Ovarian Cancer Screening

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Ovarian Cancer

- 2006: 20,180 new cases/yr; 15,310 deaths
- Fifth leading cause of cancer death among women
- Leading cause of death among gynecologic malignancies
- 5 yr survival: Stage I - ~ 90%
  Stage III/IV - 20%
- Prevalence- 50/100,00 in women > 50 yrs.
- 75% cases diagnosed with advanced disease

Ovarian Cancer Symptoms

- Abdominal bloating
- Abdominal pain
- Indigestion
- Urinary frequency
- 22% of patients ignored symptoms
- Incorrect diagnosis 30%

Goff BA et al. Cancer 89:2068-2075, 2000.

Ovarian Cancer Target Symptoms

- Abdominal pain (30%) – OR 6.0
- Abdominal swelling (16.5%) – OR 30
- Gastrointestinal symptoms (8.5%) – OR 2.3
- Pelvic pain (5.4%) – OR 4.3

Smith LH et al. Cancer 104:1398-1407, 2005.

Delay in Diagnosis

- On average patients seek medical attention 9 months after onset of symptoms
- On average patients receive a pelvic exam 9 months after seeking medical attention
- Gilda Radner, Ella Grasso, Madeline Kahn, Liz Tilberis, Cassandra Hanis-Brosnan, Coretta Scott King, Patsy Ramsey, Loretta Young, Dinah Shore, Jessica Tandy, Lauro Nyro, Joan Hackett, Dixie Lee, Rosalind Franklin (discoverer of DNA), Sandy Dennis; *Bess Myerson & Carol Channing are survivors*

Sackett, et. al., Clinical Epid., Boston: Little, Brown & Co., 1985
http://en.wikipedia.org/wiki/Ovarian_cancer#Notable_victims_of_ovarian_cancer

Accuracy of Pelvic Examination

- 289 ovaries evaluated clinically in 151 women under anesthesia
- Ovaries detected clinically in 30% of women > 55 years of age
- Ovaries detected clinically in 9% of women > 200 lbs
- Ovaries detected clinically in 12% of women with a uterine weight > 200 grams

Ueland et al. Gynecol Oncol 99:400-403, 2005.

Screening

- The identification of unrecognized disease by the application of tests or examinations to apparently well persons to distinguish those who have a disease from those who do not.

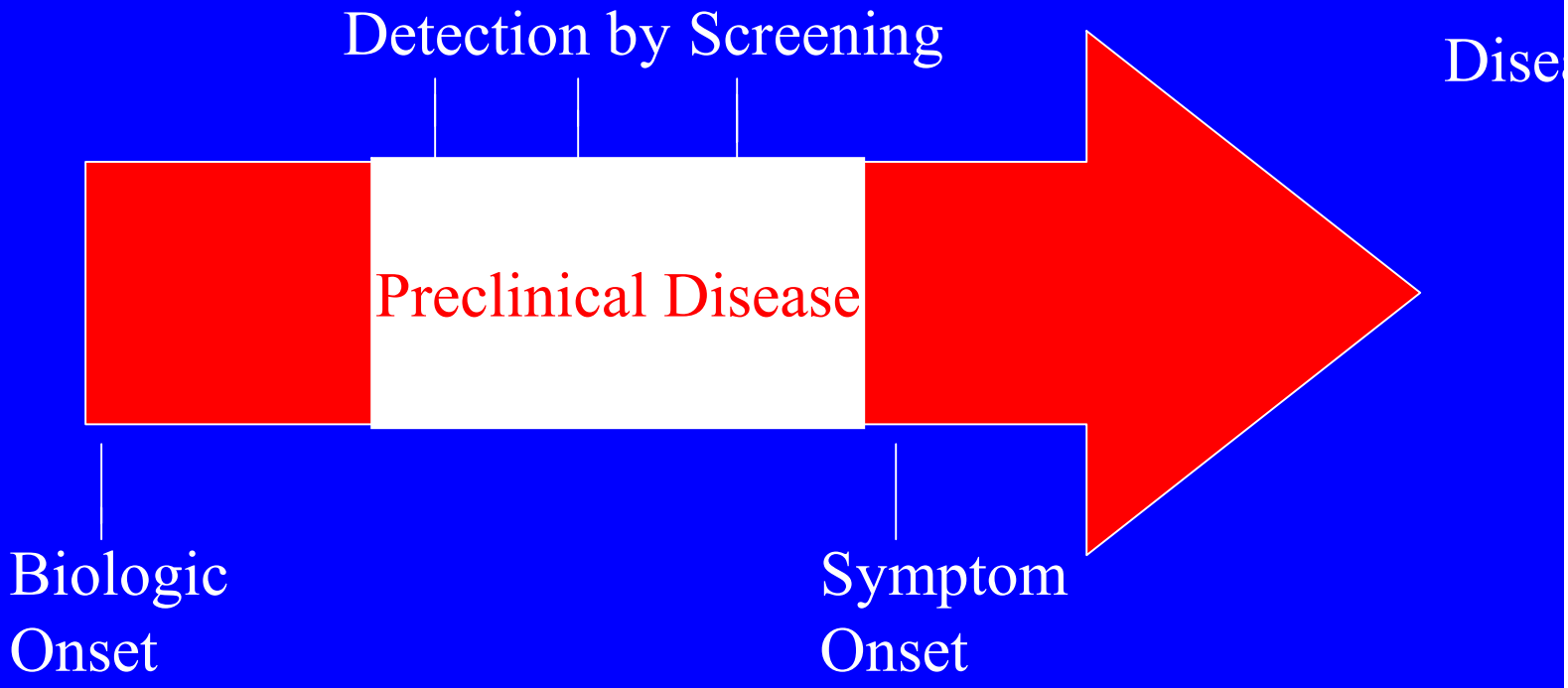
Long-term Results of a Successful Screening Test

