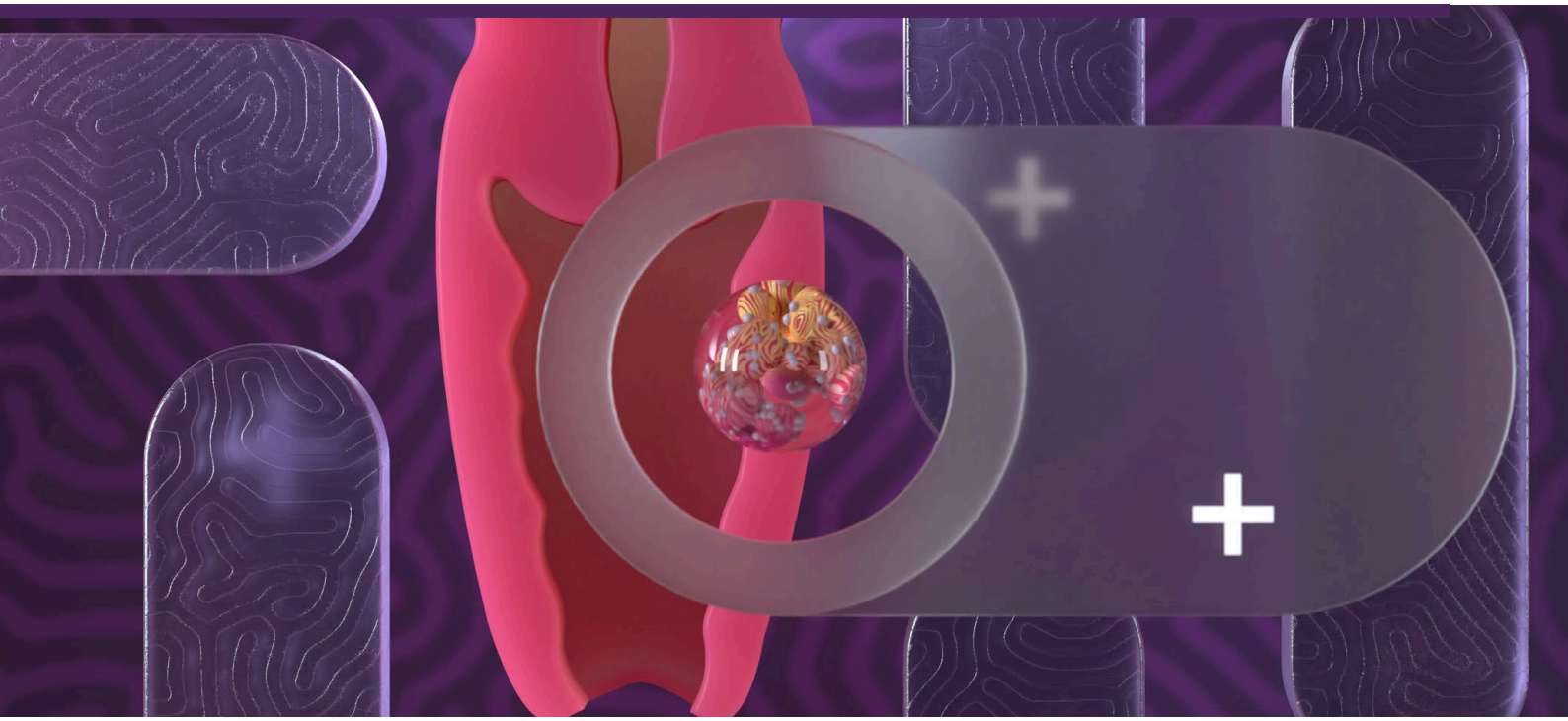

Vaginal cancer – early detection and referral

Vaginal cancer is the least common type of gynaecological cancer in New Zealand with an average of 17 females newly diagnosed each year (from 2015 – 2020). Primary vaginal cancer is very rare; most cancers affecting the vagina are secondary, involving metastases from another site such as the cervix.

