Gynecologic Malignancies

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31 March 2016

Outline

- Female Cancer Statistics
- Uterine Cancer
- Adnexal Cancer
- Cervical Cancer
- Vulvar Cancer

Estimated New Cancer Cases* in the US in 2016

Males 841,390		Females 843,820	
Prostate	21%	29%	Breast
Lung & bronchus	14%	13%	Lung & bronchus
Colon & rectum	8%	8%	Colon & rectum
Urinary bladder	7%	7%	Uterine corpus
Melanoma of skin	6%	6%	Thyroid
Non-Hodgkin lymphoma	5%	4%	Non-Hodgkin lymphoma
Kidney & renal pelvis	5%	3%	Melanoma of skin
Oral cavity & pharynx	4%	3%	Leukemia
Leukemia	4%	3%	Pancreas
Liver & intrahepatic bile duct	3%	3%	Kidney & renal pelvis
All other sites	22%	21%	All other sites

*Excludes basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder.

American Cancer Society®

The Lifetime Probability of Developing Cancer for Females, 2010-2012

Site	Risk
All sites*	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 17
Colon & rectum	1 in 23
Uterine corpus	1 in 36
Melanoma of the skin†	1 in 52
Non-Hodgkin lymphoma	1 in 53
Thyroid	1 in 58
Pancreas	1 in 67
Ovary	1 in 77
Leukemia	1 in 82

*All sites exclude basal cell and squamous cell skin cancers and in situ cancers except urinary bladder. †Statistic for white females.
Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.7.3 Statistical Research and Applications Branch, National Cancer Institute, 2015.

American Cancer Society

Estimated Cancer Deaths in the US in 2016

Males 314,290		Females 281,400	
Lung & bronchus	27%	26%	Lung & bronchus
Prostate	8%	14%	Breast
Colon & rectum	8%	8%	Colon & rectum
Pancreas	7%	7%	Pancreas
Liver & intrahepatic bile duct	6%	5%	Ovary
Leukemia	4%	4%	Uterine corpus
Esophagus	4%	4%	Leukemia
Urinary bladder	4%	3%	Liver & intrahepatic bile duct
Non-Hodgkin lymphoma	4%	3%	Non-Hodgkin lymphoma
Brain & other nervous system	3%	2%	Brain & other nervous system
All other sites	24%	24%	All other sites

American Cancer Society

Uterine Cancer

Endometrial Cancer

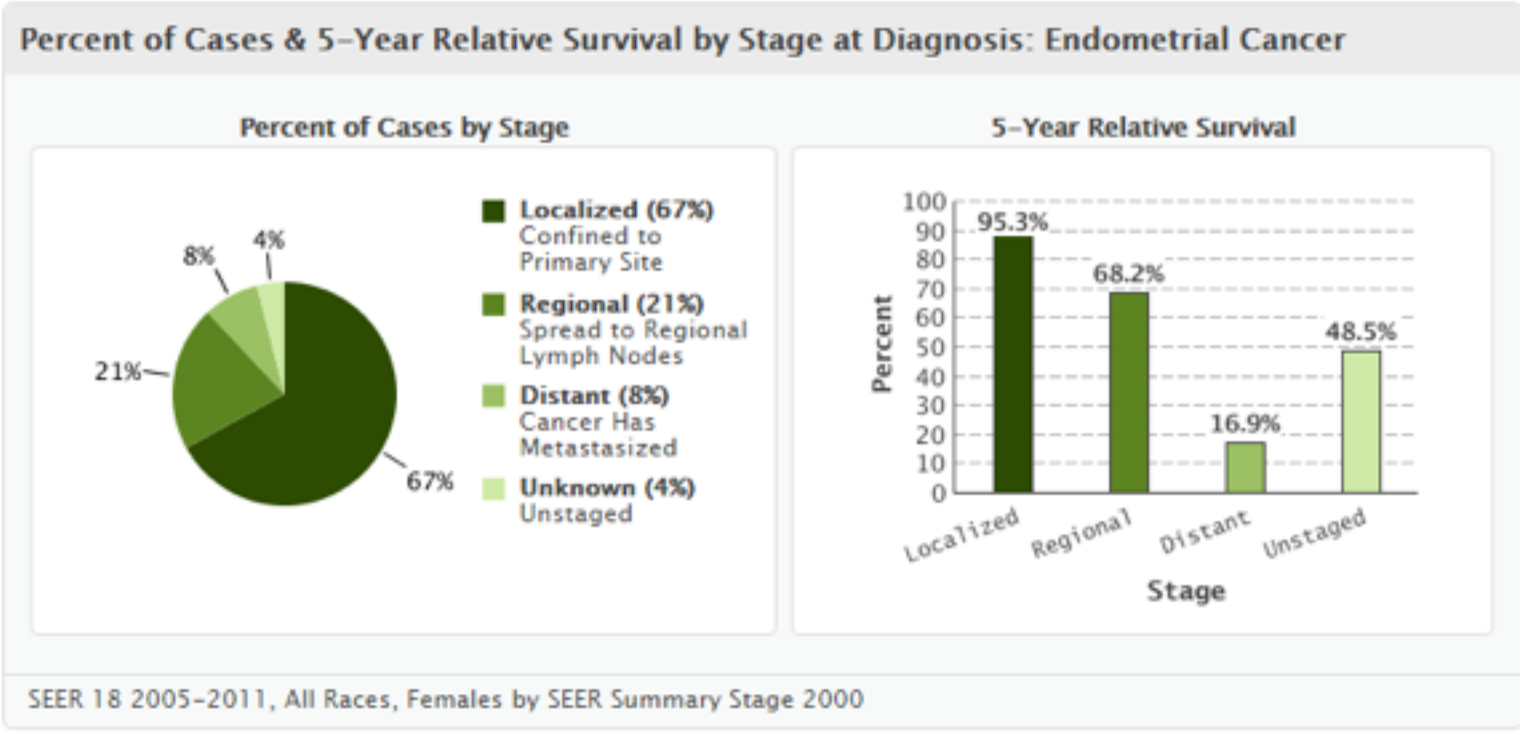
Uterine Sarcoma

Endometrial Cancer

- Epidemiology and Risk Factors
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
  - Recurrent
- Follow-Up
- Future Therapy

Epidemiology

- 60,500 cases expected in 2016
  - 25.3 per 100,000 women
- 10,470 deaths expected in 2016



Epidemiology

Increased Risk

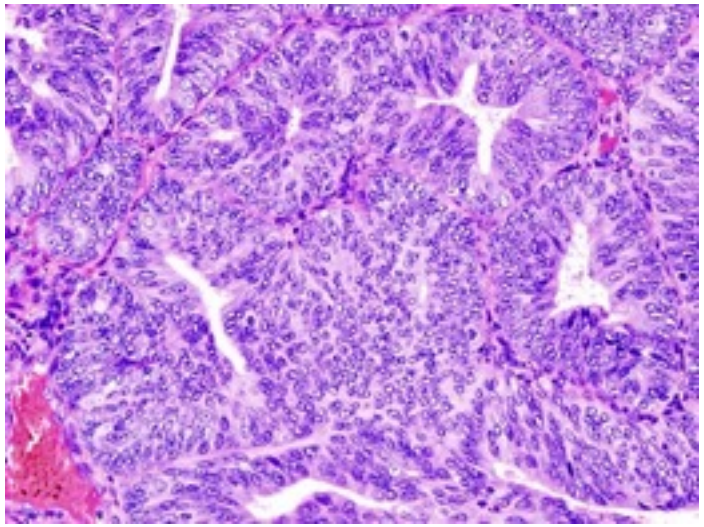
- Age
- Unopposed Estrogens
  - Exogenous
  - Tamoxifen
  - Obesity
- Genetic Risk
  - Lynch Syndrome
  - Cowden Syndrome

Decreased Risk

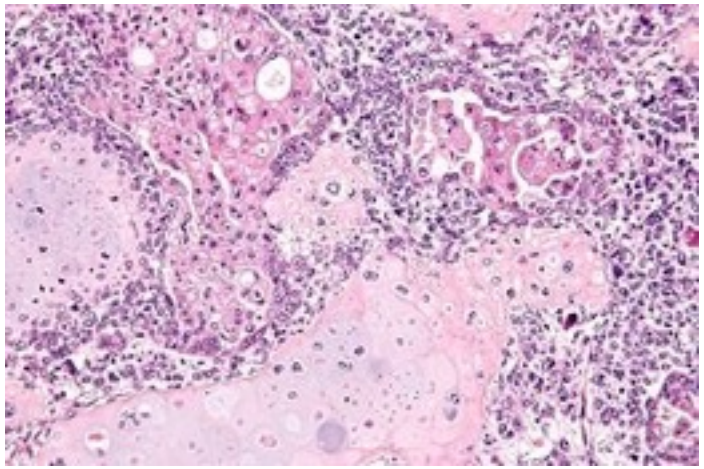
- Progestational Agents
  - Oral Contraceptive Pills
  - Levonorgestrel IUS
- Physical Activity
- Pregnancy
- Breastfeeding

Histology

- Type I
  - Endometrioid, well differentiated
  - Less aggressive
  - Usually localized
  - Good Prognosis



- Type II
  - Clear cell, papillary serous, MMMT, poorly differentiated
  - More aggressive
  - Likely to spread
  - Worse Prognosis



Histology – Molecular Features

Type I

- Diploid
- K-ras overexpression
- PTEN mutations
- Microsatellite instability

Type II

- Aneuploid
- K-ras overexpression
- P53 overexpression

Clinical Presentation

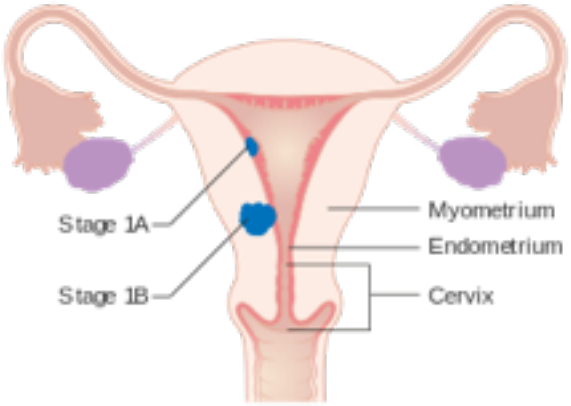
- Abnormal Uterine Bleeding
- Postmenopausal Uterine Bleeding
- Abnormal Vaginal Discharge
- Endometrial cells on a pap smear
- Bloating/pelvic pressure/pain (if advanced disease)

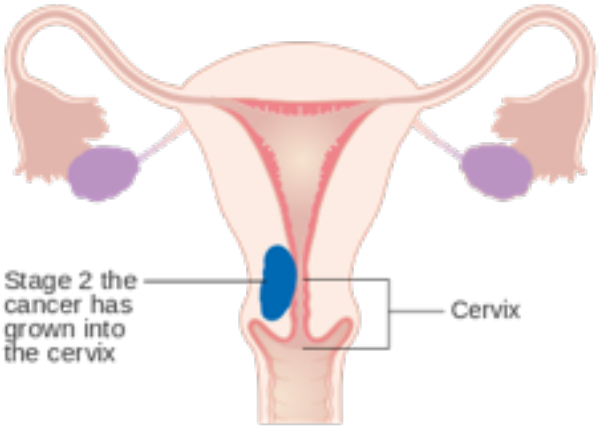
Diagnosis

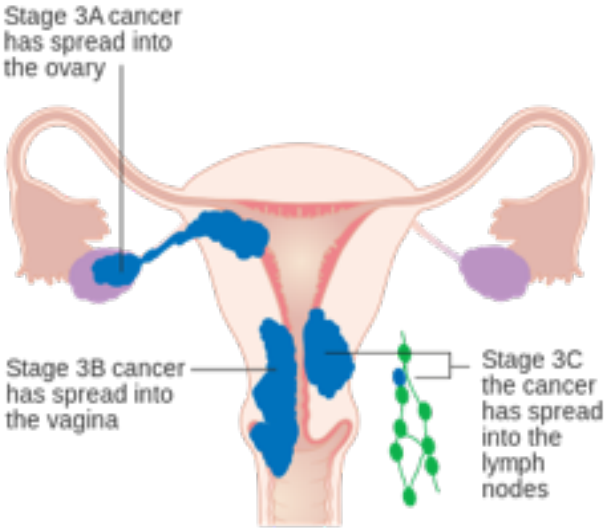
- Ultrasound
- Endometrial Biopsy
- Hysteroscopy
- Dilation and Curettage

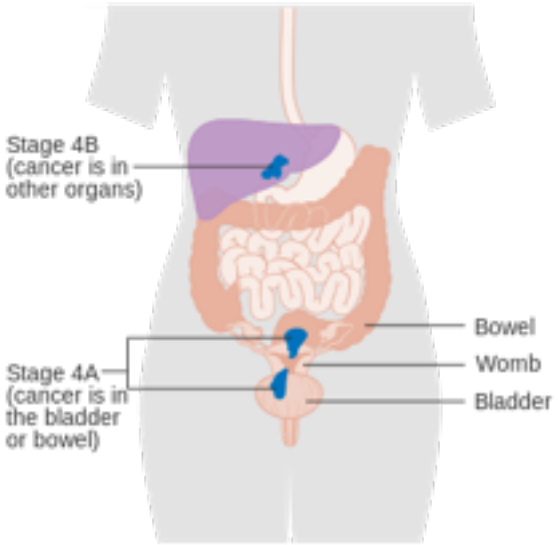
- Hysterectomy +/- BSO +/- Lymph node sampling

