

Cervical case study, cont'd.

- **Jody died less than a year later when the disease had blocked her ureters causing hydronephrosis, invaded her lymph glands causing unilateral leg and vulvar edema, a rectovaginal fistula, excruciating pelvic pressure and pain, and ultimately she succumbed to lung mets from her squamous epithelial cervical dis.**
- **Her mother & brother at her side. I still have the teddy bear she bought for me to remind of paps.**

Endometrial Cancer



Endometrial Cancer Case Study

- **Doris, a 58 y.o. WDF, G.0, LMP: age 55, with PMH of DM type 2, HTN, & obesity presents with c/o vaginal bleeding for 2 months. Her PCP referred her to an OB/GYN who performed an in-office endometrial biopsy. This returned from pathology with the diagnosis of endometrial carcinoma and she was referred to a GYN oncologist.**

Endometrial Cancer: Annual Incidence and Mortality

ACS Estimates

Year	Cases	Deaths
1987	35,000	2,900
2000	36,100	6,500*

***224% increase**
American Cancer Society 2000

- **Type I**
 - Estrogen Related
 - Younger and heavier patients
 - Low grade
 - Perimenopausal
 - Exogenous estrogen
- **Type II**
 - Aggressive
 - Unrelated to estrogen stimulation
 - Occurs in older & thinner women
 - Potential genetic basis
 - Lynch syndrome
 - Familial trend

Endometrial Cancer: Risk Factors

Characteristic	Relative Risk [X]
Obesity	
>30 LBS	3
>50 LBS	10
Nulliparous	2
Late Menopause	4
Unopposed Estrogen	9.5
Atypical Hyperplasia	29
Diabetes	2.8
Hypertension	1.5

- **Patient – Primary***
- **Cytology – Not satisfactory**
- **Histology - Secondary**
- **Hysteroscopy – Not satisfactory**
- **Sonography – Cost-effective issue**

***Patient/physician awareness**

Endometrial Cancer: Who Needs an Endometrial Biopsy?

- **Postmenopausal bleeding**
- **Postmenopausal women with endometrial cells on Pap**
- **Perimenopausal intermenstrual bleeding**
- **Abnormal bleeding with history of anovulation**
- **Thickened endometrial stripe via sonography**

Endometrial Cancer: Transvaginal Ultrasound Screening

N=250				
	Endometrial Stripe Thickness			
Diagnosis	<5mm	6-10mm	11-15mm	>15mm
Atrophy	93%	7%		
Hyperplasia		58%	42%	
Polyp		53%	47%	
Cancer		18%	41%	41%

Grigoriou: Maturitus 23:9-14,1996

Endometrial Cancer: Survival by Clinical Stage

Stage	%	Survival (%)
I	70.2	76.3
II	17.8	59.2
III	8.1	29.4
IV	3.6	10.3

Modified: FIGO 1991

Endometrial Cancer: FIGO Surgical Stage

Stage I	Confined to uterus
Stage II	Cervix involved
Stage III	Uterine serosa, adnexae, positive cytology, vaginal metastases, pelvic/aortic node metastases
Stage IV	Bladder, bowel, inguinal node, distant metastasis

Endometrial Cancer: Poor Prognostic Factors

- **Increasing age (over 65)**
- **Stage (> IB)**
- **Vascular invasion**
- **Grade**
- **Histologic Subtypes (Clear-cell, Serous, Adenosquamous)**
- **Aneuploidy**
- **Cytokinetics**
- **Altered oncogene/tumor suppressor gene expression**
- **Other**

Endometrial Cancer: Nodal Involvement

Situation	% Positive Nodes
G1, no myometrial invasion, no extrauterine disease.	<1%
G2 or G3, inner 1/3 invasion, no extrauterine disease	5-9% Pelvic 4% Aortic
G3, outer muscle, and/or extrauterine disease	20-60% Pelvic 10-30% Aortic

