radiation to the pelvis.

Early carcinomas are generally treated with either surgery or radiation therapy and chemotherapy. The radiation therapy involves radioactive material placed against the cancer (intracavitary) or radioactive material temporarily placed directly into the cancer (interstitial radiation). External radiation is given in divided doses to the pelvis five days a week for five weeks.

Advanced cancers are treated with radiation therapy with simultaneous administration of combination chemotherapy.

### **TREATMENT BY STAGE**

***STAGE 0 (squamous cell carcinoma)***

***TNM*** Tis, N0, M0

Carcinoma in situ or intraepithelial carcinoma.

**Standard Treatment** There are a number of effective treatments, including the partial or complete removal of the vagina (vaginectomy), which occasionally requires a skin graft. The tumor may also be treated with laser therapy, intravaginal chemotherapy with 5-fluorouracil cream or intracavitary radiation.

**Five-Year Survival** 100 percent.

**Investigational** None.

***STAGE I (squamous cell carcinoma or adenocarcinoma)***

**TNM** T1, N0, M0

The carcinoma is limited to the vaginal wall.

**Standard Treatment** Young women with lesions involving the upper third of the vagina can be treated by a radical vaginectomy, radical hysterectomy and removal of the pelvic and sometimes the aortic lymph nodes on both sides.

Equally effective for all Stage I tumor, regardless of age and site, is external beam radiation therapy with concurrent chemotherapy and intracavitary or interstitial radiation therapy. Smaller lesions are sometimes treated with only intracavitary or interstitial radiation therapy.

***Five-Year Survival*** 70 to 95 percent.

**Investigational**

- Meticulous laparoscopic or conventional surgical staging before radiation therapy.
- Chemotherapy given simultaneously with radiation therapy. Chemotherapeutic regimens under investigation include 5-fluorouracil (5-FU) with cisplatin.
- High-dose rate radiation therapy.
- Radiation therapy with heat (hyperthermia).

***STAGE II (squamous cell carcinoma an adenocarcinoma)***

***TNM*** T2, N0, M0

The carcinoma involves the adjacent vaginal tissue but has not extended to the pelvic wall.

**Standard Treatment** External beam radiation with chemotherapy and interstitial or intracavitary radiation.

***Five-Year Survival*** About 50-7- percent.

**Investigational** Same as Stage I.

***STAGE III AND STAGE IVA (squamous cell carcinoma and adenocarcinoma)***

***Stage III TNM*** T3 (or less), N1, M0 or T3, N0, M0.

The carcinoma has extended to the pelvic wall.

**Stage IVa TNM** Any t, N2, M0 or T4, N0, M0.

The carcinoma has extended beyond the true pelvis or involves the lining of the bladder or rectum.

**Standard Treatment** These carcinomas are generally treated with external beam with concurrent chemotherapy, intracavitary or interstitial radiation therapy. Radical surgery is an option in selected cases.

**Five-Year Survival** About 30 percent for Stage III, about 10-20 percent for Stage IVa.

**Investigational** Same as Stage I.

#### **STAGE IVB**

**TNM** Any T, any N, M1

There is spread to distant organs.

**Standard Treatment** Neither radiation nor surgery can cure women with distant metastases, but both are used for local relief of symptoms.

A number of chemotherapy regimens that are effective in the treatment of metastatic cervical cancer are also used to treat metastatic vaginal cancers-various doses and combinations of cisplatin, carboplatin, mitomycin-C, vincristine, bleomycin, cisplatin, ifosfamide, etoposide.

***Five-Year Survival*** Less than 10 percent.

### **Investigational**

- Various doses and combinations of chemotherapeutic drugs are being evaluated, including cisplatin, carboplatin, ifosfamide, etoposide, mitomycin-C, 5-FU, vincristine, vinblastine, mitoxantrone, bleomycin and methotrexate.

### **TREATING OTHER CELL TYPES**

**Endodermal Sinus Tumors** These are extremely rare and are treated with surgery and combination chemotherapy programs such as cisplatin + bleomycin + etoposide.

**Vaginal Sarcomas** Sarcomas of the botryoid type are treated with combination chemotherapy, including vincristine, actinomycin-D, Cytosan and dacarbazine (DTIC) or mitomycin, Adriamycin, and ifosfamide followed by surgery or radiation therapy as indicated. (See "*Sarcomas*")

**Malignant Melanoma** These tumors are generally treated by aggressive surgery, but the overall survival rate is extremely poor-less than 15 percent. Advanced melanomas are

treated with chemotherapy regimens including dacarbazine (DTIC) + cisplatin + Cytosan + tamoxifen (See "*Melanoma*").

### **TREATMENT FOLLOW-UP**

After therapy, women are followed every three months with a careful general physical examination, pelvic examination and Pap smear.

- A chest x-ray or an abdominal or pelvic CT scan may be obtained if symptoms warrant.
- If the serum CEA, squamous cell carcinoma antigen and/or AFP were elevated before therapy, they can be followed to detect recurrent disease.

### **RECURRENT CANCER**

Vaginal cancer can recur in the vagina, pelvis, liver, lungs and lymph nodes. Symptoms of recurrent disease include weight loss, vaginal or rectal bleeding, bleeding from the urinary tract, pain in the pelvis, back or leg, leg swelling and the development of a chronic cough.

- If the tumor is confined to the vagina, bladder and/or rectum, a recurrent vaginal carcinoma may be treated by the removal of the vagina, bladder and/or rectum (pelvic exenteration).
- Locally recurrent unresectable and/or metastatic disease is treated with single chemotherapeutic drugs such as cisplatin or carboplatin, or combination chemotherapeutic drug regimens such as mitomycin-C + vincristine + bleomycin + cisplatin, or carboplatin/or cisplatin + ifosfamide + etoposide.

## **Investigational**

- Various doses and combinations of the different chemotherapeutic drugs are being studied, including cisplatin, carboplatin, ifosfamide, etoposide, mitomycin-C, 5-FU, vincristine, vinblastine, mitoxantrone, bleomycin and methotrexate.

## **THE MOST IMPORTANT QUESTIONS YOU CAN ASK**

- What qualifications do you have for treating cancer?
- Will a gynecologic oncologist be involved in my care?
- What stage of cancer do I have?
- What is the cell type?
- Was the cancer related to DES (diethylstilbestrol)?
- What signs and symptoms should I look for after I've been treated?