Staging



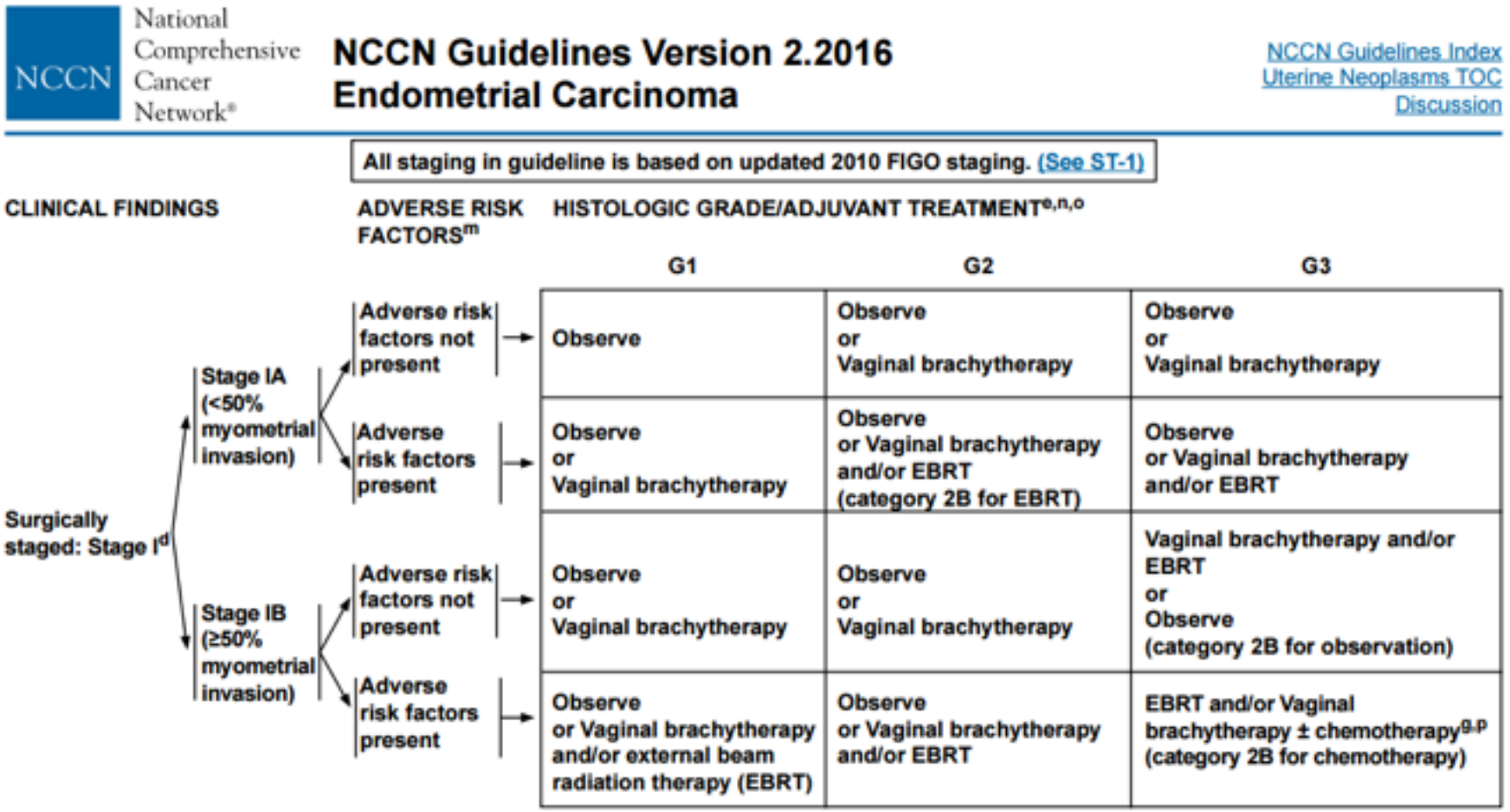






wikipedia

Therapy – Early disease



Therapy – Locally advanced disease

National Comprehensive Cancer Network®

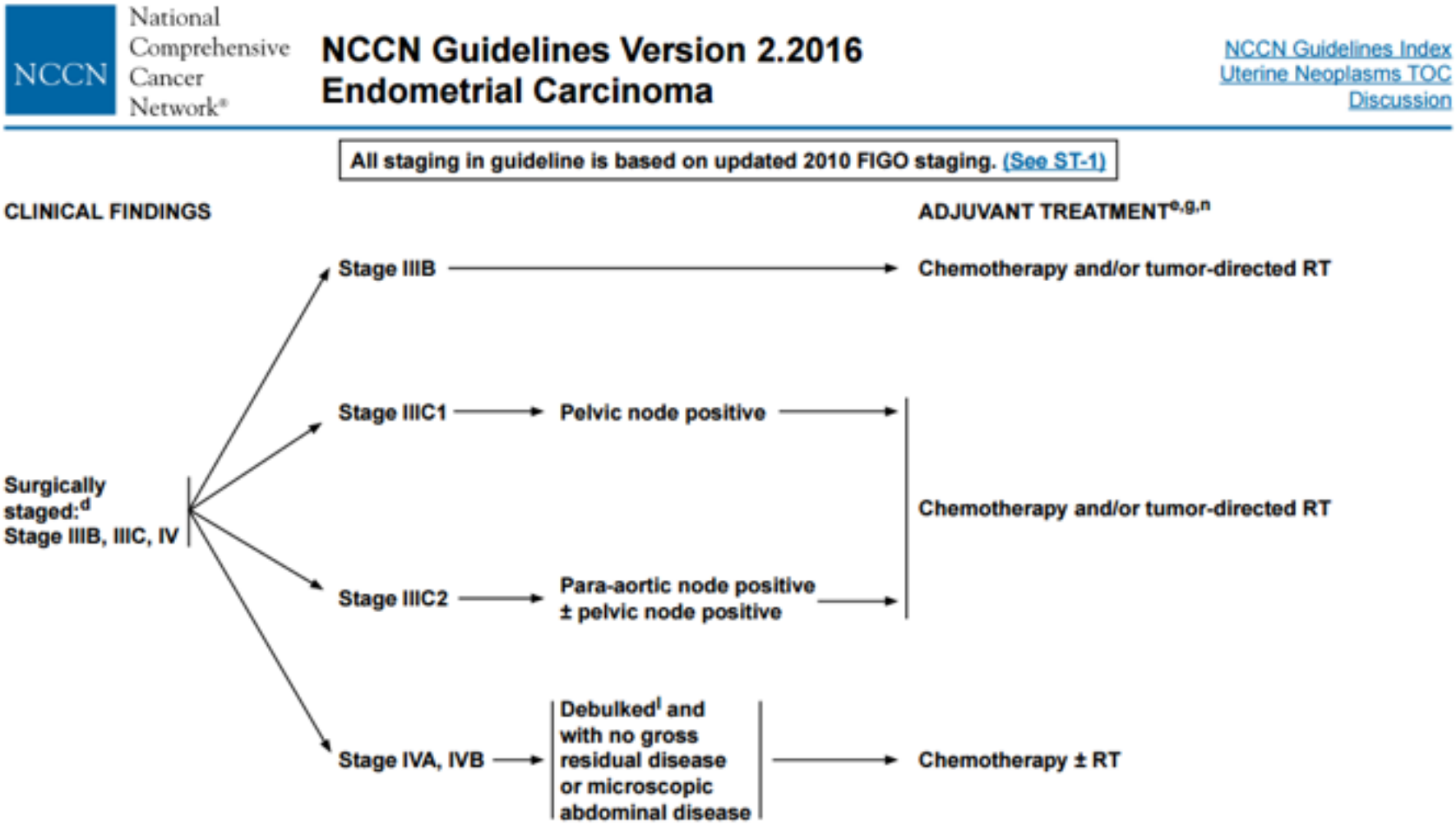
NCCN Guidelines Version 2.2016
Endometrial Carcinoma

NCCN Guidelines Index
Uterine Neoplasms TOC
Discussion

All staging in guideline is based on updated 2010 FIGO staging. (See ST-1)

CLINICAL FINDINGS	HISTOLOGIC GRADE/ADJUVANT TREATMENT[e,g,n,o]		
	G1	G2	G3
Surgically staged:[d] Stage II[q,r] →	Vaginal brachytherapy and/or EBRT	Vaginal brachytherapy and/or EBRT	EBRT ± vaginal brachytherapy ± chemotherapy[p] (category 2B for chemotherapy)
Surgically staged:[d] Stage IIIA →	Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or EBRT ± vaginal brachytherapy	Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or EBRT ± vaginal brachytherapy	Chemotherapy ± RT or Tumor-directed RT ± chemotherapy or EBRT ± vaginal brachytherapy

Therapy – Metastatic disease



Therapy - Recurrence

- Re-excision
- Radiation
- Systemic Therapies:

HORMONE THERAPY[1]

- Megestrol/tamoxifen (alternating)
- Progestational agents
- Aromatase inhibitors
- Tamoxifen

CHEMOTHERAPY REGIMENS[2,3]

- Multi-agent chemotherapy regimens preferred, if tolerated
  - Carboplatin/paclitaxel[4]
  - Cisplatin/doxorubicin[5]
  - Cisplatin/doxorubicin/paclitaxel[5,6]
  - Carboplatin/docetaxel[7]
  - Ifosfamide/paclitaxel (category 1 for carcinosarcoma)[8]
  - Cisplatin/ifosfamide (for carcinosarcoma)
- Single agents
  - Cisplatin
  - Carboplatin
  - Doxorubicin
  - Liposomal doxorubicin
  - Paclitaxel
  - Topotecan
  - Bevacizumab[9]
  - Temsirolimus[10]
  - Docetaxel[7] (category 2B)
  - Ifosfamide (for carcinosarcoma)

Follow-up

- Regular pelvic examinations
- Symptom awareness
- No role for routine imaging/vaginal cytology

Emerging Therapies

- Sentinel Node Mapping
- Fertility Preservation
- Targeted Therapies

Uterine Sarcoma

- Epidemiology and Risk Factors
- Histology
- Presentation
- Diagnosis/Staging
- Therapy
- Follow-Up
- Future Therapy

Epidemiology

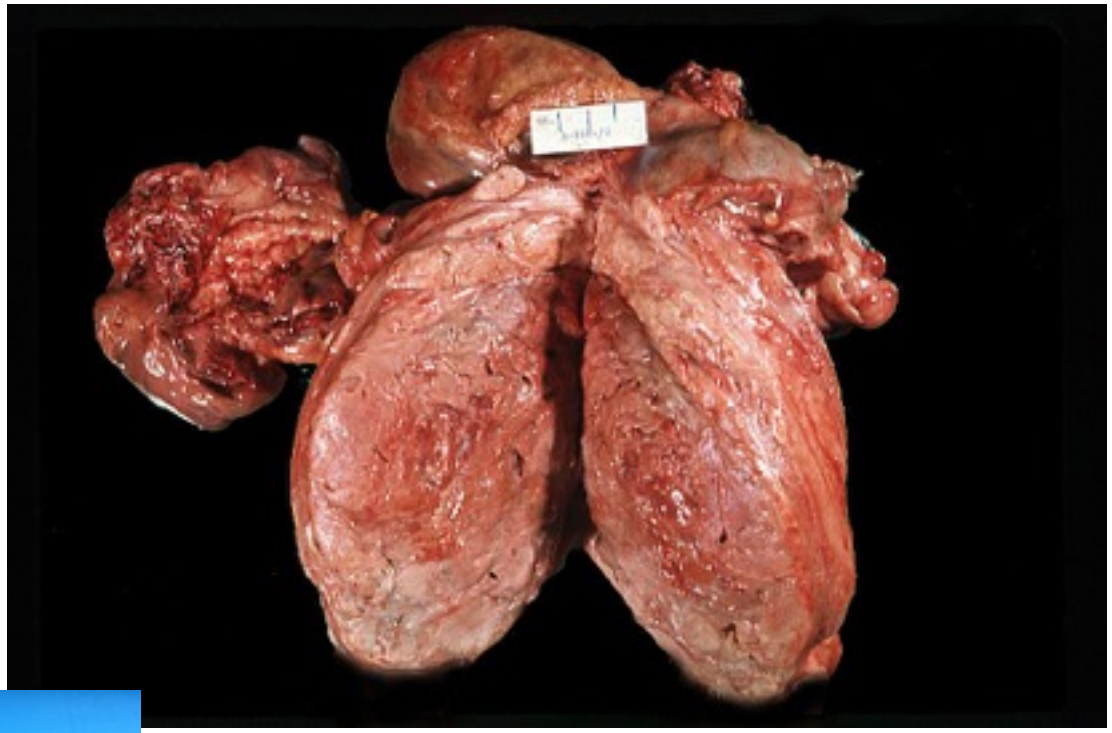
- Median age ranges is 40s to 50s based on histologic type
- Leiomyosarcomas are more common in black women than white women (age adjusted risk is 1.5 vs 0.9 per 100,000)

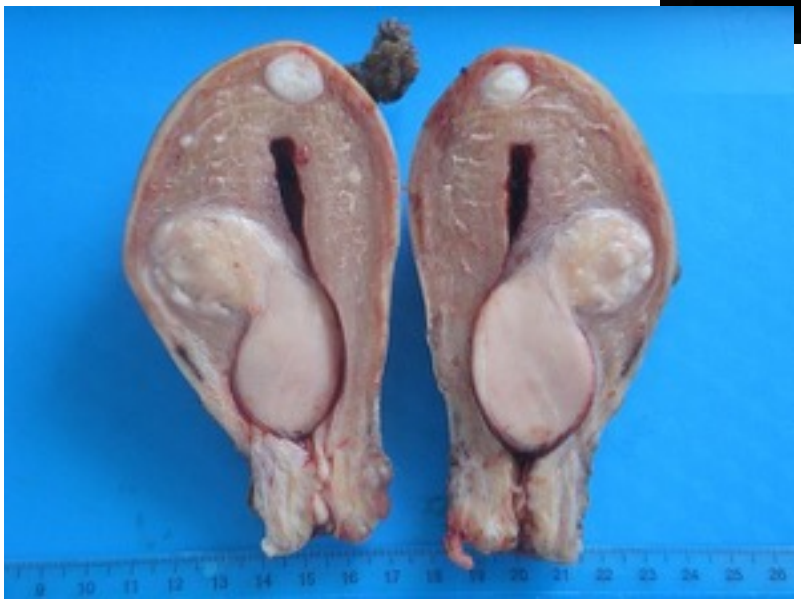
Risk Factors

- Prior radiation exposure
- Hormone exposure
  - ESS is the only true contraindication to hormone replacement after surgery for a gynecologic malignancy
- Tamoxifen Use
- Hereditary Predisposition
  - HNPCC/Lynch syndrome

