Vaginal cancer

What is vaginal cancer?[1]

Vaginal cancer is usually a squamous cell carcinoma involving the posterior wall of the upper third of the vagina. It may directly invade the bladder or rectum. Lesions may be ulcerative or exophytic.

Those in the upper vagina metastasise in a similar way to cervical carcinoma - eg, regional lymph nodes and para-aortic nodes. Those in the middle can invade in either direction. Tumours in the lower third metastasise mainly to inguinal nodes.

The distinction between squamous cell carcinoma and adenocarcinoma is important because the two types represent distinct diseases, each with a different pathogenesis and natural history:

- Approximately 80% of cases of primary vaginal cancer are squamous cell vaginal cancer. This initially spreads superficially within the vaginal wall and later invades the paravaginal tissues and the parametria. Distant metastases occur most commonly in the lungs and liver.
- Approximately 15% of cases of primary vaginal cancer are adenocarcinoma. This has a peak incidence between 17 and 21 years of age and differs from squamous cell carcinoma by an increase in pulmonary metastases and supraclavicular and pelvic node involvement.
- 80% of vaginal carcinoma is metastatic spread, such as from the urethra, bladder, Bartholin's gland, rectum, endometrium, kidney, ovary or endocervix.

Rarely, melanoma and sarcoma are described as primary vaginal cancers.

Adenosquamous carcinoma is a rare and aggressive mixed epithelial tumour comprising approximately 1-2% of cases. Clear cell adenocarcinomas plus vaginal adenosis are most often associated with in utero exposure to diethylstilbestrol.

Primary vaginal cancer can only be diagnosed if the cervix is uninvolved or only minimally involved by tumour obviously of vaginal origin. Where malignancy involves both the cervix and vagina and histology indicates either origin, then it is conventionally denoted as a cervical carcinoma.

Some vaginal cancers are preceded by vaginal intraepithelial neoplasia (VAIN).[2]

How common is vaginal cancer? (epidemiology)[3]

- Vaginal cancer accounts for less than 1% of all new cancer cases in females in the UK (2016-2018).
- Incidence rates for vaginal cancer in the UK are highest in females aged 85 to 89 (2016-2018). 37% of all new vaginal cancer cases in the UK are diagnosed in females aged 75 and over (2016-2018).
- Since the early 1990s, vaginal cancer incidence rates have remained stable in females in the UK (2016-2018). Vaginal cancer incidence rates are projected to fall by 15% in the UK between 2023-2025 and 2038-2040.
- Vaginal cancer incidence rates in England in females are 88% higher in the most deprived quintile compared with the least (2013-2017).
- Older age is the main risk factor for cancer. Most vaginal cancers occur in postmenopausal or elderly women. When occurring in younger patients, the disease seems to be aetiologically related to cervical neoplasia, and therefore HPV dependent.[2]
- 75% of vaginal cancer cases in the UK are caused by human papillomavirus (HPV) infection. Vaginal cancer risk is 5 times higher in women with HPV16 antibodies versus those without. HPV16 is present in 59% of vaginal cancers, a cross-sectional study showed.

- People with HIV infection often also have human papillomavirus (HPV), and HIV may facilitate initiation or persistence of HPV infection. Vaginal cancer risk is 9 times higher in women with HIV compared with the general population. Some studies show a particularly strong relationship for women under 30 years old.
- Vaginal clear cell adenocarcinoma (a rare subtype) risk is higher in women whose mothers took diethylstilboestrol during pregnancy.

Symptoms of vaginal cancer (presentation)

- Vaginal bleeding or bloody discharge may be seen.
- Advanced tumours may affect the rectum or bladder, or extend to the pelvic wall, causing pain or leg oedema.