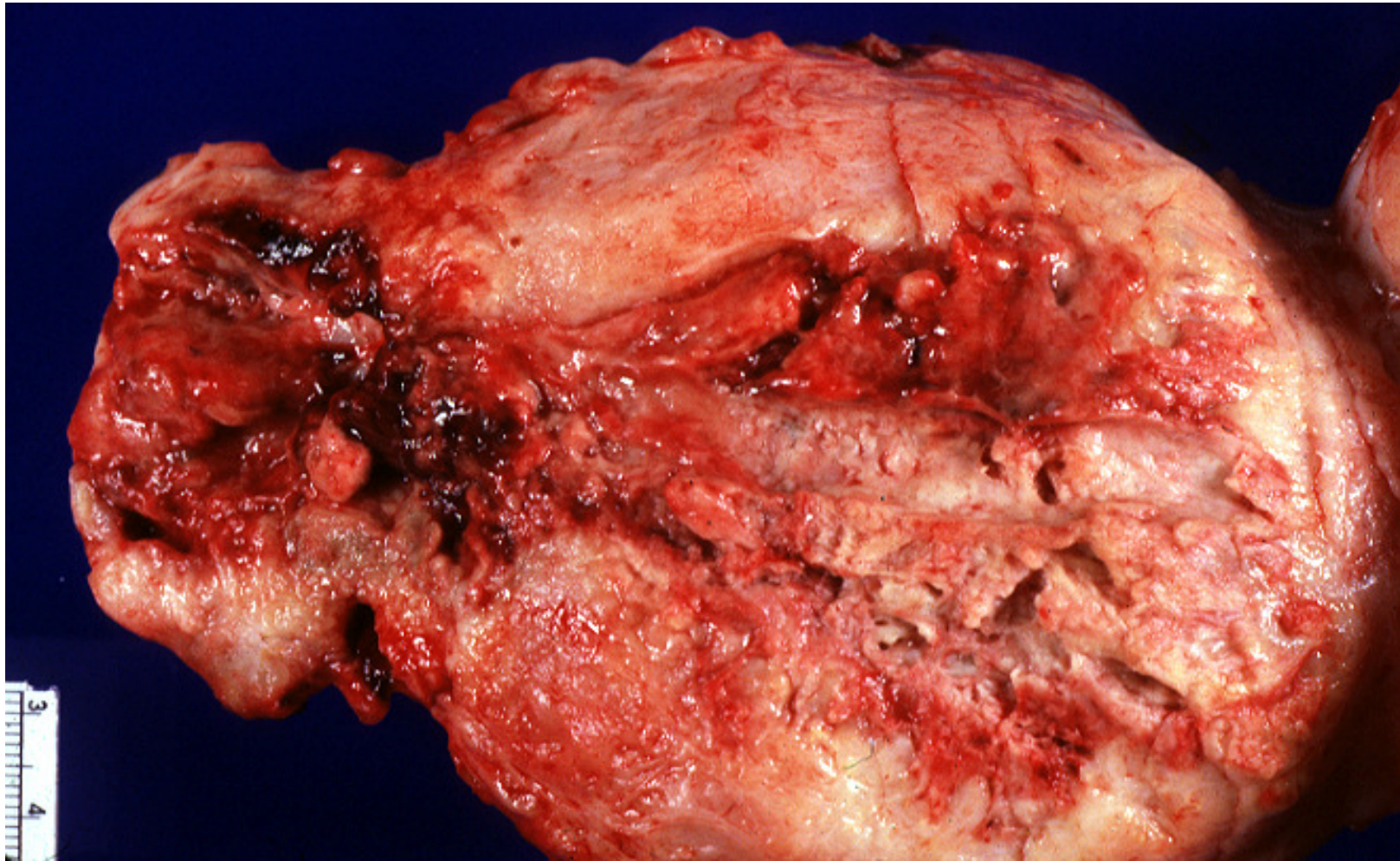
Endometrial Cancer: Pre-op Evaluation

- **CA125**
- **Chest X-ray**
- **Mammograms**
- **Colon Evaluation**
- **Transvaginal Ultrasound**
- **Others as indicated**