Histology

- Leiomyosarcoma
  - Fleshy
  - Nuclear Atypia
  - Tumor Necrosis

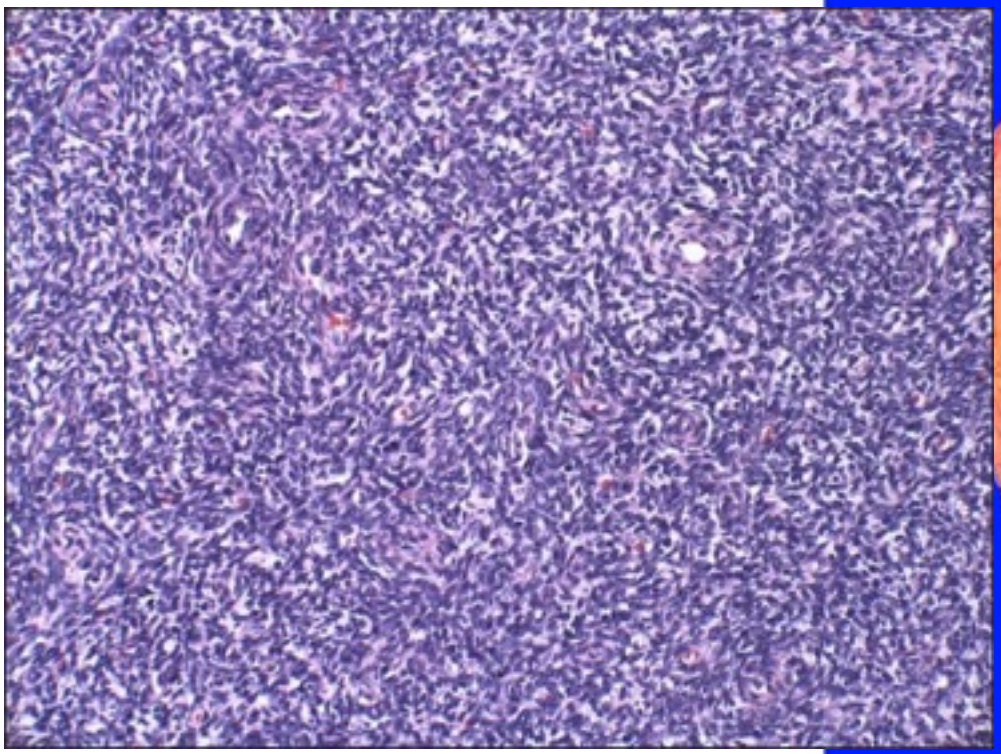


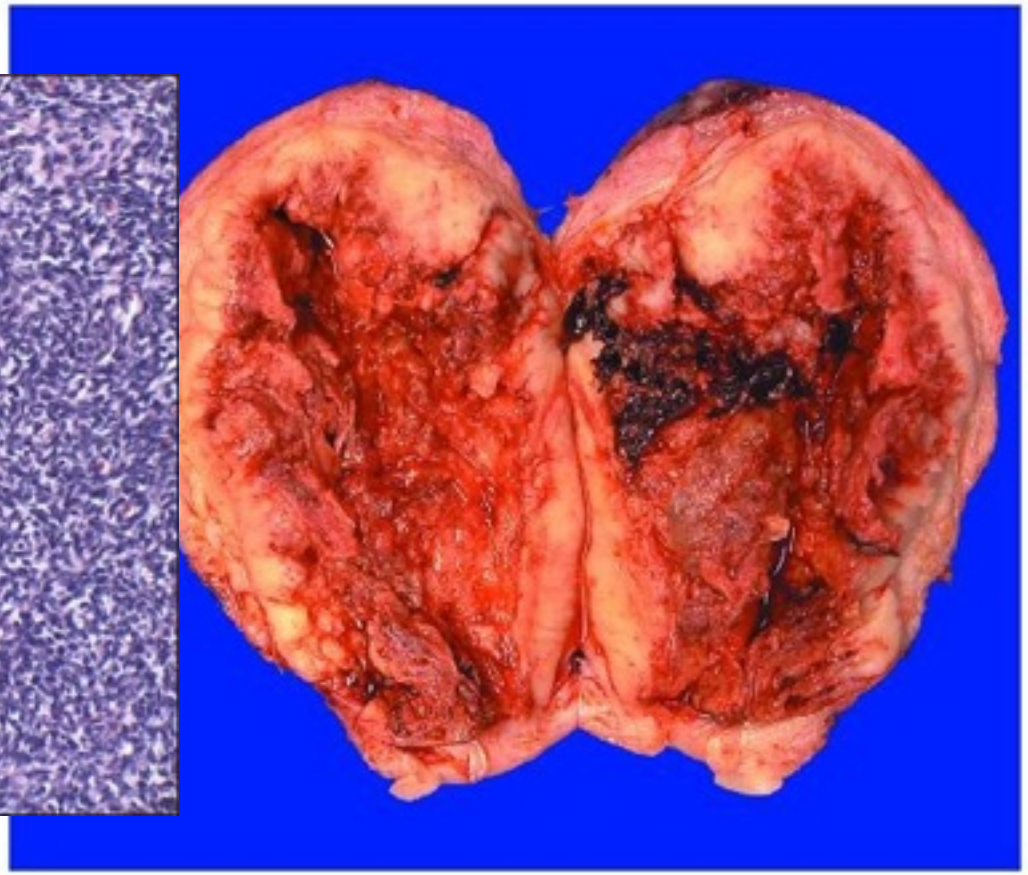


- Endometrial stromal sarcoma
  - Low Grade
  - “Bland”
  - Single mass
  - ER/PR positive

Histology

- Undifferentiated Uterine Sarcoma
  - VERY atypical cells





Presentation

- Abnormal vaginal bleeding
- Abdominopelvic mass
- Incidental diagnosis at the time of hysterectomy

Diagnosis/Staging

Staging for uterine sarcomas (leiomyosarcomas, endometrial stromal sarcomas, adenosarcomas, and carcinosarcomas)

(1) Leiomyosarcomas

Stage		Definition
I		Tumor limited to uterus
	IA	<5 cm
	IB	>5 cm
II		Tumor extends to the pelvis
	IIA	Adnexal involvement
	IIB	Tumor extends to extrauterine pelvic tissue
III		Tumor invades abdominal tissues (not just protruding into the abdomen).
	IIIA	One site
	IIIB	> one site
	IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
IV	IVA	Tumor invades bladder and/or rectum
	IVB	Distant metastasis

(2) Endometrial stromal sarcomas (ESS) and adenosarcomas*

Stage		Definition
I		Tumor limited to uterus
	IA	Tumor limited to endometrium/endocervix with no myometrial invasion
	IB	Less than or equal to half myometrial invasion
	IC	More than half myometrial invasion
II		Tumor extends to the pelvis
	IIA	Adnexal involvement
	IIB	Tumor extends to extrauterine pelvic tissue
III		Tumor invades abdominal tissues (not just protruding into the abdomen).
	IIIA	One site
	IIIB	> one site
	IIIC	Metastasis to pelvic and/or para-aortic lymph nodes
IV	IVA	Tumor invades bladder and/or rectum
	IVB	Distant metastasis

Therapy

- Endometrial Stromal Sarcoma
  - Observation
  - Hormonal Therapy
  - Consider Radiotherapy
- LMS/UUS
  - Chemotherapy
  - Radiotherapy

- Lots of negative trials… disappointing results
- Most trials have slow accrual due to rarity of tumors

Therapy

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NCCN Guidelines Version 2.2016
Uterine Sarcoma

NC
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SYSTEMIC THERAPY FOR UTERINE SARCOMA[1]
(Clinical trials strongly recommended)

Combination regimens:
- Docetaxel/gemcitabine (preferred for leiomyosarcoma)
- Doxorubicin/ifosfamide
- Doxorubicin/dacarbazine
- Gemcitabine/dacarbazine
- Gemcitabine/vinorelbine

Single-agent options:
- Dacarbazine
- Doxorubicin
- Epirubicin
- Eribulin
- Gemcitabine
- Ifosfamide
- Liposomal doxorubicin
- Pazopanib
- Temozolomide
- Trabectedin[3]
- Vinorelbine (category 2B)
- Docetaxel (category 3)

HORMONE THERAPY
(For Low-grade ESS or Hormone Receptor Positive (ER/PR) uLMS[2]):
- Medroxyprogesterone acetate (category 2B for ER/PR positive uLMS)
- Megestrol acetate (category 2B for ER/PR positive uLMS)
- Aromatase inhibitors
- GnRH analogs (category 2B for low-grade ESS and ER/PR positive uLMS)

Follow-Up

- Recurrence is common
- Routine exams
- Routine CT scans
- Patient symptom monitoring

Emerging Therapies

- Continued chemotherapy trials
- Biologic therapies
- Numerous genetic mutations in these tumors
  - Targeted therapies
    - Anti-VEGF
    - Multi-kinase inhibitors
    - mTOR inhibitors

Adnexal Cancers

Epithelial Tumors

Germ Cell Tumors

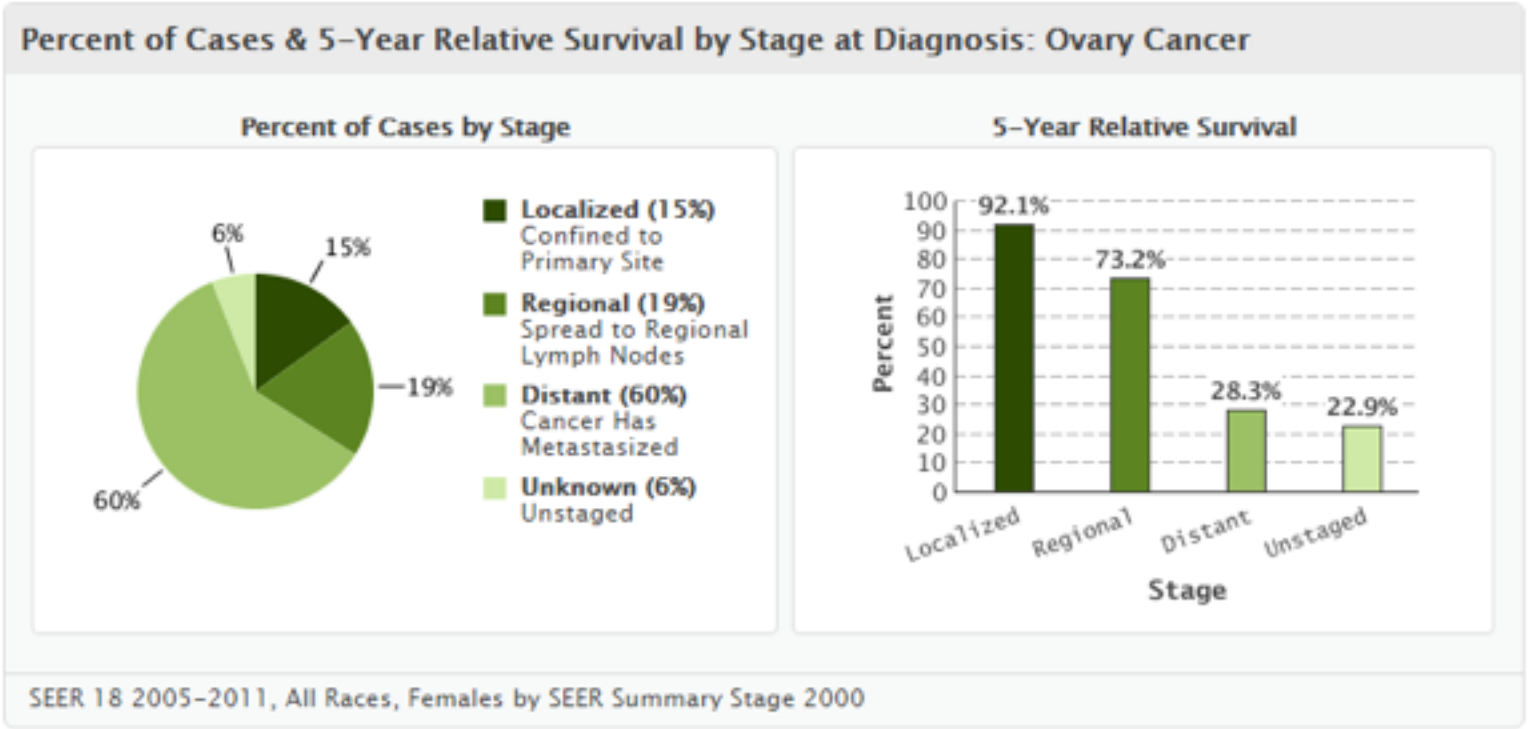
Stromal Tumors

Epithelial Cancers (OV/FT/PP)

- Epidemiology and Risk Factors
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Primary Disease
  - Recurrent
- Follow-Up
- Future Therapy

Epidemiology

- 22,280 cases expected in 2016
  - 11.9 per 100,000 women
- 14,240 deaths expected in 2016



Epidemiology

Increased Risk

- Age
- Family History
  - BRCA
  - Lynch
- PID
- Endometriosis
- Smoking (mucinous)

Decreased Risk

- Oral Contraceptive Pills
- Tubal Interruption
- Hysterectomy
- Pregnancy
- Breastfeeding
- Low fat diet

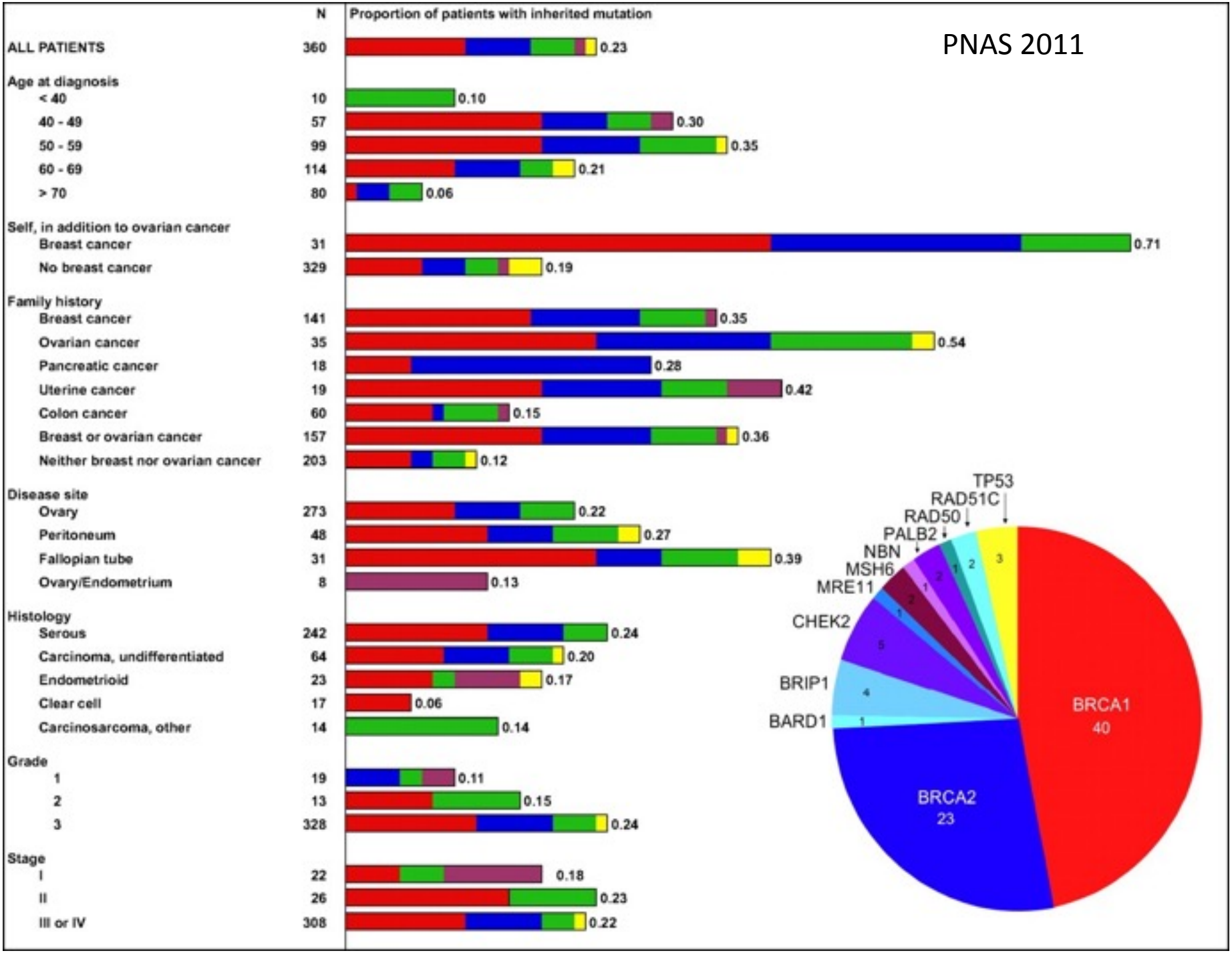
Histology

- Serous
- Mucinous
- Endometrioid
- Clear Cell
- Transitional Cell
- Squamous
- Undifferentiated
- Carcinosarcoma

Table 24.10 **Distribution of 1,247 Ovarian Epithelial Tumors by Cell Type, Washington Hospital Center, 1999 to 2011**

	Benign (%)	Atypical proliferative/ borderline (%)	Malignant (%)	Total (%)
Serous	48.6	1.8	17.8	68.2
Endometrioid	0.8	0.2	1.9	2.9
Clear cell	0	0.2	2.2	2.4
Mucinous	7.6	1.0	0.8	9.4
Seromucinous	1.8	0.3	0.2	2.3
Transitional	9.9	0.2	0.3	10.4
Mixed	0.6	0	0.7	1.3
Undifferentiated	–	–	0.1	0.1
Carcinosarcoma	–	–	1.6	1.6
Squamous	1.3	–	0.1	1.4
Totals	70.6	3.7	25.7	100

Seidman, unpublished data.