KEY PRACTICE POINTS

- Primary vaginal cancers are rare and are defined as cancer found in the vagina without clinical or histological evidence of cervical or vulval cancer, or a prior history of these cancers within the past five years
  - Most tumours in the vagina (80%) are metastases from other gynaecological cancers. Less commonly, vaginal metastases occur with other cancer types, such as breast cancer.
- Squamous cell carcinoma is the predominant type of primary vaginal cancer, followed by adenocarcinoma. Rarely, melanomas, sarcomas and lymphomas are reported as primary vaginal cancers.
- As the majority of vaginal cancers are squamous cell carcinomas, risk factors are similar to those for cervical cancer, with human papillomavirus (HPV) infection being the most significant. Other risk factors include increasing age, history of cervical cancer or pre-cancerous cervical lesions, immunosuppression and cigarette smoking.
- Vaginal cancers typically arise from pre-cancerous vaginal lesions which occur from infection with HPV. Prophylactic HPV vaccination can prevent the acquisition of new HPV infections. Gardasil 9 is the currently recommended vaccine and is most effective when administered prior to the onset of sexual activity; it is funded for eligible females (and males) aged 9 – 26 years.
- Abnormal vaginal bleeding or malodorous discharge are the most frequently reported symptoms of vaginal cancer. Some people may be asymptomatic. People with advanced vaginal cancer typically experience pelvic pain and urinary and bowel dysfunction.
- There are no screening programmes for the early detection of vaginal cancer, but some people are diagnosed incidentally after an examination for other reasons, e.g. cervical screening. Most people are diagnosed with targeted investigations after symptoms are reported.
- The diagnostic workup of a patient with suspected vaginal cancer includes:
  - A focused history, considering relevant risk factors
  - A pelvic examination, including bimanual and speculum examination. Take a vaginal sample for cytology/HPV testing.
  - Additional laboratory tests, depending on individual factors. These may include: full blood count, ferritin, liver function tests, coagulation tests, thyroid stimulating hormone, urine pregnancy test or serum hCG.
- If the results from cytology are abnormal, or if the vagina is visually abnormal upon examination (irrespective of HPV and cytology results), refer the patient directly for a colposcopy or to gynaecology. Note "urgent" on the referral if there are specific concerns on examination. Patients will undergo further investigations, e.g. vaginal biopsy, and management in secondary care or a Gynaecological Oncology centre if required.

N.B. The term "female" is used in this article to describe the biological sex of the patient population at risk for vaginal cancer. However, we acknowledge that this may not reflect the identity of all patients, which will include transgender boys or men, intersex and non-binary individuals.

For information on the follow-up and surveillance of a patient after curative-intent treatment for vaginal cancer, see: **bpac.org.nz/2023/gynaecological-cancers.aspx**

Vaginal cancer is the least common type of gynaecological cancer

Vaginal cancer is the rarest type of gynaecological cancer in New Zealand with an average of 17 new diagnoses (0.4 per 100,000 females; from 2015 – 2020) and nine deaths (0.2 per 100,000 females; from 2015 – 2018) each year.*[1] Data in New Zealand are similar to the world age-standardised incidence and mortality rates (published in 2018).[2] Since vaginal cancers are rare, data are limited to single institutions or cohort studies with different patient demographics and treatment options;[3] five-year survival rates therefore vary widely. Some studies report overall five-year survival rates as 47 – 52%, while others report considerably higher (e.g. 95% for stage I) and lower (e.g. less than 20% for stage IV) rates.[4, 5]

* Data on vaginal cancer incidence and mortality rates are not published in the **Cancer: Historical summary 1948 – 2020** document that has been the primary source of data for the other gynaecological cancers in this series. Data reported here have been obtained directly from Te Whatu Ora/Health New Zealand. Mortality data are available for 2019, but are preliminary so have not been included.