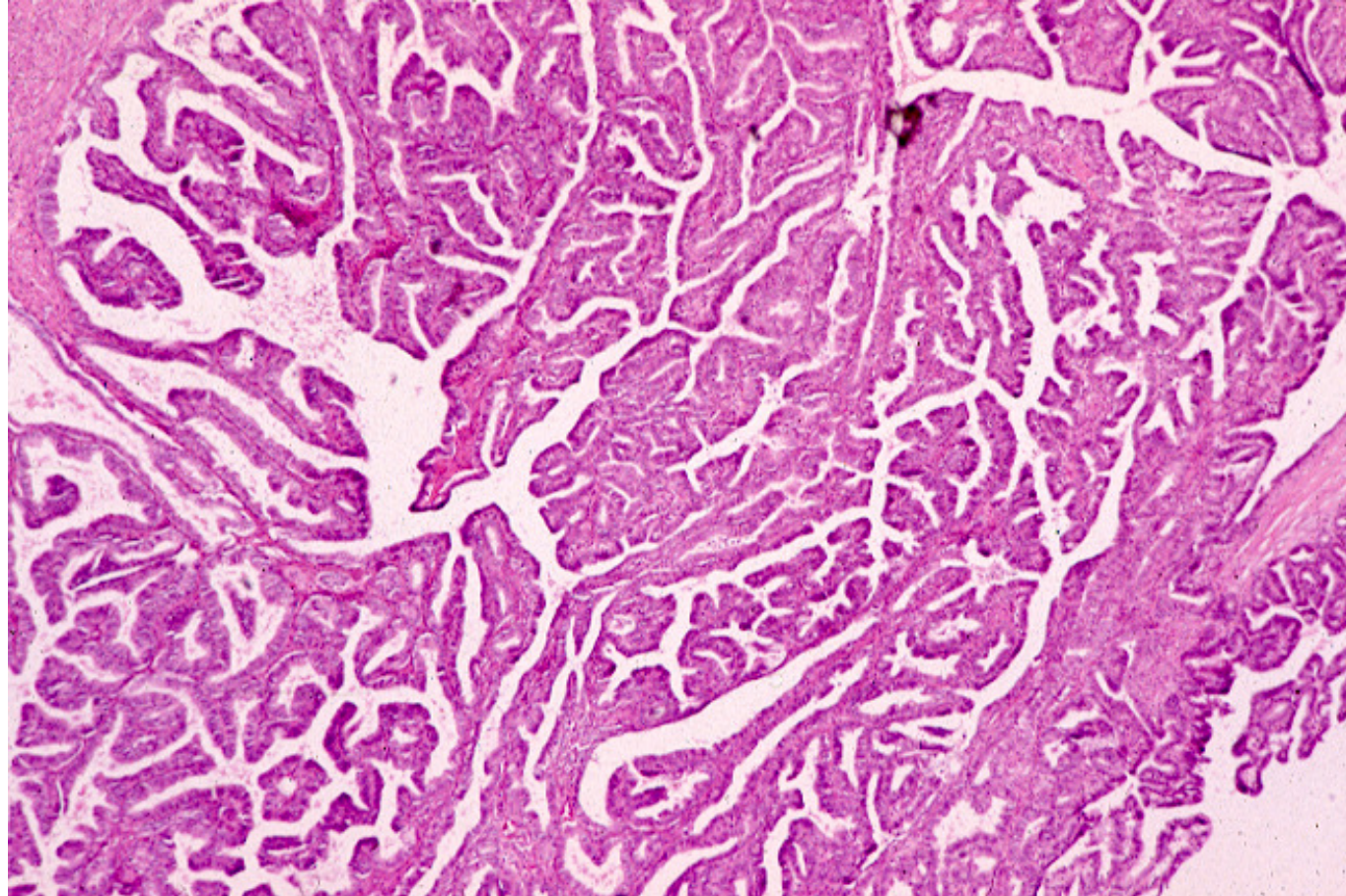
Endometrial Cancer: Intra-operative Surgical Principals