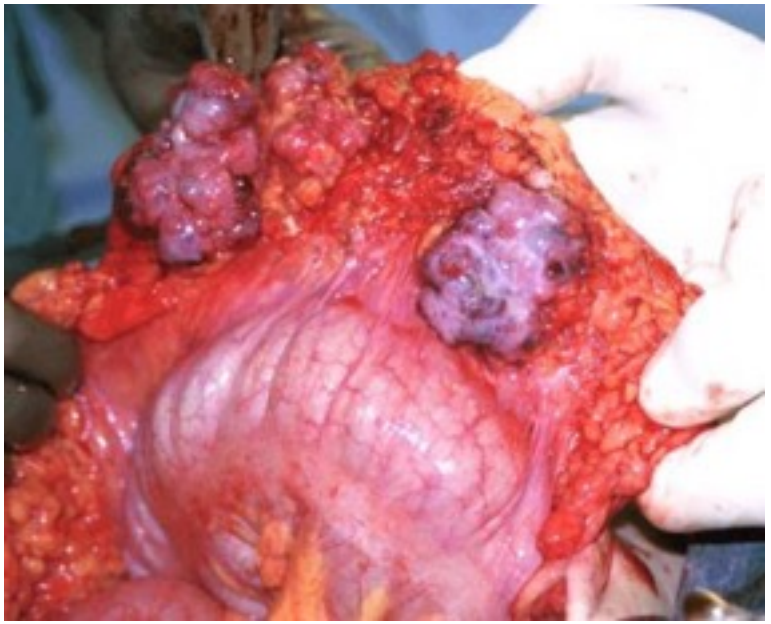

N
Proportion of patients with inherited mutation
PNAS 2011
ALL PATIENTS 360 0.23
Age at diagnosis
< 40 10 0.10
40 - 49 57 0.30
50 - 59 99 0.35
60 - 69 114 0.21
> 70 80 0.06
Self, in addition to ovarian cancer
Breast cancer 31 0.71
No breast cancer 329 0.19
Family history
Breast cancer 141 0.35
Ovarian cancer 35 0.54
Pancreatic cancer 18 0.28
Uterine cancer 19 0.42
Colon cancer 60 0.15
Breast or ovarian cancer 157 0.36
Neither breast nor ovarian cancer 203 0.12
Disease site
Ovary 273 0.22
Peritoneum 48 0.27
Fallopian tube 31 0.39
Ovary/Endometrium 8 0.13
Histology
Serous 242 0.24
Carcinoma, undifferentiated 64 0.20
Endometrioid 23 0.17
Clear cell 17 0.06
Carcinosarcoma, other 14 0.14
Grade
1 19 0.11
2 13 0.15
3 328 0.24
Stage
I 22 0.18
II 26 0.23
III or IV 308 0.22
TP53
RAD51C
RAD50
PALB2
NBN
MSH6
MRE11
CHEK2
BRIP1
BARD1
BRCA1
40
BRCA2
23

Clinical Presentation

- Early disease is usually asymptomatic
- Symptoms are generally benign and non-specific
  - Anorexia
  - Fatigue
  - Early satiety
  - Loss of appetite
  - Bloating
  - Diffuse/dull/constant abdominal pain

“The cancer that whispers”

Diagnosis

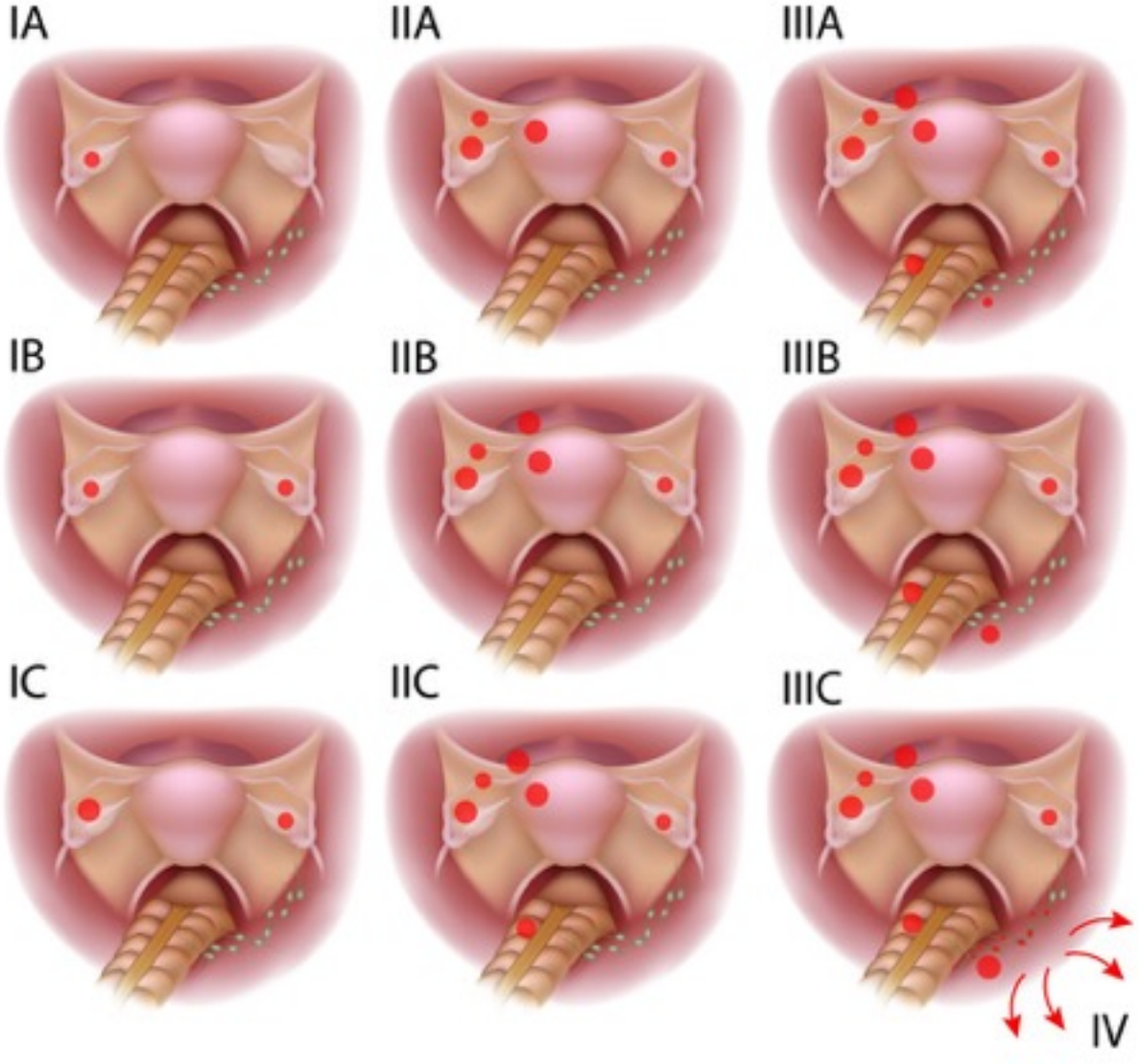


- Ultrasound
- CA 125
- CT for extent of disease spread
- Paracentesis/thoracentesis

- Limited role for screening patients at population risk

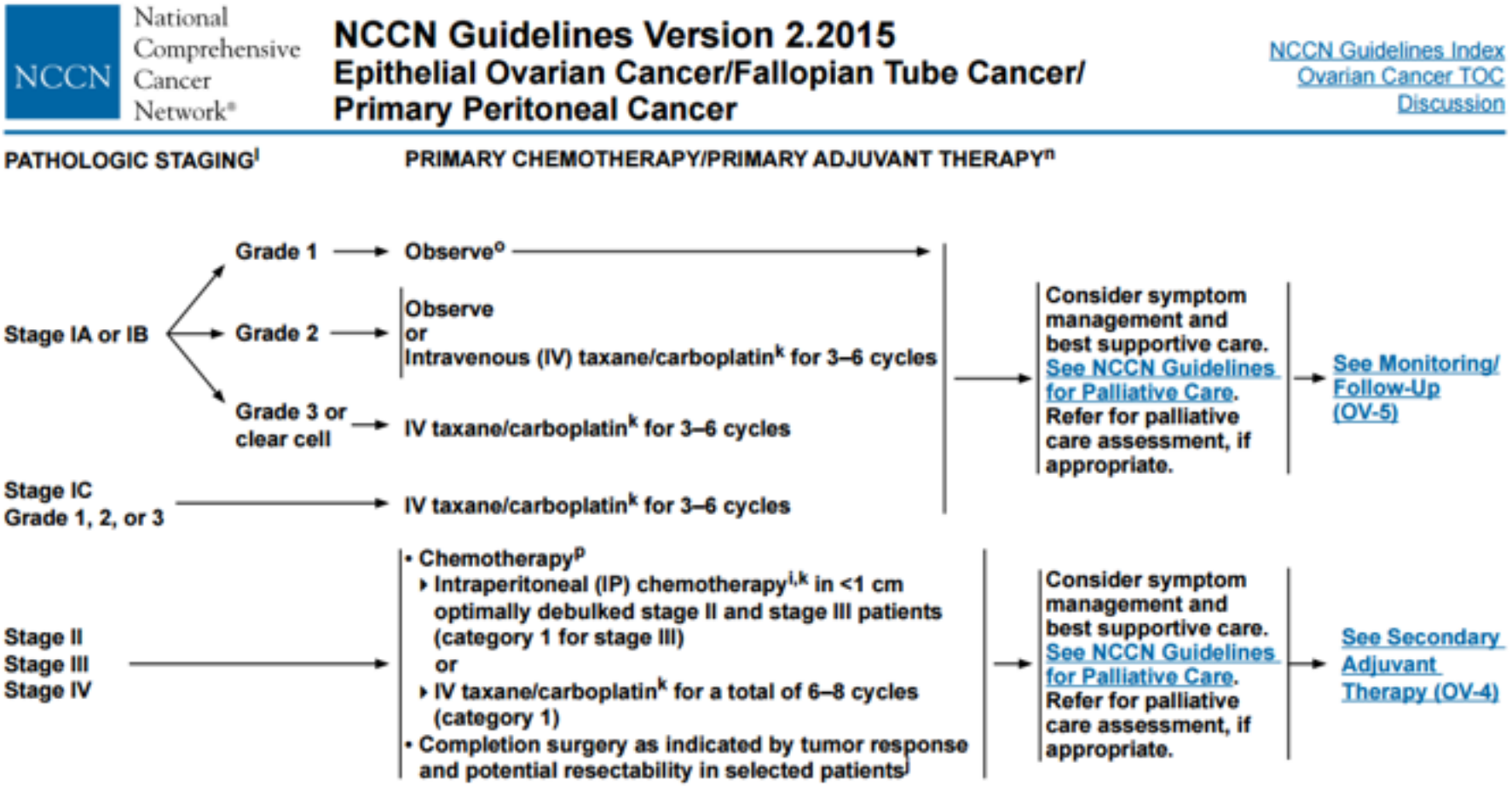
- Surgical evaluation

Staging



Nethealthbook.com

Therapy – Primary disease



Therapy – Recurrence

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2015
Epithelial Ovarian Cancer/Fallopian Tube Cancer/ Primary Peritoneal Cancer

NCCN Guidelines Index
Ovarian Cancer TOC
Discussion

ACCEPTABLE RECURRENCE THERAPIES (1 OF 2)[a]

	Cytotoxic Therapy (In alphabetical order)	Hormonal Therapy	Targeted Therapy	Radiation Therapy
Preferred Single Agents or Combinations	**Platinum-Sensitive Disease[b,c]** Carboplatin[1] Carboplatin/docetaxel[2,3] Carboplatin/gemcitabine[1] Carboplatin/gemcitabine/bevacizumab[d,e] (category 2B)[4] Carboplatin/liposomal doxorubicin[5] (category 1) Carboplatin/paclitaxel (category 1)[6] Carboplatin/paclitaxel (weekly)[7] Cisplatin[6] Cisplatin/gemcitabine[8]		Bevacizumab[d,e,17,18] Olaparib[9,19,20]	
	Platinum-Resistant Disease Docetaxel[9] Etoposide, oral[10] Gemcitabine[11,12] Liposomal doxorubicin[11,12] Liposomal doxorubicin/bevacizumab[d,e,13] Paclitaxel (weekly)[14] Paclitaxel (weekly)/bevacizumab[d,e,13] Topotecan[15,16] Topotecan/bevacizumab[d,e,13]		Bevacizumab[d,e,17,18] Olaparib[9,19,20]	
Other Potentially Active Agents[f]	**Single Agents[21]** Altretamine Capecitabine Cyclophosphamide Doxorubicin Ifosfamide Irinotecan Melphalan Oxaliplatin Paclitaxel Paclitaxel, albumin bound (nab-paclitaxel) Pemetrexed Vinorelbine	Aromatase inhibitors Leuprolide acetate Megestrol acetate Tamoxifen		Palliative localized radiation therapy

Follow-up

- Regular pelvic examinations
- Monitor CA 125 - controversial
- Imaging for symptoms (or elevated CA 125)
- GENETIC COUNSELING/TESTING
- Cascade Testing for family members
- Clinical trials

Emerging Therapies

- Targeted therapies
- Cytotoxic agents
  - HIPEC
  - Alternate dosing schemes
- Vaccine therapies
- Revisiting radiotherapy

Germ Cell Tumors

- Epidemiology
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
  - Recurrent
- Follow-Up
- Future Therapy

Epidemiology

- Approximately 5% of ovarian tumors
- “Juvenile Ovarian Cancer”
  - Median age 16-20 years depending on histology
- 10-year survival up to 88.6%

Histology

- Dysgerminoma
  - Most common malignant ovarian germ cell tumor
  - 5-10% associated with gonadoblastomas
  - 10% bilateral on gross exam and another 10% have microscopic involvement
- Yolk Sac Tumor (endodermal sinus tumor)
  - Tan-gray
  - Abundant hemorrhage and necrosis
  - AFP is elevated

Histology

- Choriocarcinoma
  - Rare as a primary tumor of the ovary
  - Syncytiotrophoblast/cytotrophoblast admixture
  - Spreads by vascular invasion
- Teratomas
  - Mature cystic teratomas (Benign, “dermoids”)
  - Immature (malignant) teratomas = 3% of teratomas
  - Most are unilateral

