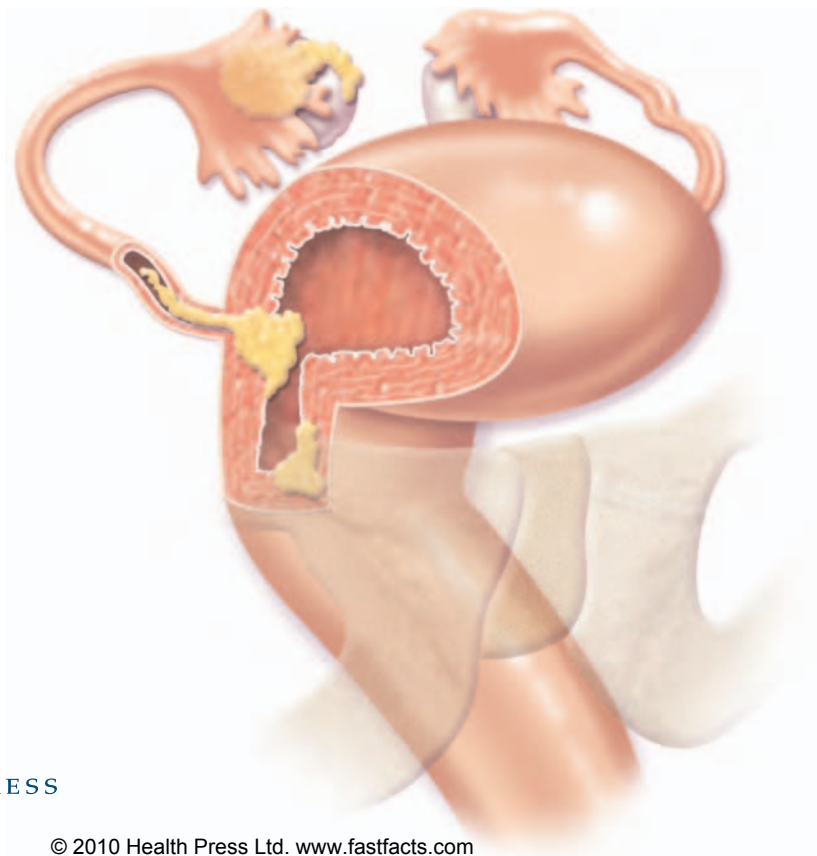


Fast Facts



# Fast Facts: Gynecologic Oncology

**Shohreh Shahabi, J Richard Smith, Giuseppe Del Priore**  
Second edition





# Fast Facts: Gynecologic Oncology

Second edition



**Shohreh Shahabi MD FACOG**

Chair, Department of Obstetrics & Gynecology  
Danbury Hospital and Chair, Reproductive Tumor Biology  
Biomedical Research Laboratory, Danbury  
Connecticut, USA



**J Richard Smith MD FRCOG**

Consultant Gynaecological Surgeon  
West London Gynaecological Cancer Centre  
Queen Charlotte's and Chelsea Hospital  
Imperial College Healthcare NHS Trust, London, UK, and  
Adjunct Associate Professor, New York University Medical  
Center, New York, USA



**Giuseppe Del Priore MD MPH**

Mary Fendrich Hulman Professor  
Director of Gynecologic Oncology  
Indiana University School of Medicine  
Indianapolis, USA

**Declaration of Independence**

This book is as balanced and as practical as we can make it.  
Ideas for improvement are always welcome: [feedback@fastfacts.com](mailto:feedback@fastfacts.com)

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Shohreh Shahabi, J Richard Smith, Giuseppe Del Priore

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## Glossary of abbreviations