- **Availability of frozen section**
- **Capability of complete surgical staging**
- **Capability of tumor reduction if indicated**

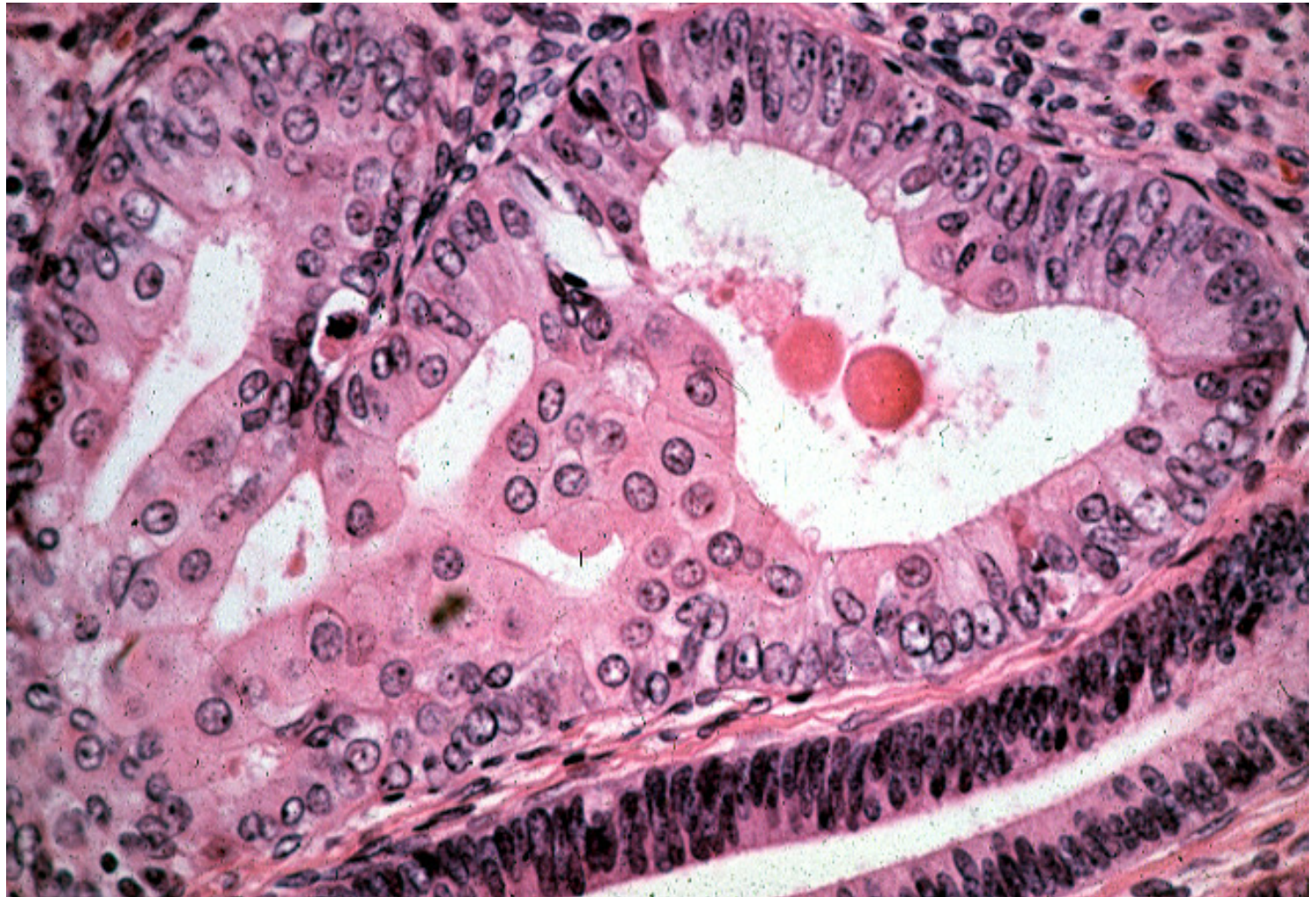
Uterine carcinoma, endometrial involvement