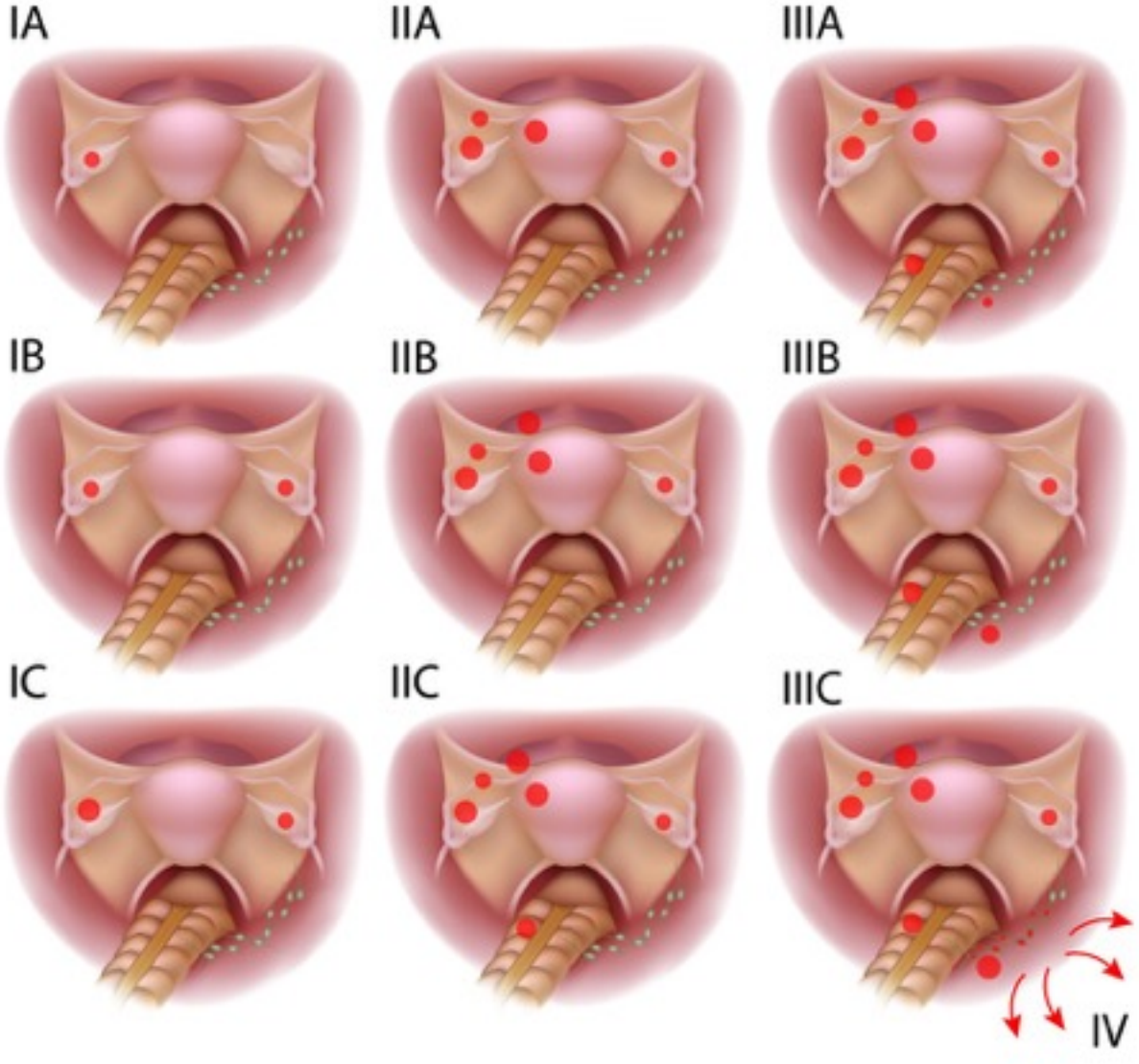
Presentation

- Abdominal pain associated with a palpable abdominopelvic mass (85% of patients)
- Acute abdominal pain (10%)
  - Due to rupture, hemorrhage, or torsion
- Abdominal distension (35%)
- Fever (10%)
- Vaginal bleeding (10%)

Diagnosis

- Large mass, generally found at the time of surgery
- Primary surgery is often required for diagnosis and therapy (resolution of symptoms)
- Fertility preservation:
  - removal of abnormal ovary and sampling of other pelvic tissues
  - preferable if possible (young patient ages)

Staging



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Therapy – Primary Setting

- Observation for:
  - Stage I Grade 1 immature teratomas
  - Stage I dysgerminoma
- Systemic cytotoxic chemotherapy for everyone else
  - Bleomycin/Etoposide/Clisplatin (BEP)
    - 5 days of therapy every 3 weeks for 3-4 cycles
  - Etoposide/Carboplatin
    - 3 days of therapy every 3 weeks for 3 cycles
    - Selected patients only based on risk of toxicity and disease

Therapy – Recurrence

Malignant Germ Cell Tumors[2]

High-dose chemotherapy[2,3]

Cisplatin/etoposide

Docetaxel

Docetaxel/carboplatin

Paclitaxel

Paclitaxel/ifosfamide

Paclitaxel/carboplatin

Paclitaxel/gemcitabine

VIP (etoposide, ifosfamide, cisplatin)

VeIP (vinblastine, ifosfamide, cisplatin)

VAC (vincristine, dactinomycin, cyclophosphamide)

TIP (paclitaxel, ifosfamide, cisplatin)

Radiation therapy

Supportive care only

Borrowed from testicular cancer studies

Follow-up

- Psychosocial Support
- Routine exams
- Serum biomarkers (if indicated)

Emerging Therapies

- Clinical trials
- Less extensive surgery
- Less cytotoxic treatment
- Targeted therapies

Stromal Tumors

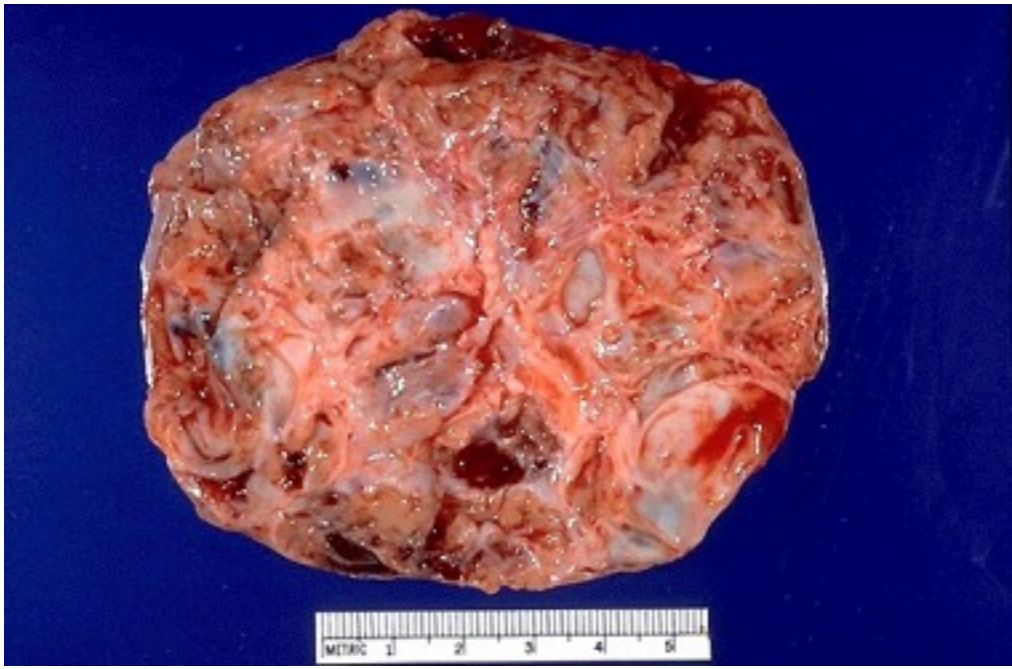
- Epidemiology
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
  - Recurrent
- Follow-Up
- Future Therapy

Epidemiology

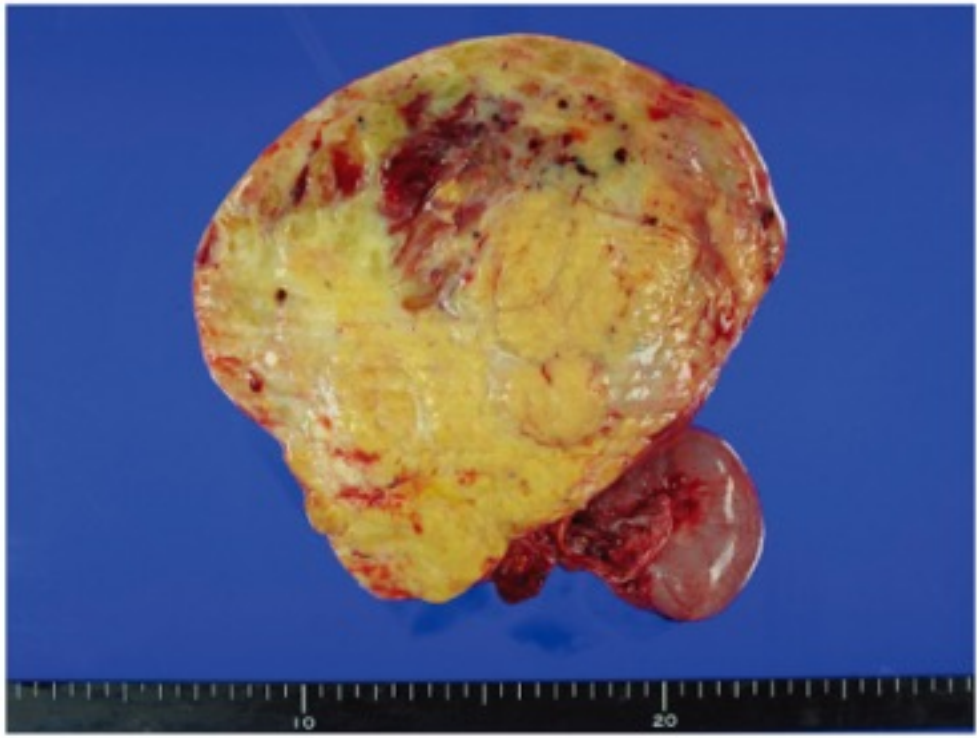
- Account for 7% of malignant ovarian neoplasms
- Account for 90% of functional tumors
- Annual incidence between 0.5 and 1.7 cases per 100,000 women

Histology

- Granulosa Cell Tumors
  - Estrogen producing
  - Inhibin as a biomarker
    - B is better than A
  - Adult type
    - Low grade/indolent
    - Diagnosed later in life
  - Juvenile type
    - 44% diagnosed before age 10
    - Isosexual precocious puberty



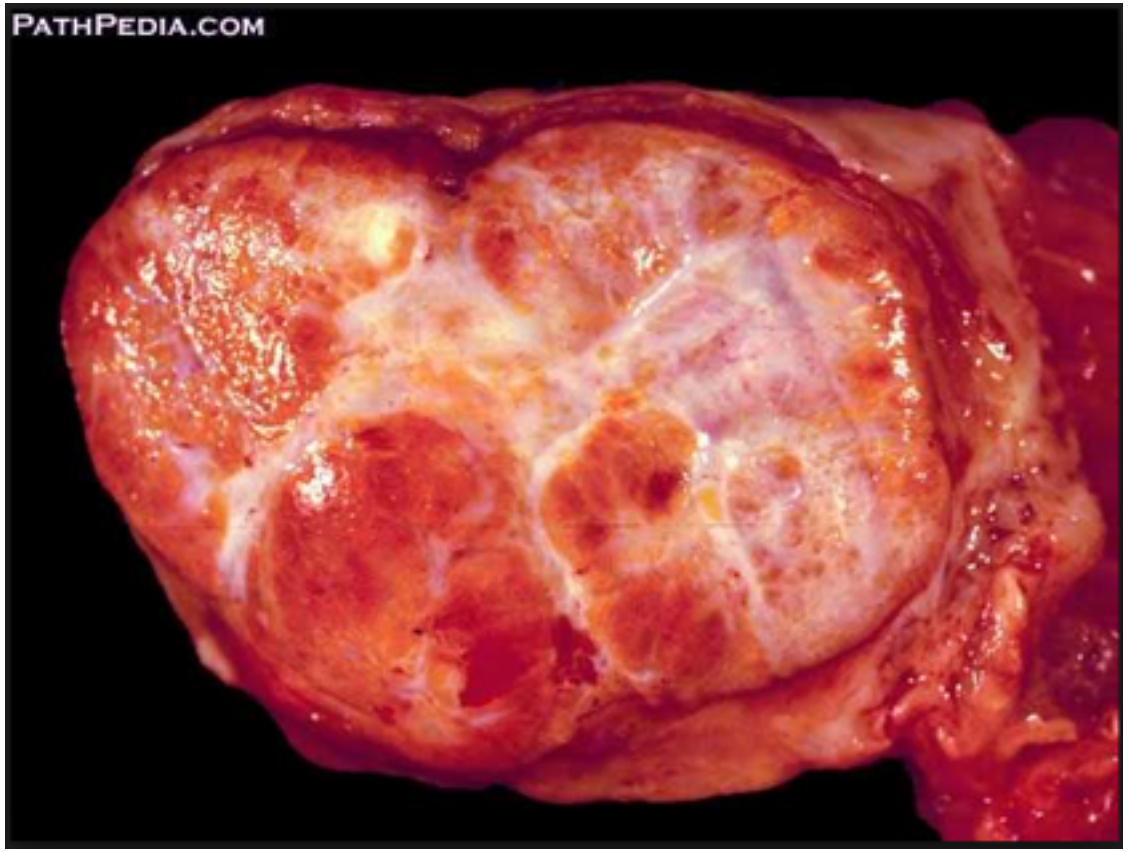
Histology



- Thecoma/Fibroma
  - Lipid-laden stromal cells
  - Occur later than other stromal tumors (most in 30s/40s)
  - Abnormal bleeding and/or a pelvic mass

Histology

- Stertoli-Leydig Tumors
  - Less than 0.2% of ovarian tumors
  - Androgen producing tumors leading to virilization



Presentation

- Abdominopelvic mass
- Abnormal bleeding
- Virilization (Sertoli-Leydig cell tumors)

Staging / Therapy / Follow-up

- Staging
  - Same as other ovarian tumors
- Therapy
  - Hybrid of germ cell and epithelial cancers
- Follow-up
  - Routine exams
  - Serum markers if appropriate