NICE recommends considering a suspected cancer pathway referral (for an appointment within 2 weeks) for vaginal cancer in women with an unexplained palpable mass in or at the entrance to the vagina. Urgent investigations/referral should also be considered for any woman presenting with abnormal vaginal bleeding or unexplained vaginal discharge.[4]

Editor's note
Dr Krishna Vakharia, 16th October 2023 **Suspected cancer: recognition and referral**[4] The National Institute for Health and Care Excellence (NICE) has recommended that a person should receive a diagnosis or ruling out of cancer within 28 days of being referred urgently by their GP for suspected cancer.

Diagnosing vaginal cancer (investigations)[1]

Investigations include:

- Colposcopy; because vaginal intraepithelial neoplasia (VAIN) is associated with other genital neoplasias, the cervix (when present) and vulva should be examined carefully.
- Biopsy, cervical cytology, endometrial biopsy.

- CT scan.
- Fluorodeoxyglucose-positron emission tomography (FDG-PET) - may be more sensitive than CT scanning.[5]
- CXR.
- Cystoscopy, sigmoidoscopy.

Staging[6]

International Federation of Gynaecology and Obstetrics (FIGO) staging system

- Stage 0 - squamous cell carcinoma in situ; this disease is usually multifocal and commonly occurs at the vaginal vault.
- Stage I - the disease is limited to the vaginal wall mucosa.
- Stage II - the disease involves the subvaginal tissue, but not the pelvic wall.
- Stage III - the disease extends to pelvic wall.
- Stage IV - the disease either extends beyond the true pelvis or involves the bladder or rectal mucosa:
  - Stage IVA - the disease has spread to adjacent organs.
  - Stage IVB - the disease has spread to distant organs.

Management of vaginal cancer[1]

Treatment options depend on tumour stage; surgery and radiotherapy are very effective in early-stage disease, whereas radiation therapy is the primary treatment for more advanced stages.

In general, surgery has a limited role in treating vaginal cancer due to the proximity of the cancer to normal tissues such as the bladder, rectum, and urethra. The general recommendation is that surgery might be considered in small stage I tumours (<2 cm in diameter) that are limited to the proximal part of the vagina.

Pelvic exenteration may play a role in patients with stage IV disease with recto-vaginal or vesico-vaginal fistula. In this case, the surgery may be done with pelvic node dissection. Pelvic exenteration may also play a role is when a patient has a central recurrence after radiation therapy.

Radiation therapy is the treatment of choice in most patients with vaginal cancer, especially in patients with advanced-stage disease. Radiation therapy usually consists of a combination of external beam radiation therapy and brachytherapy.

Chemoradiation therapy (CCRT) has been increasing in use for the treatment of vaginal cancer, mirroring the rates for the treatment of cervical cancer. Various retrospective studies have demonstrated a potential benefit of the use of CCRT for vaginal cancer. The most common agents used are cisplatin and 5-fluorouracil.[7]

Local recurrences in vaginal cancer are common, occurring in 23–26% of patients at 5 years, and about 80% of them occur within the first 2 years and 90% at 5 years.

Prognosis[3]

More than 8 in 10 women in England diagnosed with vagina or vulva cancer aged 15-49 survive their disease for five years or more, compared with almost 6 in 10 women diagnosed aged 70-89 (2009-2013).

For vaginal cancer, like other cancer sites, survival trends reflect a combination of changes in treatment and stage distribution. These factors themselves can vary by age, sex and deprivation.

Further reading

- Gynaecological cancers - recognition and referral; NICE CKS, February 2021 (UK access only)
- Adams TS, Rogers LJ, Cuello MA; Cancer of the vagina: 2021 update. Int J Gynaecol Obstet. 2021 Oct;155 Suppl 1(Suppl 1):19-27. doi: 10.1002/ijgo.13867.

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6. General Information About Vaginal Cancer; (US) National Cancer Institute
7. Kulkarni A, Dogra N, Zigras T; Innovations in the Management of Vaginal Cancer. Curr Oncol. 2022 Apr 27;29(5):3082-3092. doi: 10.3390/curroncol29050250.

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Originally Published: 20/11/2023	Next review date: 22/06/2023	Document ID: doc_1041