



Winning the War on Women's Cancer *Gynecologic Cancer Prevention*

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6 Week Course Agenda

- I. Introduction to Women's Cancers
- II. Genetics of Gynecologic Cancers
- III. Gynecologic Cancer Surgery
- IV. Gynecologic Cancer Prevention
- V. Gynecologic Cancer Treatment
- VI. Sexual Health & Survivorship



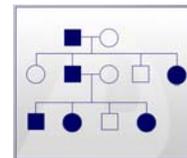
Today's Agenda

- I. Ovarian cancer
- II. Uterine (endometrial) cancer
- III. Cervical cancer



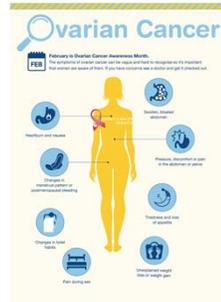
Ovarian Cancer: Risk Factors

- Increasing age
- Family history of ovarian, fallopian tube, primary peritoneal cancer, or premenopausal breast cancer
- Personal history of premenopausal breast cancer
- Intertility / never becoming pregnant
- Oral contraceptive pill use is protective



Ovarian Cancer: Know the symptoms

- Pelvic or abdominal pain
- Difficulty eating or feeling full quickly
- Bloating
- Urinary symptoms (urgency & frequency)



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Ovarian Cancer: Routine Screening is NOT recommended

- Screening test must be noninvasive
- Screening test must be inexpensive
- Detection of tumors at an **early stage** to allow more successful treatment

▪ CA125

Elevated in 80% of epithelial ovarian cancers but only 25-50% of Stage I. May be elevated in benign conditions: fibroids, adenomyosis, endometriosis, pelvic inflammatory disease, pregnancy, menstruation

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Ovarian Cancer: Prevention

Oral contraceptive pills decrease ovarian cancer risk by up to 50%
Even 6 months is beneficial
Benefits last for 15 years

Even in BRCA1/BRCA2 mutation carriers, any use of OCPs yields odds ratio of 0.5.



CASH Study, N Eng J Med 1987
Narod et al, N Engl J Med 1998

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Risk reducing Salpingo-oophorectomy (RRSO)

- 90% ovarian cancer risk reduction in BRCA1/2 mutation carriers
- Up to 60% breast cancer risk reduction

- Does not eliminate peritoneal carcinoma
- Induces surgical menopause
- Occult cancer found in 10-20% surgeries



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Risk Reducing Salpingo-oophorectomy (RRSO)

N=551 BRCA1/2 mutation carrier women, 259 cases of RRSO vs. 292 controls of surveillance

2.3% occult ovarian CA

Mean follow-up 8.8 years

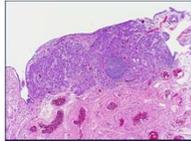
0.8% subsequent PPC

20% ovarian cancer incidence in control group

0.04 Hazard Ratio (0.01-0.16 95% CI)

0.47 HR for breast cancer

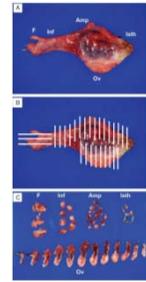
Rebbeck et al, N Engl J Med, 2002



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RRSO Protocol

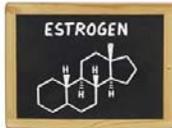
- Complete bilateral salpingo-oophorectomy +/- omental/peritoneal biopsies
- Cytologic examination of peritoneal washings
- Fine sectioning of ovaries and fallopian tubes with complete pathologic examination



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Uterine Cancer: Risk Factors

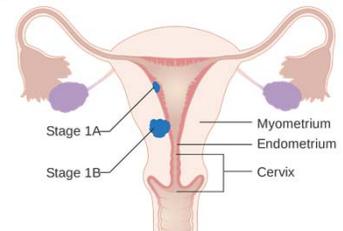
- Taking estrogen alone without progesterone
- Obesity
- Later menopause
- Diabetes
- Never becoming pregnant
- Hypertension
- Family history of endometrial or color cancer
- Use of tamoxifen



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Uterine Cancer: Know the symptoms

- Abnormal bleeding or discharge
- Postmenopausal bleeding
- Pressure in pelvis



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Endometrial Cancer: Routine Screening is NOT recommended

- Screening test must be noninvasive
- Screening test must be inexpensive
- Detection of tumors at an early stage to allow **more successful** treatment

- 90% of women with endometrial cancer present with postmenopausal bleeding
- No satisfactory or cost-effective screening for endometrial cancer
- Consider ultrasound or biopsy for Lynch Syndrome family members

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Endometrial Cancer: Prevention

Obesity increases endometrial cancer risk by as much as 10-fold.

Obesity may affect how cancer is treated (surgery, chemotherapy, radiation) and how well these treatments may work

Diet, exercise, and weight loss may decrease risk of cancer, diabetes, heart disease, death

CALCULATE YOUR BMI

Weight (kg) / Height (cm) squared= Body Mass Index

- Normal = 18.5-24.9
- Overweight = 25-29.9
- Obesity \geq 30

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Lynch Syndrome & Risk-reducing Surgery

N=380 women with MLH1, MSH2, and MSH6 mutations from 3 HNPCC registries, 1973-2004

Median age 41 years at prophylactic surgery

46 at endometrial cancer diagnosis

42 at ovarian cancer diagnosis

Incidence of endometrial CA

0% after prophylactic hysterectomy (13 year follow-up)

33% controls (7 year follow-up)

Incidence of ovarian CA

0% after prophylactic oophorectomy (11 yr follow-up)

5.4% controls (11 yr follow-up)

Schmeler et al, *N Engl J Med*, 2006

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Cervical cancer screening and prevention