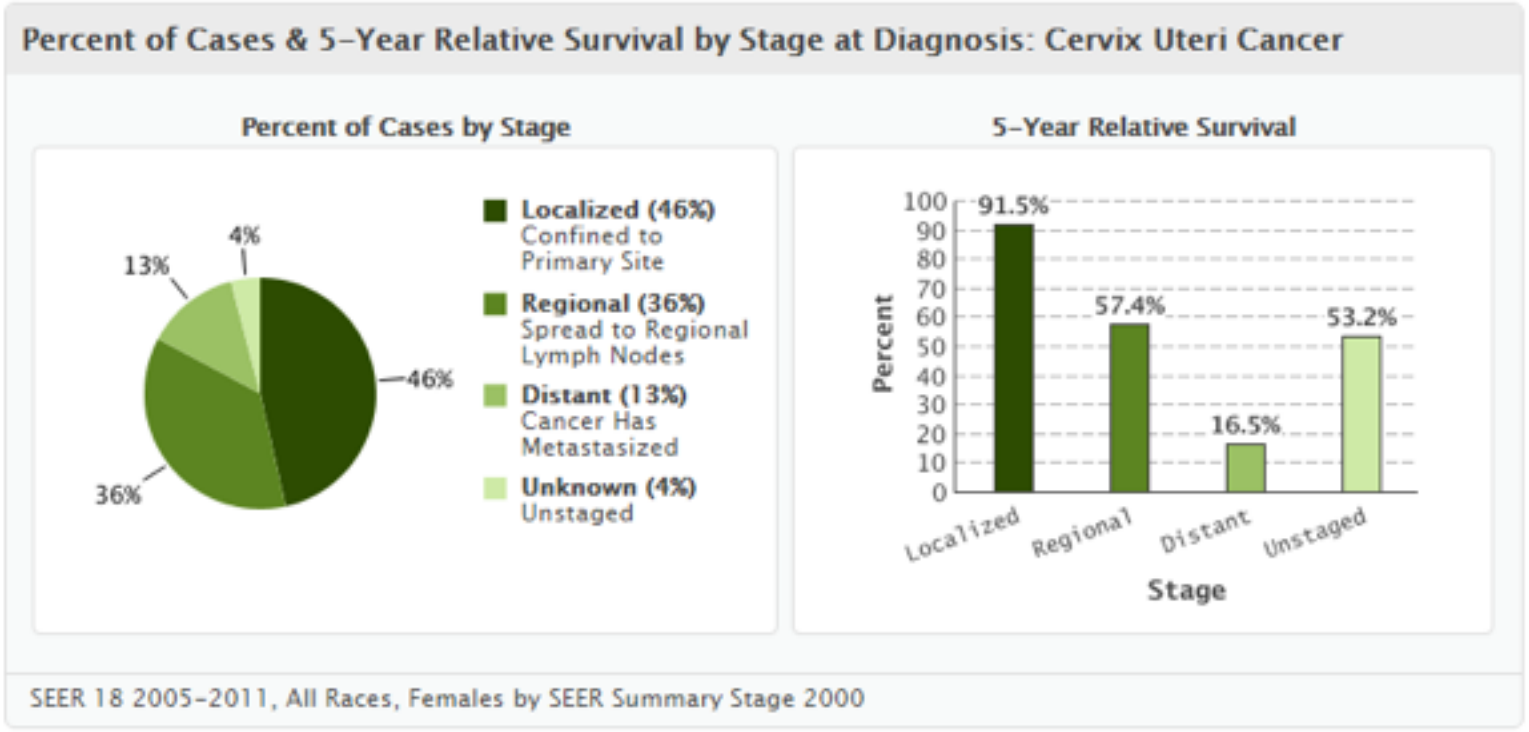
Cervical Cancer

Cervical Cancer

- Epidemiology and Risk Factors
- Histology
- Presentation
- Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
  - Recurrent
- Follow-Up
- Future Therapy

Epidemiology

- 12,990 cases expected in 2016
  - 7.7 per 100,000 women
- 4,120 deaths expected in 2016

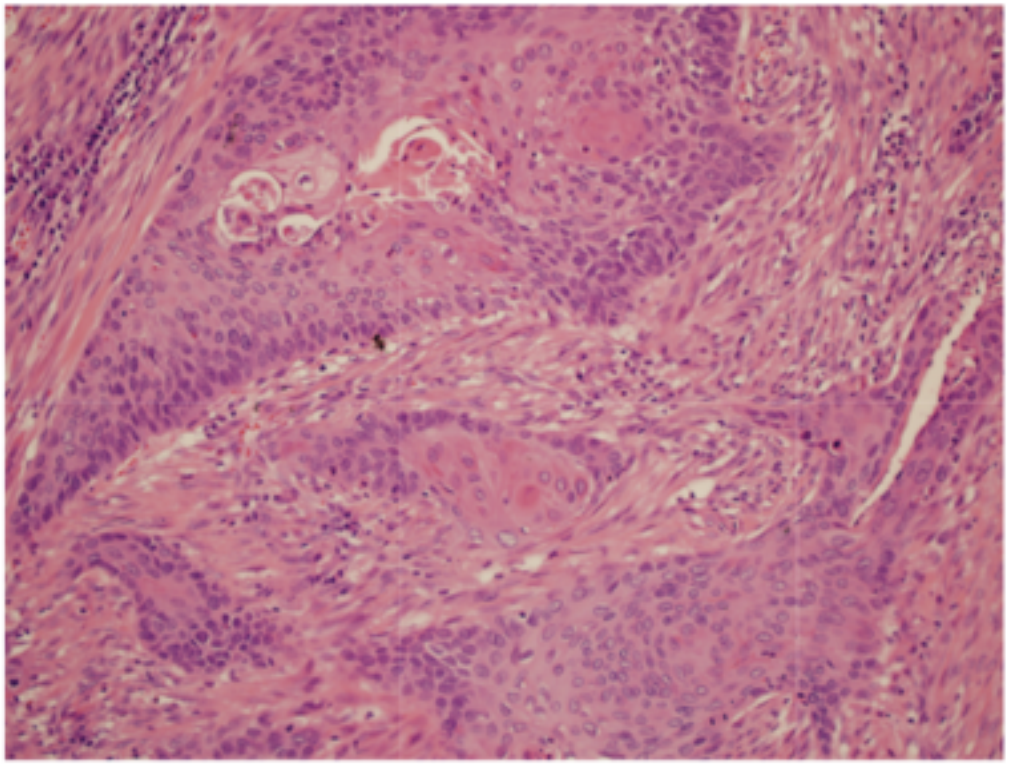


Epidemiology

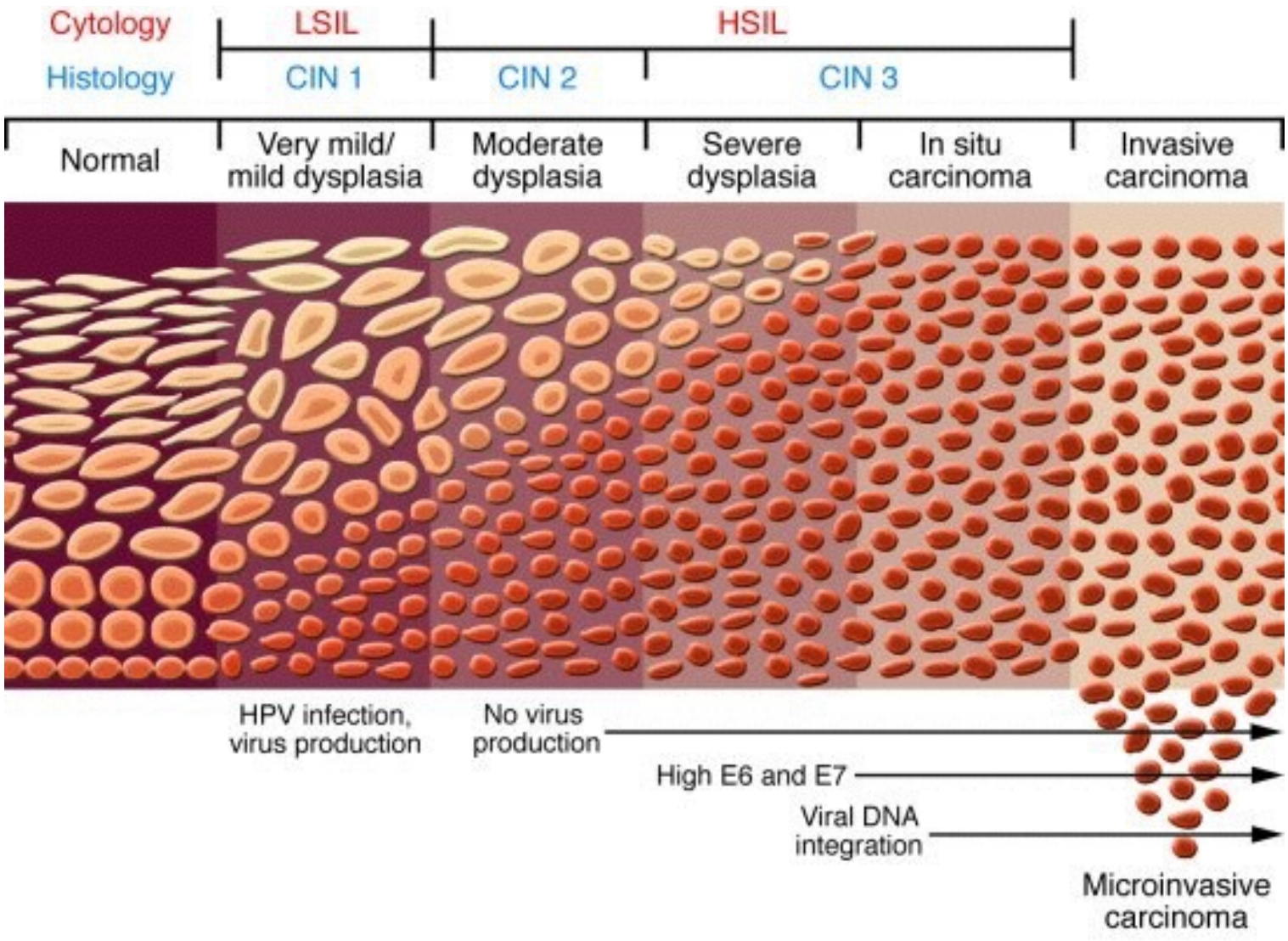
- HPV infection
- High parity
- Increased number of sexual partners
- Young age at time of first sexual intercourse
- Low socioeconomic status
- History of smoking
- Long-term use of oral contraceptives
- Physical inactivity

Histology

- Squamous
- Adenocarcinoma
- Rare histologies
  - Clear cell
  - Serous
  - Glassy Cell
  - Neuroendocrine
  - Mesenchymal tumors



Pathogenesis



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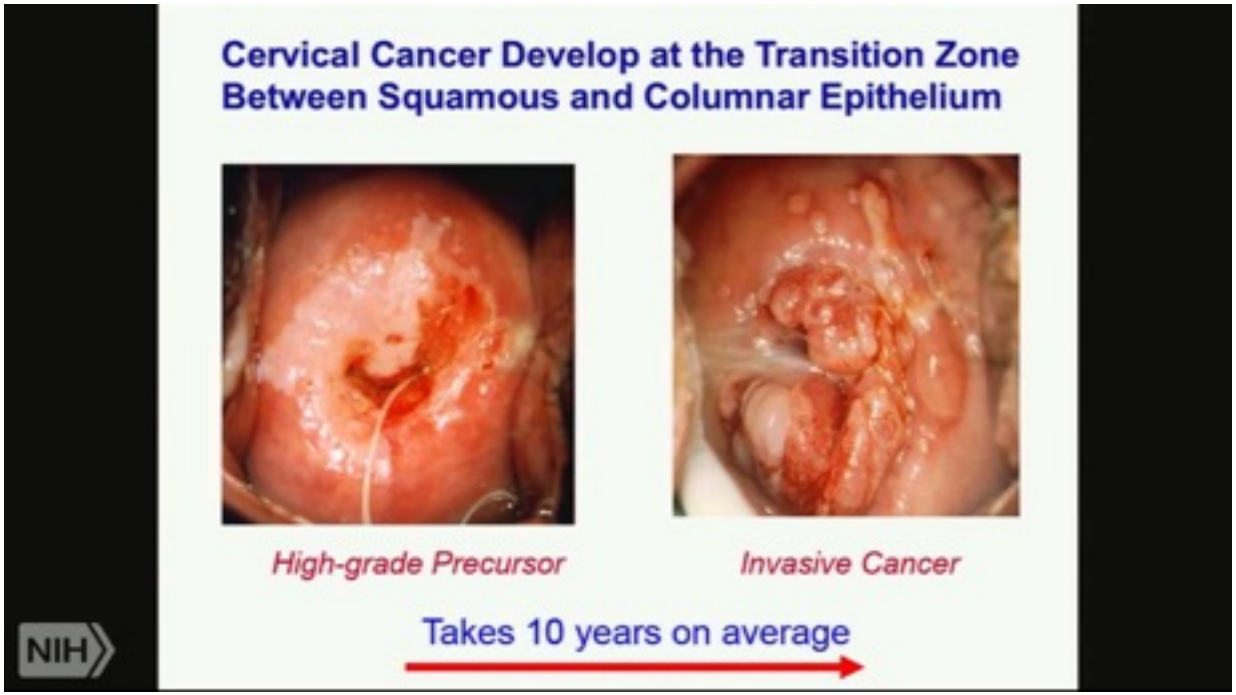
Clinical Presentation

- Post-coital bleeding
- Abnormal uterine bleeding
- Abnormal Pap smear
- Pelvic pain
- Flank pain
- Uncontrolled leakage of urine/stool from vagina

Diagnosis

- Pelvic examination/biopsies
- Cone biopsy
- Chest x-ray
- IVP
- Cystoscopy
- Proctoscopy



Staging

- Clinically staged
- PET CT often used in western countries but not available in the highest prevalence regions of the world

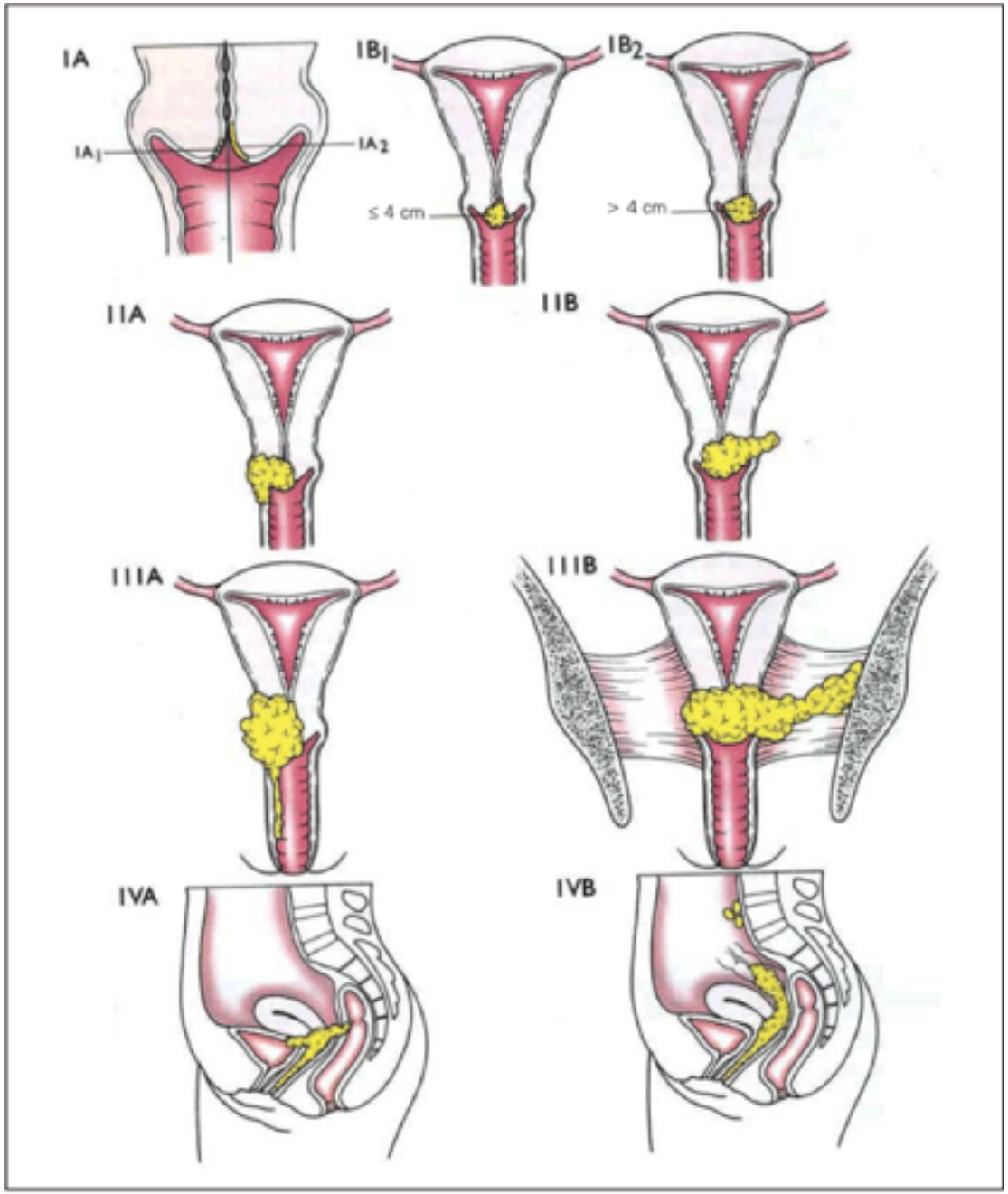


Figure 1. Staging of uterine cervix carcinoma according to FIGO[3].