The risk of vaginal cancer increases with age; it primarily affects older females with an average age at diagnosis of 60 – 70 years.[4, 6] However, vaginal cancer can still occur in younger females; vaginal adenocarcinomas have a peak incidence between the ages of 17 and 21 years.[4, 7]

Most vaginal cancers are secondary to another cancer

In the majority of cases (80%), a tumour in the vagina is attributed to metastases from another gynaecological cancer by either direct invasion from adjacent tumours (e.g. cervical or vulval) or through the lymphatic system (e.g. endometrial).[5, 7] Vaginal metastases can also rarely occur from other cancers such as breast, kidney, lymphoma or gestational trophoblastic disease.[3, 5, 7]

Primary vaginal cancers are rare and are defined as cancer found in the vagina without clinical or histological evidence of cervical or vulval cancer, or a prior history of these cancers in the past five years.[3] The vaginal apex or upper one-third of the vagina are the most common sites for vaginal cancer to develop.[7]

Squamous cell carcinoma is the predominant type of primary vaginal cancer, representing 80 – 90% of all cases, followed by adenocarcinoma for which the prognosis is worse.[6, 7] Other types of primary vaginal cancer such as melanoma (which typically occur in the distal vagina, on the anterior vaginal wall), sarcomas, e.g. leiomyosarcoma, and lymphomas are very rare.[4, 5]

Squamous cell carcinomas of the vagina typically arise from pre-cancerous lesions – vaginal intraepithelial neoplasia – that occur from infection with HPV (see: "HPV infection is the main cause of vaginal cancer").[3, 6] Low-grade squamous intraepithelial lesions (LSIL) represent a transient infection that will resolve for the majority of people. However, for some people, infection persists and high-grade squamous intraepithelial lesions (HSIL) develop which can then progress to invasive vaginal cancer.[7] The risk of progression from HSIL to invasive vaginal cancer is relatively low and ranges from 2 – 12%.[7]

HPV infection is the main cause of vaginal cancer

As the majority of primary vaginal cancers are squamous cell in origin, they share common risk factors with cervical cancer, the most significant being HPV infection (particularly with high-risk HPV type 16 and to a lesser extent, type 18).[6, 7] HPV is associated with 75 – 88% of all vaginal cancers.[4] See: "**Cervical cancer – early detection and referral**" for further information on HPV.

A personal history of cervical cancer or pre-cancerous cervical lesions also increases the risk of developing vaginal cancer.[4, 7] Up to 30% of people diagnosed with primary vaginal cancer have a history of *in situ* or invasive cervical cancer treated in the past five years.[5]

Other risk factors for vaginal cancer may include:*[3, 4, 7]

- Increasing age
- Immunosuppression
- Cigarette smoking
- Young age at sexual activity onset
- Increasing number of lifetime sexual partners
- *In utero* exposure to diethylstilboestrol (DES)†
- Pelvic radiation treatment for cervical cancer
- Low socioeconomic status
- History of genital warts

* It is unclear how significant some of these risk factors are given the limited data available. Many risk factors are based on older population or case-control studies.

† DES was used by approximately 1,000 pregnant females in New Zealand between the 1940s and 1960s to reduce the risk of miscarriage.[8] Female offspring exposed *in utero* prior to 18 weeks' gestation have an increased risk of clear cell adenocarcinoma of the vagina (and cervix), HSIL and cervical cancer. As DES has not been used during pregnancy for more than 45 years, the problem is declining.[9] N.B. Offer referral for colposcopy (if not previously done) to affected offspring to determine whether vaginal adenosis is present.[14] Annual colposcopic assessment is recommended for people with vaginal adenosis.[14] If vaginal adenosis is absent, routine interval cervical screening is appropriate.[14]

Prophylactic HPV vaccination can reduce the risk of vaginal cancer

Persistent infection with high-risk HPV types (i.e. 16/18) is associated with the development of high-grade squamous intraepithelial lesions (HSIL) and vaginal cancer.[3] Therefore, prophylactic HPV vaccination can be a prevention strategy against the development of pre-cancerous vaginal lesions and invasive vaginal cancer.[3]

HPV vaccination can protect against the acquisition of new HPV infections; it does not reduce the progression of established vaginal lesions or cancer.[10] HPV vaccination is most effective when administered prior to HPV exposure, however, it is still effective after exposure to HPV (see: "Expert tip"), and can prevent the development of up to 100% of pre-cancerous vaginal lesions and vaginal cancers.[11, 12] There is also emerging evidence that HPV vaccination may be beneficial in reducing recurrence risk after treatment, however, further studies are required.[13]

Gardasil 9 is the currently recommended vaccine in New Zealand and has been used since 2017. It protects against nine types of HPV (6, 11, 16, 18, 31, 33, 45, 52, 58); seven of which cause HPV-related cancers and two cause genital warts (6, 11).[10]

HPV vaccination is recommended for all females (and males) ideally before the onset of sexual activity, and is funded for eligible people aged 9 – 26 years inclusive*.[10] School immunisation programmes and general practices generally offer HPV vaccination to students in Year Eight (around age 12 years).