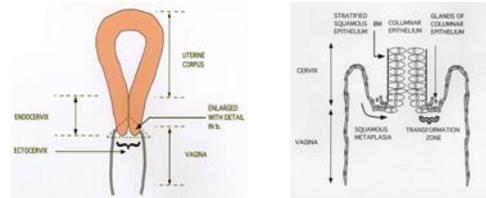
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Overview

- Risk factors
- Protective factors
- Signs and symptoms
- Screening methods
- Prevention

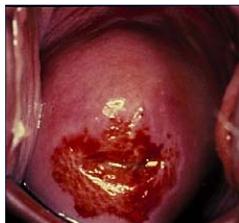
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Cervical Cancer: Anatomy



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Cervical Transformation Zone



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Cervical Cancer—Risk Factors

- HPV infection
- Smoking
- Early age at 1st birth
- Early age at 1st intercourse
- High parity
- Low socioeconomic status

- ?Genetic factors
- ?Other sexually transmitted agents (chlamydia)

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Protective Factors

- Cesarean section
- Circumcision of male partner
- Prior Pap smear screening

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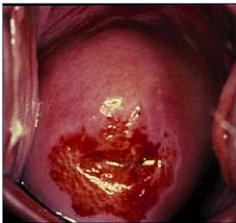
Cervical CA--Signs and Symptoms

- Irregular vaginal bleeding or postmenopausal bleeding
- Bleeding after sex
- Vaginal discharge
- Pelvic pain
- Unilateral leg swelling or pain
- Pelvic/cervical mass or swelling

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Cervical Cancer

Normal cervix

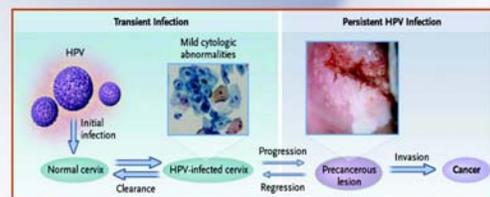


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Natural History of HPV Infections



Wright and Schiffman (2003) NEJM

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HPV and Cervical CA

▪ Cofactors that enhance the malignant potential of HPV:

- Smoking
- Immunocompromise

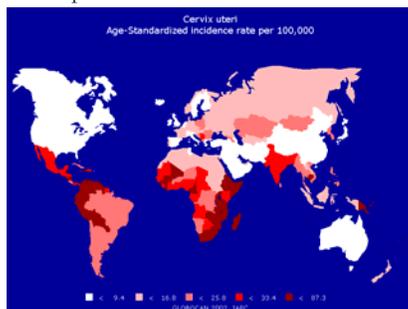
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HPV types cancer risk

HPV TYPE	CANCER RISK
6,11, 42-44	Low to nil
31,33,35,39,51-53,58,59,66,68	Intermediate
16,18, 45, 56	High

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Cervical cancer screening is an effective way to prevent cervical cancer



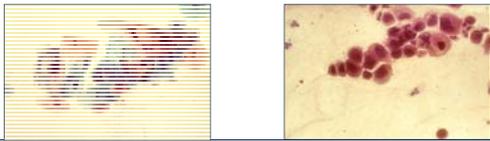
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Screening for cervical cancer

- 2 approaches are currently in use in the USA
 - Cytology (Pap test) every 3 years
 - Cytology (Pap test) plus HPV testing every 5 years
 - HPV testing detects the high risk HPV types associated with cervical cancer

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Cervical Cancer screening- Pap test



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HPV testing

Component Results

Component	Value	Ref Range & Units	Status
HPV High-Risk DNA Types	DETECTED		Final

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Management of abnormal screening results

- Repeat in 6 months- 12 months (equivocal results)
- Colposcopy and treatment

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Colposcopy is a binocular microscopic examination of the cervix, vagina and vulva

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Colposcopy allows identification of abnormal areas on the cervix



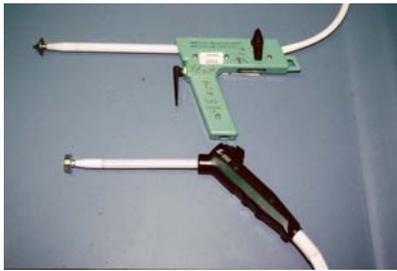
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Treatment options

- Ablative therapy (cryotherapy, laser therapy)
- Excisional therapy (LEEP, cone biopsy)

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Cryotherapy freezes the transformation zone



Courtesy E.J. Mayeux

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LEEP allows excision of the abnormal area of the transformation zone



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Primary prevention: HPV vaccines

Bivalent (2vHPV): HPV16 and18

Quadrivalent (4vHPV): HPV 6, 11, 16 and 18

9-valent (9vHPV): HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58

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CDC Recommendations for HPV vaccination

- routine HPV vaccination be initiated at age 11 or 12 years.
- The vaccination series can be started beginning at age 9 years.

MMWR March 27, 2015 / 64(11);300-304

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CDC Recommendations for HPV vaccination

- vaccination is also recommended for females aged 13 through 26 years and for males aged 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series
- males aged 22 through 26 years may be vaccinated.

MMWR March 27, 2015 / 64(11);300-304

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Safety

- Vaccines are associated with local reactions including pain, erythema and swelling, as well as systemic reactions such as fatigue, headache and myalgia
- No obvious safety issues were identified in Phase III trials

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HPV vaccination

- Population impact is under investigation but suggest reduction in cervical dysplasia in populations with high vaccine coverage
- Vaccine uptake is expected to result in reduced rates of cervical cancer

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Summary

- Primary prevention of cervical cancer: HPV vaccination before exposure to HPV
- Secondary prevention of cervical cancer: screening for detection and treatment of cancer precursors

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Homework

- Calculate your BMI

https://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm

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