http://dx.doi.org/10.1590/S0100-39842007000300014

Therapy

- Stage IA1 – Cone biopsy, hysterectomy
- Stage IA2 – modified radical hysterectomy
- Stage IB and IIA – radical hysterectomy OR pelvic RT
  - Add chemotherapy to RT in IB2 and IIA2
  - Can add to RT in IB1 and IIA1
- Stage IIB to IVA – pelvic RT with chemotherapy
- Stage IVB – systemic chemotherapy/clinical trials

Follow-up

- Psychosocial Support
- Routine exams
- Cytologic testing

Emerging Therapies

- Sentinel Node Mapping
- Fertility Preservation
- Targeted Therapies

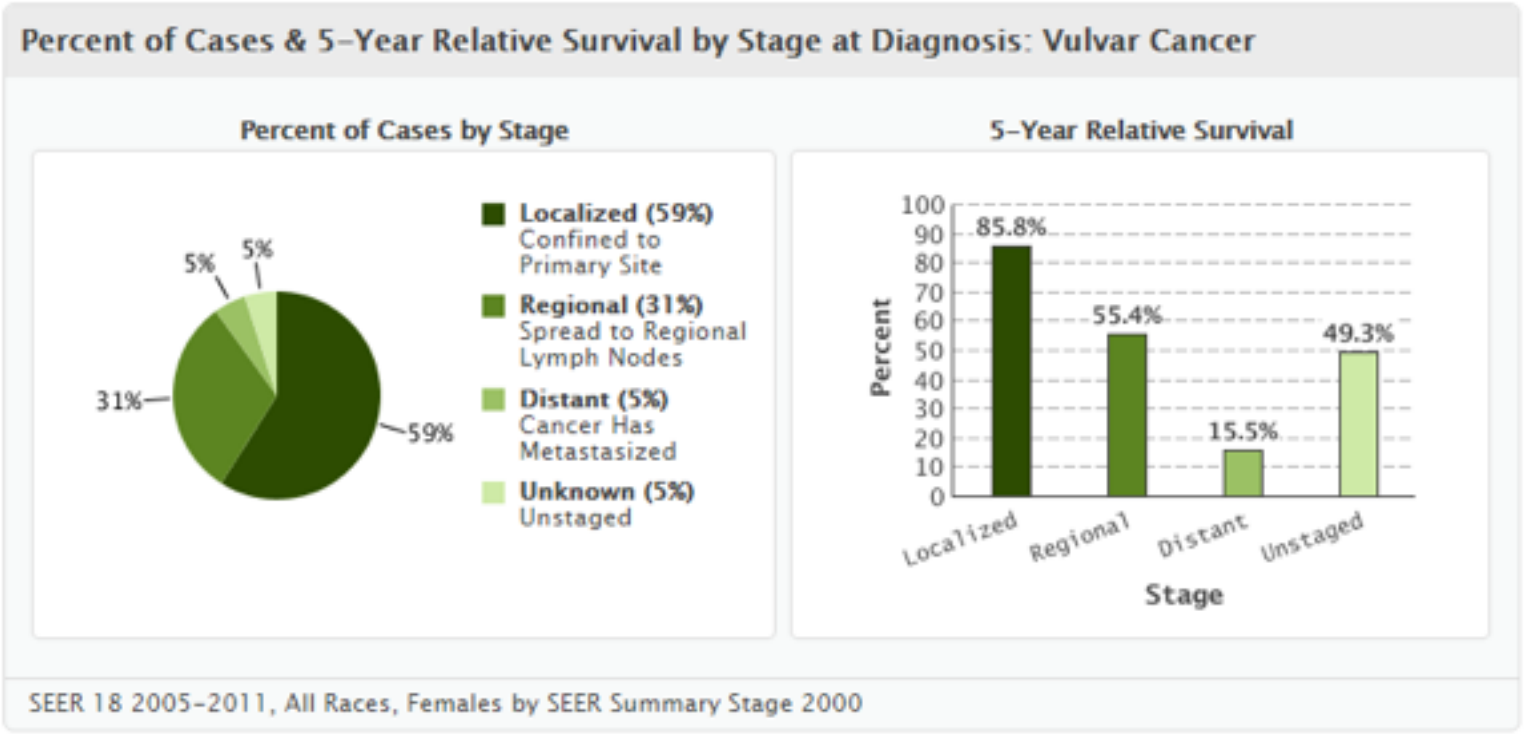
Vulvar Cancer

Vulvar Cancer

- Epidemiology and Risk Factors
- Histology
- Presentation / Diagnosis
- Staging
- Therapy
  - Early
  - Locally Advanced
  - Metastatic
- Follow-Up

Epidemiology

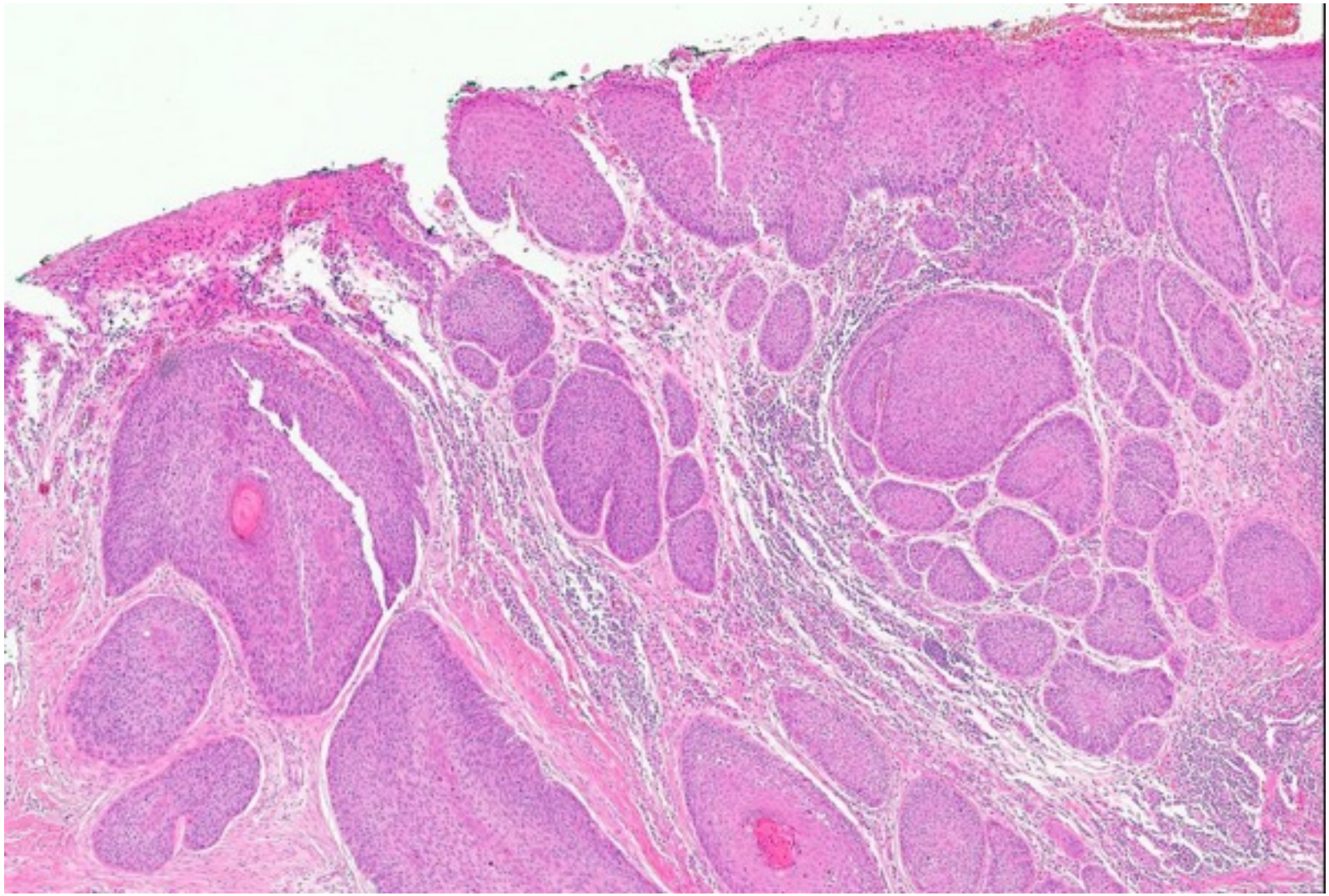
- 5,950 cases expected in 2016
- 1,110 deaths expected in 2016



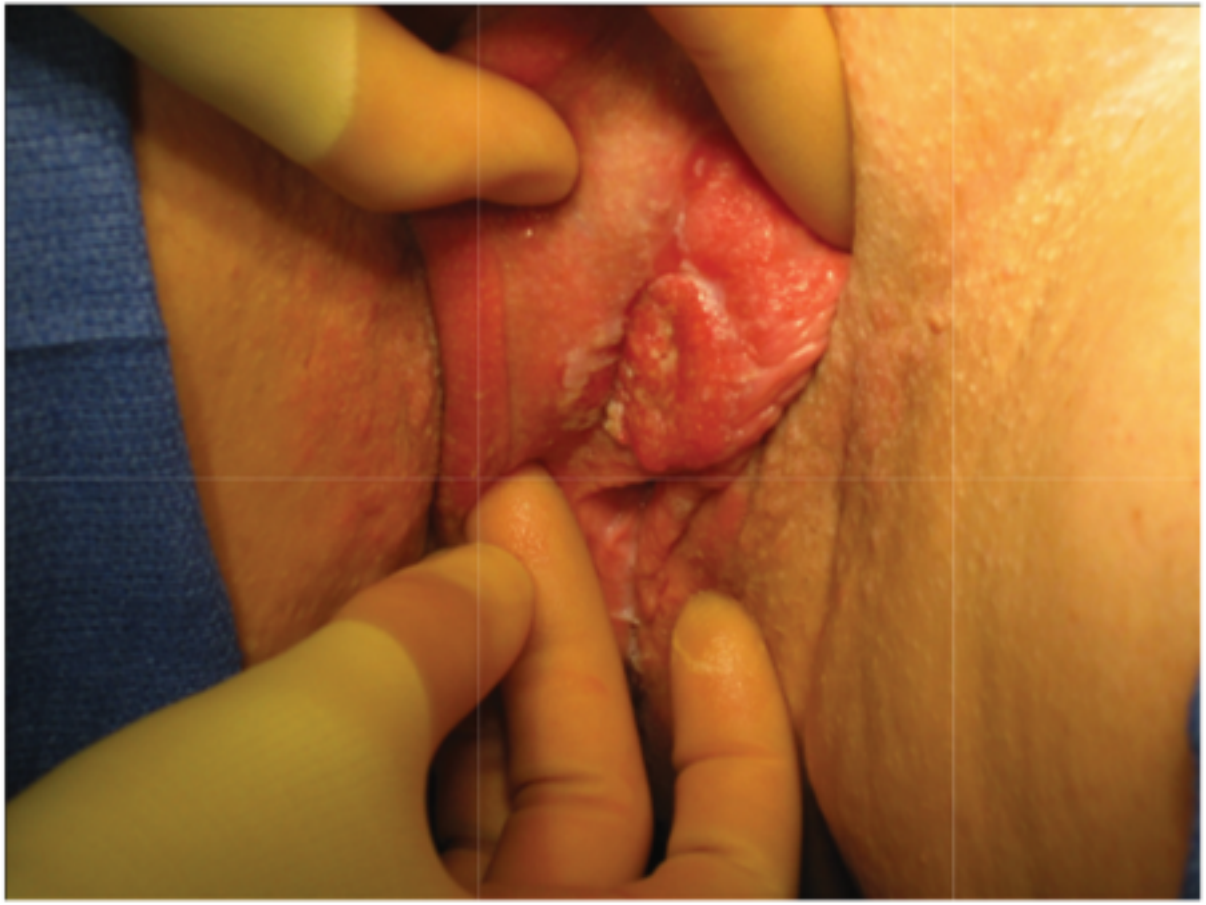
Epidemiology

- Condyloma
- History of squamous dysplasia
- HPV infection in basaloid or warty types
- Common risk factors with cervical cancer
  - Multiple sex partners
  - Early age at initiation of sexual intercourse
  - History of abnormal Pap smears
- HPV associated more common in women < 50 years
- Non-HPV is more common in older women