Expert tip. Vaccinating people who have already commenced sexual activity is still recommended as even if they have been infected with one or more HPV types, there are still other HPV types that are associated with malignancy, and so it is unlikely that someone will have been infected with all of them.

N.B. Gardasil 9 is registered for use in females aged 9 – 45 years and in males aged 9 – 26 years. However, there are no theoretical concerns that the efficacy or safety of the vaccine in males aged up to 45 years will differ significantly from females of the same age or younger males.[10] The vaccine may have efficacy in peopled aged > 45 years, however, there is a lack of evidence of this.

* If the course is started prior to the patients 27th birthday, the rest of the course is funded. For further information on funded indications, see: **www.health.govt.nz/publication/immunisation-handbook-2020**

For further information on HPV vaccination, see: "**Cervical cancer – early detection and referral**"

Most people are diagnosed with vaginal cancer with targeted investigations after symptoms are reported

There are no specific screening programmes available or recommended for the early detection of vaginal cancer, however, cervical screening, particularly once HPV testing is introduced in New Zealand, is likely to be useful in detecting vaginal cancers in people who are asymptomatic. Some people who are asymptomatic may be diagnosed with vaginal cancer incidentally after an examination for other reasons.[4, 7] Most people are diagnosed with targeted investigations after symptoms are reported.

Symptoms of vaginal cancer, e.g. abnormal vaginal bleeding or malodorous discharge, tend to be non-specific and are commonly related to another cause, e.g. medicines, vaginal infection.[3] In some cases, the patient or their partner will have detected a possible mass or lesion in the vagina. In more advanced vaginal cancer, symptoms may include, pelvic pain, urinary retention, dysuria, haematuria, tenesmus, constipation or melaena.[3, 4, 7]

Take a patient history and perform a pelvic examination for patients with suspicion of vaginal cancer

Begin by taking a focused history with particular attention to risk factors, e.g. a history of cervical cancer. **Perform a pelvic examination**, including bimanual and speculum examination. Ideally use a clear plastic disposable speculum and gently move it around so that the whole vagina can be seen, paying close attention to the upper one-third and apex as this is the most common site of vaginal cancer.[7] Examination may reveal small lesions such as a plaque or ulcer on the vaginal wall, or an ulcerating, fungating or annular constricting mass.[4] Palpate the groin to assess for any enlarged lymph nodes as more than one-third of vaginal cancers have spread to the pelvic or inguinal lymph nodes by the time of diagnosis, and indicate a later stage cancer.[4]

Take a vaginal sample (using a cervibroom) for cytology/HPV testing. If the results from cytology are abnormal, or if the vagina is visually abnormal upon examination (irrespective of HPV and cytology results), refer the patient directly for a colposcopy or to gynaecology. Note "urgent" on the referral if there are specific concerns on examination. Patients will undergo further investigations, e.g. vaginal biopsy, and management in secondary care or a Gynaecological Oncology centre if required.[3, 5]

Cervical screening should be offered to patients who are due. Swabs for **sexually transmitted infections**, e.g. chlamydia, gonorrhoea, trichomoniasis, are not usually required if a tumour is present, but may be useful to exclude other potential causes of the patients symptoms as indicated.

There are no specific **laboratory tests** (other than analysis of biopsy if performed) for the diagnosis of vaginal cancer, but they may be requested (as indicated) to assess other aspects of the patient's health and to identify other potential causes of the symptoms. Most laboratory test results will be normal except in patients with significant bleeding, who may be anaemic. Tests may include:

- Full blood count
- Ferritin
- Liver function tests
- Coagulation tests (prothrombin time, international normalised ratio, activated partial thromboplastin time and fibrinogen)
- Thyroid stimulating hormone
- Urine pregnancy test or serum hCG

For information on the follow-up and surveillance of a patient after curative-intent treatment for vaginal cancer, see: **bpac.org.nz/2023/gynaecological-cancers.aspx**

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