- Decreased stage of detection
- Decreased case-specific mortality rate
- Decreased site-specific mortality rate

Characteristics of A Disease Suitable for Screening

- Serious consequences (morbidity/mortality)
- Effectively treated when diagnosed early
- High prevalence among screened population
- Detectable preclinical phase

Disease Progression



Characteristics of Tests Suitable for Screening

- Safe
- Simple to perform/time efficient
- Cost-effective
- Acceptable to patients/non-invasive
- Valid : High Sensitivity
  High Specificity
  High Positive Predictive
  High Negative Predictive Value

Statistical Definitions

Screening Test Result	Preclinical Disease: Present	Preclinical Disease: Absent
Positive	A (TP)	B (FP)
Negative	C (FN)	D (TN)

Sensitivity = TP/(TP+FN) = A / A+C

Specificity = TN/(TN+FP) = D / B+D

PPV= TP/(TP+FP)= A / A+B

NPV= TN/(TN+FN)= D / C+D

Transvaginal Sonography (TVS)

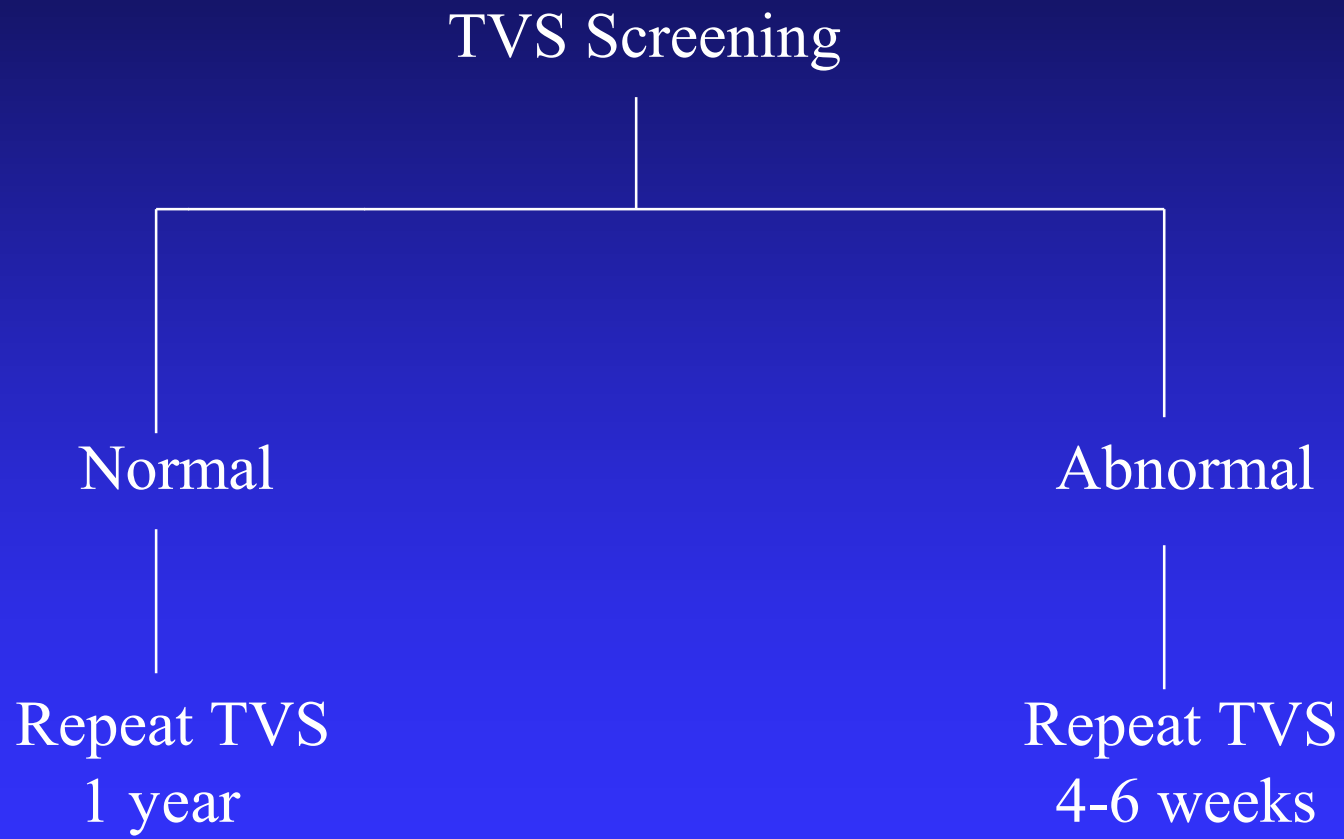
Transvaginal Sonography (TVS)