Histology



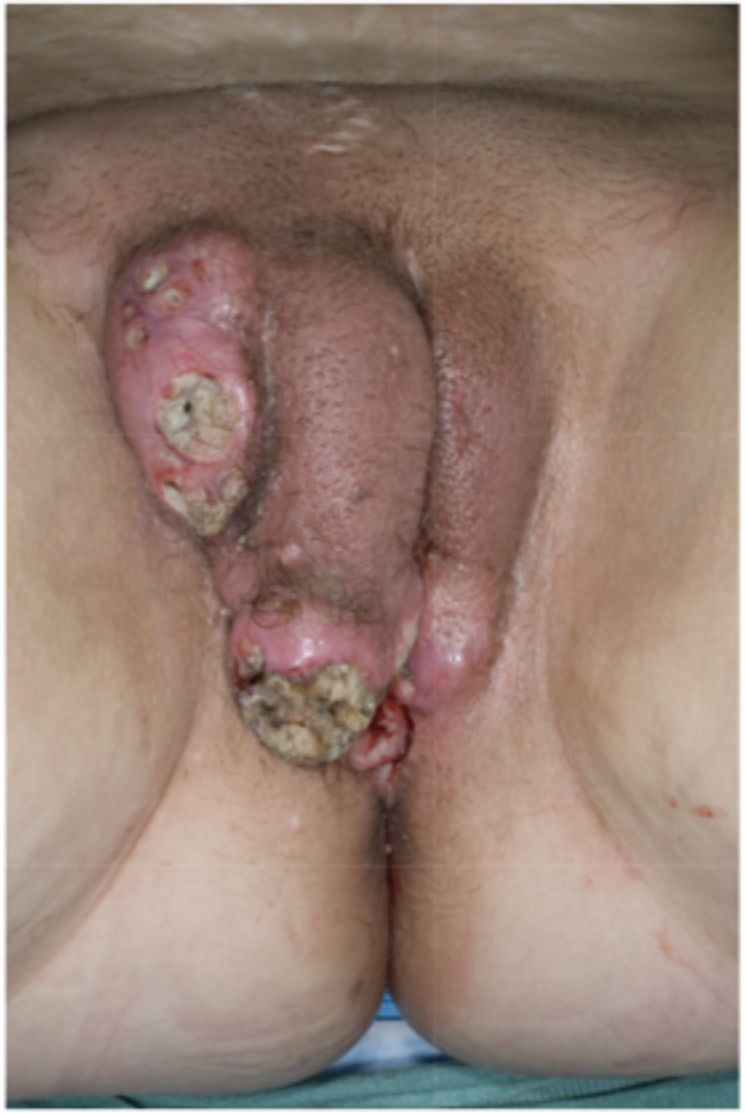
Presentation – Early disease



Persistent Irritation
Discoloration
Bleeding

Presentation – Late disease

Pain
Bleeding
Pressure from enlarged masses
Foul odor



Staging

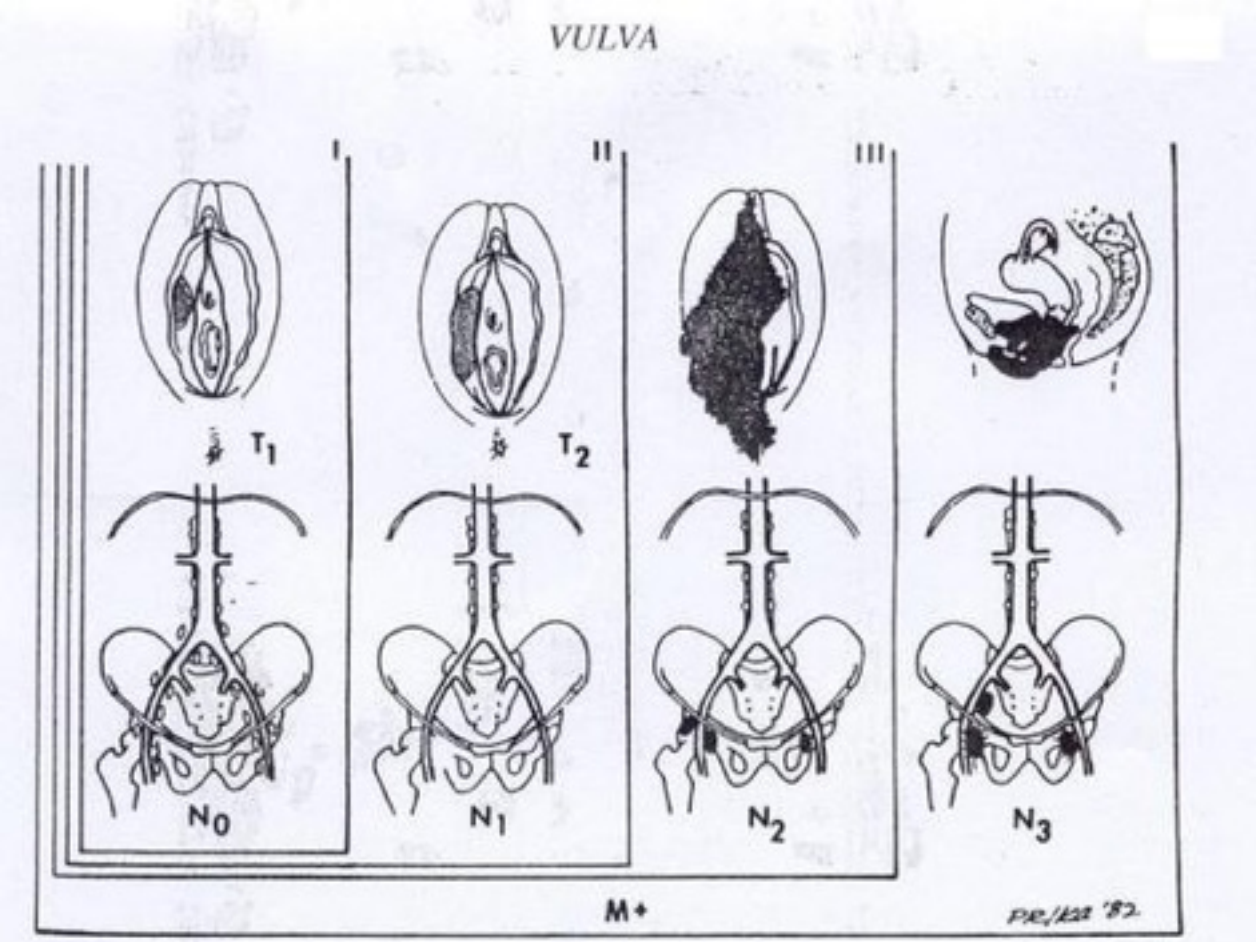


FIG. 50-2. Anatomic staging for vulva cancer. (From DuBeshter B, Lin J, Angel C, et al. Gynecologic tumors. In: Rubin P, ed. *Clinical oncology for physicians and medical students: a multidisciplinary approach*, 7th ed. Philadelphia: WB Saunders, 1993:363–418, with permission.)

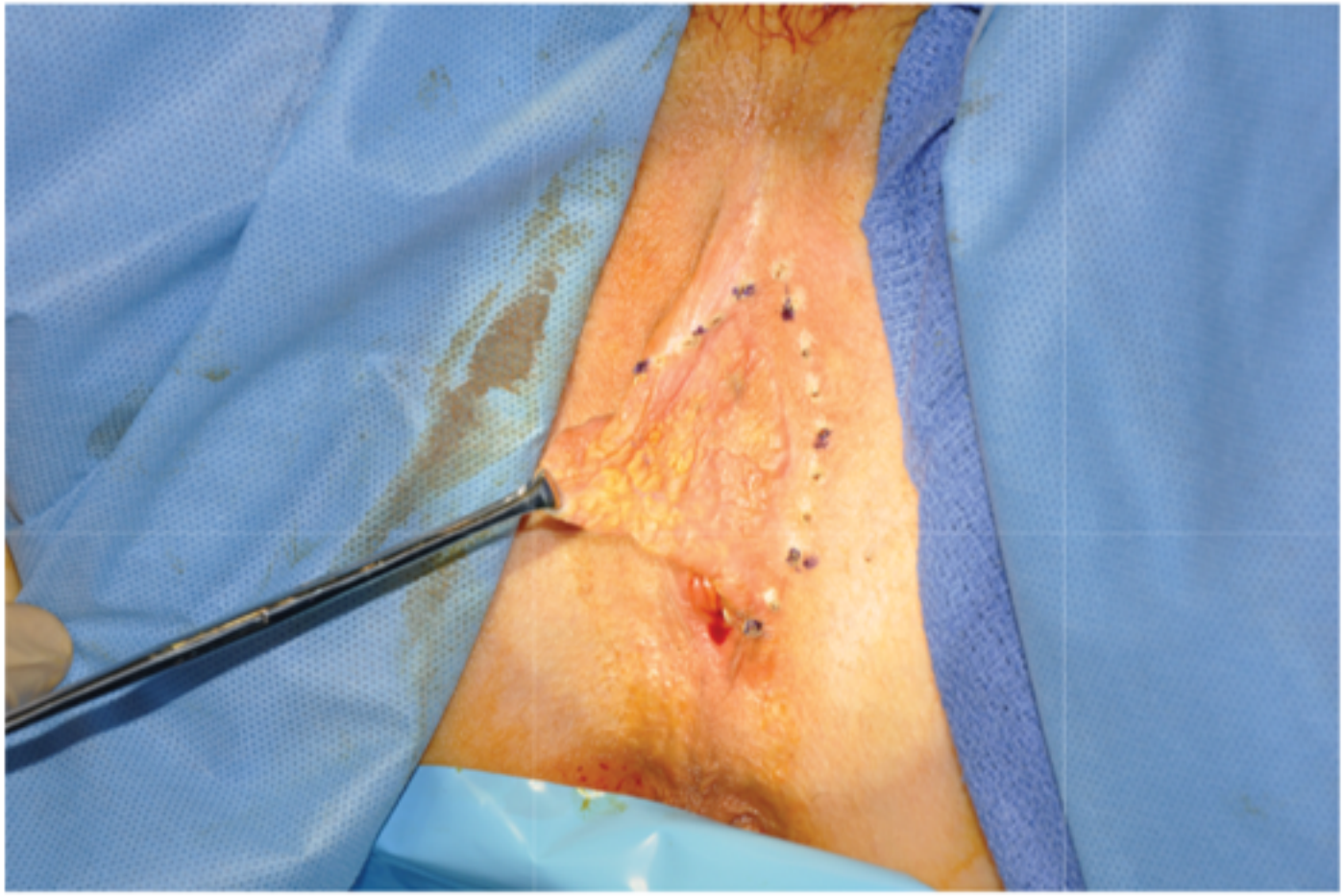
Staging

Table 19.2 Integrated 2009 FIGO and AJCC Staging System for Squamous Cell Carcinoma of the Vulva

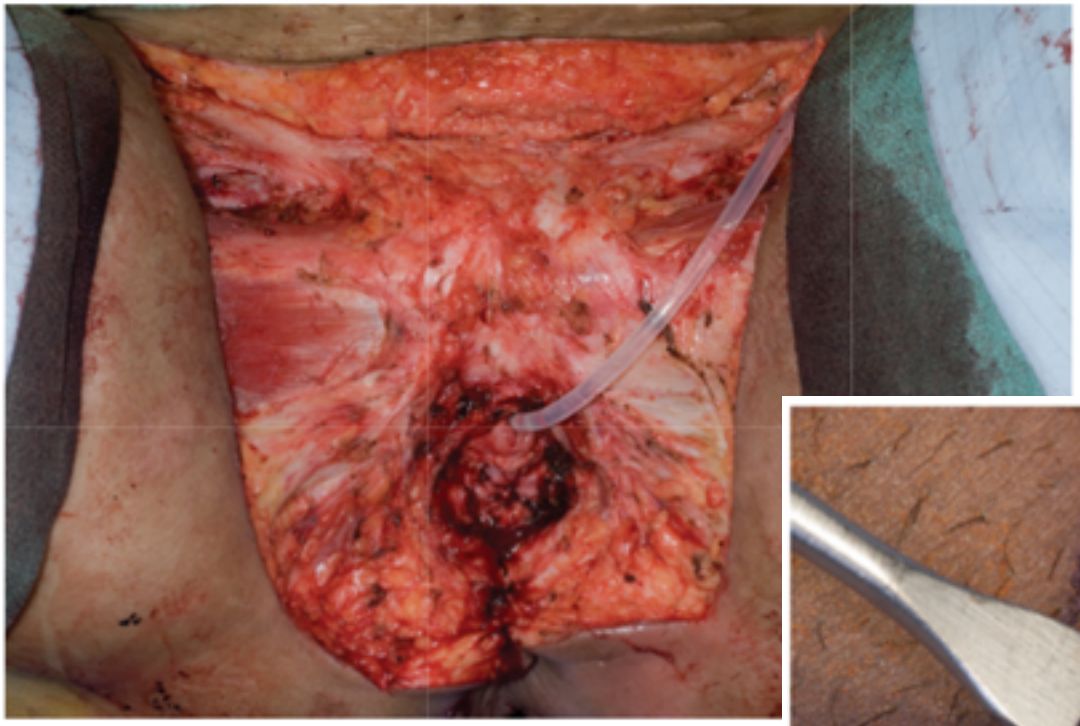
FIGO		AJCC		
		T	N	M
		Tis: No invasion past basement membrane (not in FIGO system)		
I: Tumor confined to the vulva				
IA	Lesions ≤ 2 cm in size, confined to vulva or perineum and with stromal invasion ≤ 1.0 mm, no nodal metastasis	T1a	N0	M0
IB	Lesions > 2 cm in size or with stromal invasion > 1.0 mm, confined to the vulva or perineum, with negative nodes	T1b	N0	M0
II	Tumor of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus), with negative nodes	T2	N0	M0
III	Tumor of any size with or without extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus), with positive inguinofemoral lymph nodes	T1 or T2	N1-N3	M0
IIIA	(i) 1–2 lymph node metastasis(es) (< 5 mm), or (ii) 1 lymph node metastasis (≥ 5 mm)	T1 or T2	N1a = (i) N1b = (ii)	M0
IIIB	(i) 3 or more lymph node metastases (< 5 mm) or (ii) 2 or more lymph node metastases (≥ 5 mm)	T1 or T2	N2a = (i) N2b = (ii)	M0
IIIC	Positive nodes with extracapsular spread	T1 or T2	N2c N3 = inguinal skin ulceration or fixed nodes	M0
IV	Tumor invades other regional (2/3 upper urethra, 2/3 upper vagina), or distant structures	T3 = any size, involves upper urethra, bladder, rectum, bone		
IVA	Tumor invades: (i) upper urethral and / or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or (ii) fixed or ulcerated inguinofemoral lymph nodes	T3		M0
IVB	Distant metastasis: includes pelvic nodes	T1, T2 or T3		M1

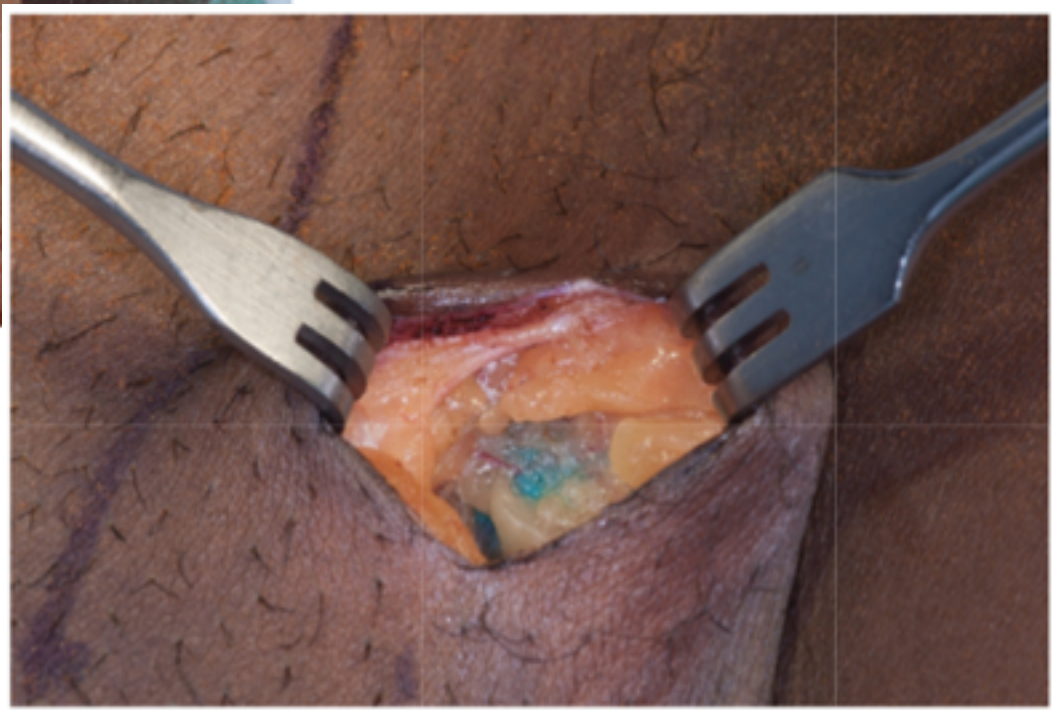
Therapy – Early

- Local excision (simple or radical)



Therapy – Locally Advanced





Therapy – Metastatic

- Systemic cytotoxic therapy is disappointing
- Targeted therapies are under development

Follow-up

- Psychosocial Support
- Routine exams

Summary

- Risk can be reduced by modifying risk factors
- Most cancers are responsive to front-line therapy
- Management of recurrent disease varies by site of origin/histology but is often sub-optimal
- More discoveries are needed to overcome these diseases