**ACOG:** American College of Obstetricians and Gynecologists

**ASC-H:** atypical squamous cells, cannot exclude high-grade cytology

**ASC-US:** atypical squamous cells of undetermined significance

**BMI:** body mass index

**BSO:** bilateral salpingo-oophorectomy

**CA125:** cancer antigen 125

**CA19-9:** cancer antigen 19-9

**CIN:** cervical intraepithelial neoplasia

**CT:** computed tomography

**D&C:** dilatation and curettage

**EBRT:** external beam radiotherapy

**FDA:** Food and Drug Administration

**FIGO:** International Federation of Gynecology and Obstetrics

**GTN:** gestational trophoblastic neoplasia

**hCG:** human chorionic gonadotropin

**HIV:** human immunodeficiency virus

**HNPCC:** hereditary non-polyposis colorectal cancer

**HPV:** human papillomavirus

**HSIL:** high-grade squamous intraepithelial lesion

**HSV:** herpes simplex virus

**5HT<sub>3</sub>:** type three 5-hydroxytryptamine

**IMRT:** intensity-modulated radiotherapy

**LDH:** lactate dehydrogenase

**LEEP:** loop electrosurgical excision procedure

**LLETZ:** large loop excision of the transformation zone

**LSIL:** low-grade squamous intraepithelial lesion

**LVSI:** lymph–vascular space invasion

**MRI:** magnetic resonance imaging

**NSAID:** non-steroidal anti-inflammatory drug

**Pap smear:** Papanicolaou smear

**PCA:** patient-controlled analgesia

**PCOS:** polycystic ovary syndrome

**PET:** positron emission tomography

**SIL:** squamous intraepithelial lesion

**STD:** sexually transmitted disease

**TNM:** tumor–node–metastasis

**TVUS:** transvaginal ultrasound

**VAIN:** vaginal intraepithelial neoplasia

**VIN:** vulvar intraepithelial neoplasia

**VLP:** virus-like particle

**WHO:** World Health Organization

## Introduction

Gynecologic oncology is a well-established subspecialty of gynecology. However, management of gynecologic malignancy is still often shared between the general gynecologist, gynecologic oncologist, radiation oncologist, medical oncologist, primary care provider and, occasionally, the palliative care specialist. Women, too, are requesting information as they become increasingly aware of their risk of genital tract malignancy, particularly as a result of the cervical screening program, the increasing publicity given to attempts to develop screening tests for ovarian cancer, and the increased risk of endometrial cancer among an aging and more obese population.

To put the burden of gynecologic cancers into perspective, the estimated numbers of new cases and deaths in the USA in 2009 are shown in Table 1.

The incidence of cervical cancer is declining in industrialized countries, almost certainly because of the implementation of cervical smear programs. It remains true, however, that those women most in need of screening or human papillomavirus vaccines are those least likely to be included in such programs. There is still much room for

TABLE 1

### Estimated new cases of, and deaths from, gynecologic cancers in the USA in 2009

Site	New cases	Deaths
Uterus	42 160	7780
Ovary	21 550	14600
Cervix	11 270	4070
Vulva	3580	900
Vagina and other	2160	770

Data from Jemal A, Siegel R, Ward E et al. Cancer statistics, 2009. *CA Cancer J Clin* 2009;59:225–49.

improvement as the projected number of new cervical cancers worldwide is anticipated to reach 2 million by 2020.

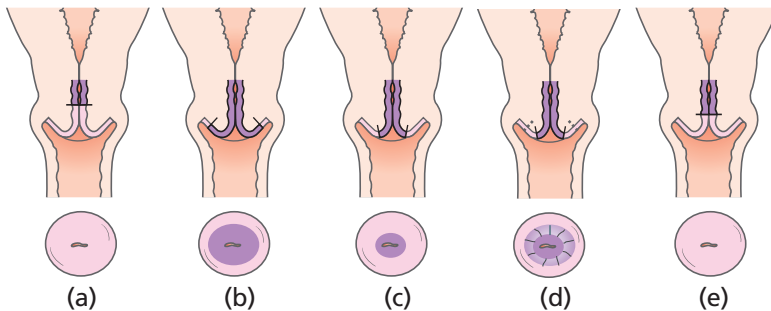
At present, 21 000 new cases of ovarian cancer are diagnosed each year in the USA, and over 14000 deaths occur annually. Worldwide, it is a leading cause of cancer deaths in women. This disease accounts for 4% of all tumors in women. Unfortunately, many women present to primary care providers early in their disease with vague, non-specific complaints, making it easy to miss the underlying diagnosis. This may represent an opportunity for well-informed clinicians to intervene in a meaningful manner.

Gynecologic tumors that have a low incidence are seen infrequently by the non-subspecialist, but nevertheless they require prompt recognition and management to minimize their potentially devastating effects.

*Fast Facts: Gynecologic Oncology* aims to update the primary care provider and non-specialist who see these tumors infrequently on current management and prognosis. It also provides a useful starting point for medical students and junior doctors on a gynecologic oncology rotation.

## The cervix

The area of the cervix with premalignant potential is the transformation zone, which is formed after puberty. Before puberty, the squamocolumnar junction is found inside the endocervical canal (Figure 1.1a). At puberty, cervical eversion occurs under the influence of estrogens, resulting in cervical ectopy (Figure 1.1b). The vagina is then colonized by lactobacilli and the acidity increases. This encourages squamous cell metaplasia, covering the area of cervical ectopy (columnar epithelium) with squamous epithelium (Figure 1.1c). Thus, there are two squamocolumnar junctions: the original one and the new one (Figure 1.1d). The area between these is the transformation zone, and it is this area that has the greatest premalignant potential. This is also the area examined cytologically. Cervical ectopy is a physiological state stimulated by increased estrogen levels; it can occur



**Figure 1.1** The physiological states of the cervix according to age: (a) before puberty, the squamocolumnar junction is inside the endocervical canal; (b) at puberty, cervical eversion occurs; (c) following puberty, the area of cervical ectopy becomes covered with squamous epithelium; (d) two squamocolumnar junctions result (distal older, proximal newer), and the area between them is the transformation zone; (e) after the menopause, the squamocolumnar junction formed following puberty ascends into the cervical canal.

at puberty as described previously, but also occurs in women taking the combined oral contraceptive pill and during pregnancy. After the menopause, the new squamocolumnar junction ascends into the cervical canal (Figure 1.1e).