Uterine—microscopic view



Uterine carcinoma—microscopic view



- **Conceptual rationale**
 - **Defines extent of disease**
 - **Minimizes over/under treatment**
 - **Minimally increases perioperative morbidity/mortality**
 - **Decreases overall Rx risks and costs**
 - **Allows comparison of therapeutic results**

Endometrial Cancer: Surgical Approach

- **TAH-BSO/washings only**
 - **Grades 1, 2***
 - **< 50% myometrial invasion***
 - **Endometrioid***
 - **< 2 cm tumor diameter***

***Verified via frozen section**

- **Complete Surgical Staging***
 - **Grade 3**
 - **> 50% myometrial invasion**
 - **>2 cm tumor diameter**
 - **Serous/clear cell subtypes**
 - **Advanced stages**

***TAH-BSO, washings, lymphadenectomy, omental/peritoneal biopsy**

- **Brachytherapy**
- **External beam radiotherapy**
- **Hormonal therapy**
- **Cytotoxic chemotherapy**
- **Combination therapy**

Endometrial Cancer: Determinants of Adjuvant Therapy

- **Stage**
- **Histologic subtype**
- **Staging completeness**
- **Tumor biology**
- **Medical conditions**

Endometrial Cancer: Recurrence

Moderate-/High-Risk Node Negative Stage I Recurrence After Formal Lymphadenectomy (No WPRT)

	Pt (no.)	Mean nodes	Postop BRT	F-U (mo)	Recur (no.)
Fanning	22	28	+	34	1
Orr	115	24	+	39	6
Larson	105	-	-	43	8
Mohan	63	33	+	96	5
Total	305				20 (6.6%)*

*15 distant (4.9%), 4 vag (1.3%)** , 1 unknown (0.3%)

** All salvaged with RT

Endometrial Cancer: Adjuvant Hormonal Therapy

	Number	Deaths
Progestagens x 1 yr	553	61
Placebo	531	62

Vergote et al: *Cancer* 64:1011, 1989

Endometrial Cancer: Chemotherapy Response Rates

Single Agent	11-37%
CAP	45-56%
AP	33-81%
CA	31-46%
TAX/CARBO	63%
TEP	73%
AP-VP-16	75%
GOG Symposium July, 1999, Goff	

- **Pelvic examination**
- **Pap smears**
- **CA125 high-risk**
- **Chest X-ray high-risk**

- **80% of recurrences happen first 3 years**
- **Most will be symptomatic**
- **Rare to cure distant recurrences**
- **50% vaginal recurrences cured**

Endometrial Cancer: Site of Recurrence

Site	%
Distant	65
Pelvic and distant	15
Pelvis only	15
Vagina	6

- **3 published studies**
- **GOG ongoing study**
- **No evidence that ERT/HRT adversely influences the disease-free survival of women treated for endometrial cancer**

Endometrial Cancer: Principles for Management

- **Knowledge of natural history**
- **Intraoperative skills**
- **Postoperative management**
- **Indications for adjuvant treatment**

Endometrial Cancer: Treatment Reassessment

- **Clinical trials**
- **Surgical management**
- **Adjuvant therapy**
- **Salvage therapy**

- **Objective**
 - Pretreatment risk assessment using molecular determinants
- **Aim**
 - Triaging of patients at risk for advanced disease and/or recurrence
- **Purpose**
 - Facilitate evaluation of treatment approaches via clinical trials

Endometrial Cancer: Molecular Staging

- **Pretreatment risk identification**
- **Readily affords high-risk patients access to special expertise in managing advanced or recurrent disease**
- **Would facilitate the evaluation and application of new or modified therapeutic modalities**

Endometrial Cancer: Evolution of Molecular-based Therapies