- Easy to perform
- Well-accepted
- Cost-effective when performed in screening setting

The University of Kentucky Ovarian Cancer Screening Program

- Initiated in 1987
- Eligible if $\geq$ 50 years old or $\geq$ 25 with family history of ovarian cancer

TVS Screening Algorithm

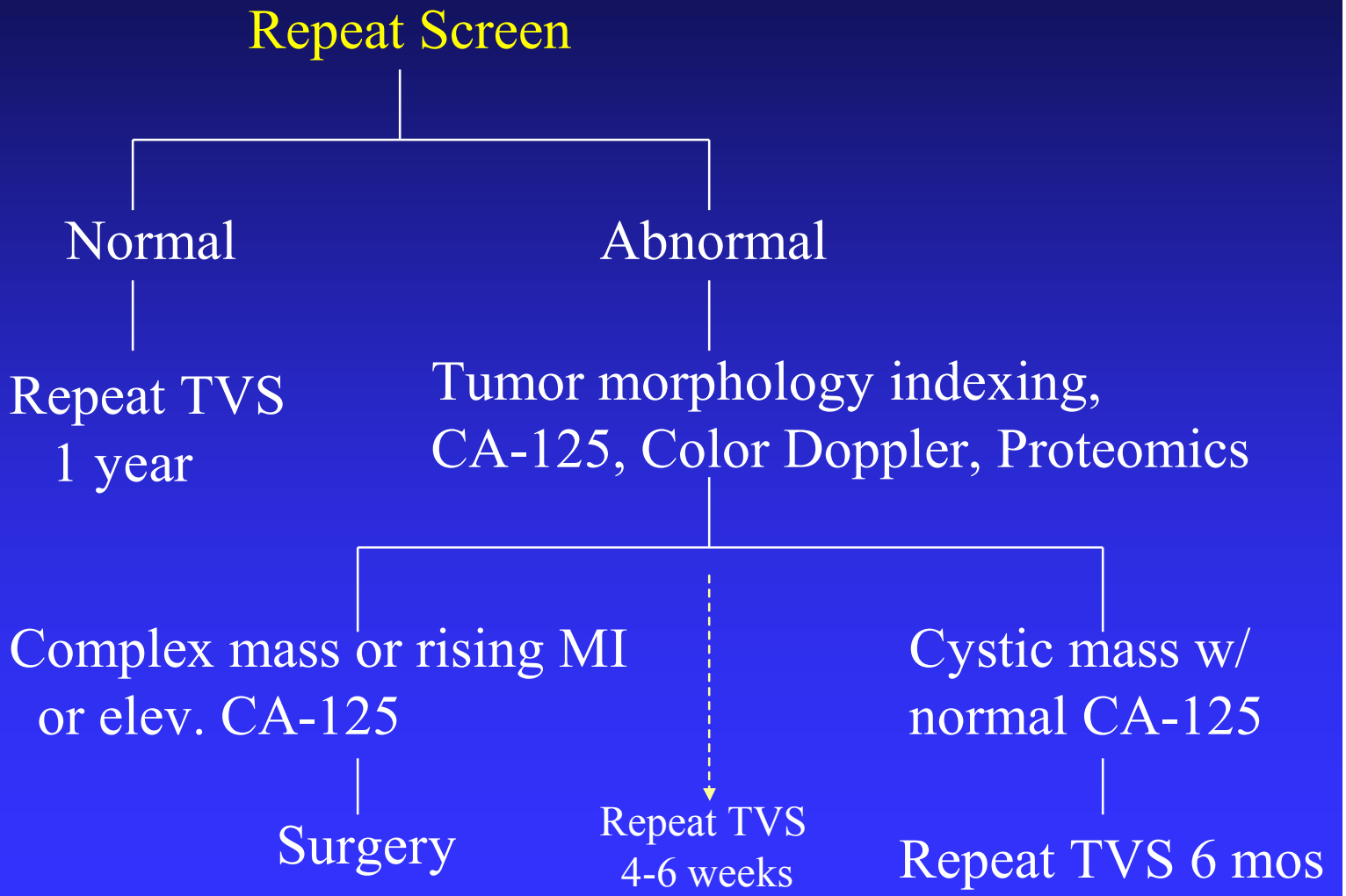


Criteria for Abnormal TVS

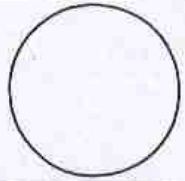
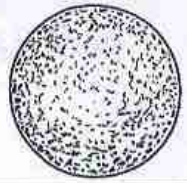
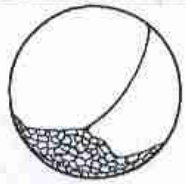
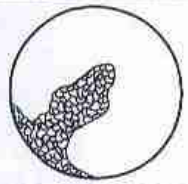
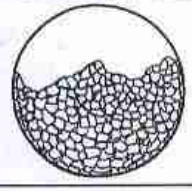
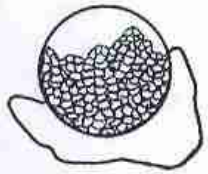
- Volume > 20 cm^3 premenopausal
- Volume > 10 cm^3 postmenopausal
- Tumor complexity - any solid or papillary projection into a cystic lumen

Pavlik, E.J., *et. al.* Relating Ovarian Size to Age, Menopausal Status, and Use of Hormones. Gynecol. Oncol. 80:333-334, (2001).