## Epidemiology

**Incidence.** Cervical cancer has a bimodal onset in the third and sixth decades of life. The incidence of cervical cancer in the general population is uncertain, but it probably affects 8–10 women/100 000/year. However, global incidence and mortality rates are disparate. In developed countries, the incidence and mortality figures for cervical cancer have fallen by 75% over the past 50 years. In the USA from 1995 to 1999, the incidence of cervical cancer in girls aged under 20 years was 0/100 000/year, rising to 1.7/100 000/year in women aged 20–24 years, and peaking at 16.5/100 000/year in women aged 45–49 years. Only 10% of affected women were 75 or older. UK data show a similar distribution.

Approximately 60% of women who are newly diagnosed with cervical cancer in developed countries have either never been screened or not been screened in the preceding 5 years. Cervical cancer is more common in metropolitan areas than in rural areas, and the incidence is higher in populations with lower socioeconomic status and low levels of education. Central and South America, southern and eastern Africa, and the Caribbean have the highest incidence of the disease.

**Risk factors.** Cervical cancer is a disease associated with chronic infection by oncogenic types of human papillomavirus (HPV). The most important cofactors that affect the persistence and progression of HPV infection are HPV type and viral load. Other cofactors that may influence the outcome of HPV infection include diet, unidentified genetic factors and, possibly, other sexually transmitted disease. Host factors that influence infection include cellular and humoral immunity, parity, multiple sexual partners, smoking, pregnancy and use of oral contraceptive.

**Diet.** Folate deficiency is reported to enhance the effects of other risk factors such as parity, infection with type 16 HPV and cigarette

Cancer of the ovary is the second most common gynecologic cancer – it accounts for 26% of tumors, but 52% of the total mortality. The probability of a newborn girl developing ovarian cancer over the course of her lifetime is 1.4% (i.e. 1 in 70). The lifetime chance of dying from ovarian cancer is 1.05% or 1 in 95.

Ovarian cancer is most common in women aged 55–59 years, but it can occur at any age. The incidence is higher among white women than black women, and it is increasing. This is in contrast to the incidence of breast cancer, which has remained constant, and cervical and endometrial cancers, which have fallen in incidence. The incidence trend may possibly be a reflection of women having smaller families and, with increasing affluence, an increasingly high-fat diet.

### Risk factors

Some of the epidemiological risk factors associated with ovarian cancer are shown in Table 4.1. There is also an association with colon, breast and endometrial cancer (all four cancers are associated with high-fat diets).

**Exposure to ovarian stimulatory drugs** has been linked with ovarian cancer, a finding that is consistent with the observation that factors that suppress ovulation (e.g. pregnancy and the oral contraceptive pill) are protective. However, successfully treated infertility is actually associated with a reduction in the risk of ovarian and endometrial cancer. If there is a causal association, it is not excessive. Certainly, in pursuit of the goal of having a child, a small risk is not unreasonable.

**Postmenopausal hormone replacement therapy** is reported to be associated with an increased risk of ovarian cancer. The Cancer Prevention Study II, with more than 200 000 postmenopausal women, revealed a two-fold increase in risk of mortality from ovarian cancer if estrogen had been used for more than 10 years. The Women's Health

TABLE 4.1

**Risk factors for ovarian cancer**

- Nulliparity
- Infertility
- A high-fat diet
- Higher socioeconomic status
- Family history
- Celibacy
- Irradiation of pelvic organs
- Early menarche
- Exposure to talc and asbestos

Initiative study revealed an increased relative risk of developing ovarian cancer with the use of combined hormone replacement therapy. However, the absolute attributable risk was actually quite small (< 1/10 000 women treated). Once a woman has developed ovarian cancer, estrogen therapy does not appear to affect the likelihood of recurrence.

**Genetic susceptibility.** Hereditary ovarian cancer accounts for 5–10% of all ovarian cancers. Two susceptibility genes for breast and ovarian cancer, *BRCA1* and *BRCA2*, have been determined. The presence of mutations in *BRCA1*, located on chromosome 17, increases the lifetime risk of ovarian cancer by 28–44%. Mutations in *BRCA2*, which is located on chromosome 13, increase the lifetime risk of ovarian cancer by up to 27%.

Mutations in mismatch repair genes increase the risk of ovarian cancer about three-fold. Other genetic mechanisms and genes associated with ovarian cancer include:

- mutation in tumor suppressor genes
- loss of heterozygosity
- p53 mutations
- c-myc
- *ERBB2*
- *AKT2*
- *PIK3C*
- ras mutations (more common in borderline ovarian tumors).