TVS Screening Algorithm



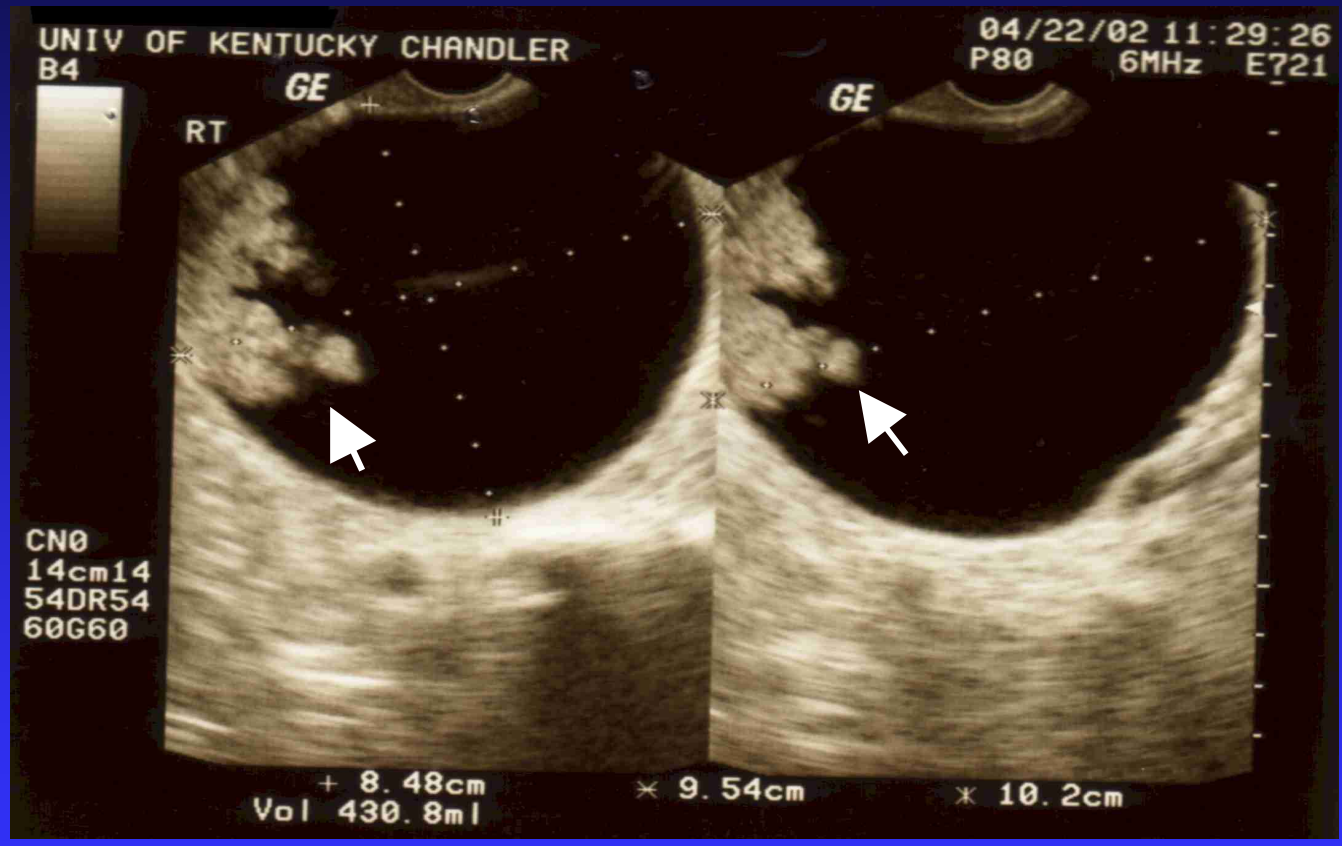
MORPHOLOGY INDEX

	TUMOR VOLUME	TUMOR STRUCTURE
0	<10 cm^3	
1	10-50 cm^3	
2	>50-100 cm^3	
3	>100-200 cm^3	
4	>200-500 cm^3	
5	>500 cm^3	

Morphology Indexing: MI = 0

- Cystadenoma

Morphology Indexing MI = 6



- Cystadenocarcinoma

Morphology Index (MI)

- Preoperative MI was performed on 442 ovarian tumors (0-10)
- 1/314 tumors with MI < 5 found to be malignant
- 52/127 tumors with MI ≥ 5 found to be malignant
- Sens. 98.1%, Spec. 80%, PPV 40.1%, NPV 99.7%

Ueland et al. Gynecol. Oncol. 91: 46-50 (2003).

The University of Kentucky Ovarian Cancer Screening Program 1987 - 2006

- 25,327 women screened
- 120,569 free screens
- 116,568 screening years
- 364 patients (1.4%) with persisting ovarian tumors operated upon

Histology of Ovarian Tumors Discovered by TVS Screening (n=364)

Primary ovarian cancer	44
Serous cystadenoma	153
Endometrioma	30
Mucinous cystadenoma	19
Cystic teratoma	18
Fibroma/thecoma/Brenner	25
Leiomyoma	4
Hydrosalpinx/paratubal cyst	25
Other	39
Non-ovarian malignancies	7

Summary of Primary Ovarian Cancers Detected by Screening (N = 44)

- Stage I – 28
- Stage II – 8
- Stage III – 8

The University of Kentucky Ovarian Cancer Screening Program 1987 - 2006

- 9 patients with ovarian cancer detected within 12 months of negative screen (false negative)
- NED = 6
- DOD = 3

The University of Kentucky Ovarian Cancer Screening Program 1987 - 2006

Statistical Data

- Sensitivity = 85.0%
- Specificity = 98.8%
- Positive Predictive Value = 13.8%
- Negative Predictive Value = 99.9%

Survival of Ovarian Cancer Patients in the Annually Screened Group

- 2 yr – 92.1%
- 5 yr – 82.4%

Conclusions

- TVS screening is safe, time-efficient, and well-accepted by patients
- Annual TVS screening causes a significant decrease in stage at detection and case-specific ovarian cancer mortality.
- The cost of each screen is approximately $50 which is well within the range of other screening methods
- TVS screening is not effective in detecting primary peritoneal cancer or ovarian cancer in which the ovarian volume is normal

Unresolved Issues

- Who should be screened?
- What is the optimal screening interval?
- What is the optimal screening algorithm?