

## **Silent and deceptive: Current Trends in the Diagnosis and Treatment of Ovarian Cancer**



### **Objectives**

- ⌘ To understand the risks for developing ovarian cancer including genetic
- ⌘ To review preventive strategies developing for ovarian cancer
- ⌘ Understand the present issues in treating ovarian cancer

### **Ovarian Cancer**

- ⌘ The most deadly gynecologic cancer
- ⌘ 28,000 women per year incidence
- ⌘ 14,000 women per year deaths

### **Who is at risk?**



- ⌘ Older women 1.2/100,000 under 40 but 68/100,000 over 60
- ⌘ Nulliparous
- ⌘ Infertility
- ⌘ No history of birth control
- ⌘ Late childbearing
- ⌘ Early menarche, late menopause
- ⌘ Other cancer history

### **In sum: "Incessant ovulation"**

- ⌘ Altered by: Use of BCP
- ⌘ Kerlikowski: greater than 2 years use, 50% reduction in life time risk
- ⌘ Thought be be related to disordered differentiation and stimulation of cytokines at the epithelial surface

### **Hereditary Ovarian Cancers**

- ⌘ Only 10%
- ⌘ If 1 first degree: 5%
- ⌘ If 2 first degree: 7%
- ⌘ Hereditary Ov Ca syndrome: 40%
- ⌘ Known BRCA1,2 or other: 35-65%

## BRCA 1 and 2

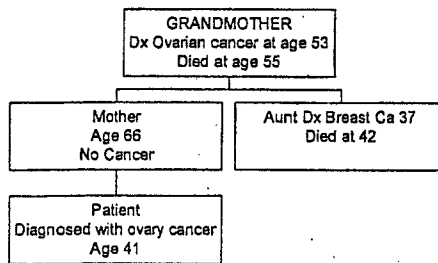
- |   |                                      |
|---|--------------------------------------|
| ⌘ BRCA 1                                    | ⌘ BRCA 2                             |
| ⌘ Tumor suppressor                          | ⌘ Tumor suppressor                   |
| ⌘ Chromosome 17                             | ⌘ Chromosome 13                      |
| ⌘ >500 mutations                            | ⌘ >300 mutations                     |
| ⌘ IF +: Breast 60-80%, Second breast 40-60% | ⌘ Breast 50-80%                      |
| ⌘ Ovary 15-45%                              | ⌘ Male breast 6%                     |
| ⌘ 3x prostate, 4x colon                     | ⌘ Ovary ?10%?<br>Pancreas, prostate? |

## Family History:

- ⌘ Father can be carrier
- ⌘ 3 generations
- ⌘ Try to get data
- ⌘ Incomplete penetrance causes problems
- ⌘ Surgery: Hyst/BSO for other causes creates confusion
- ⌘ Ethnic background



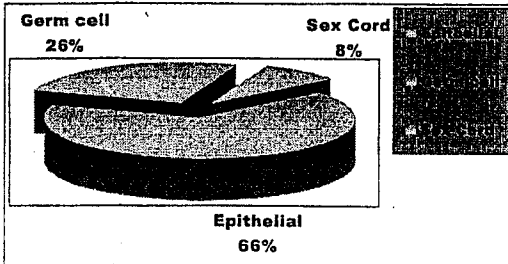
## Reduced Penetrance may cause problems:



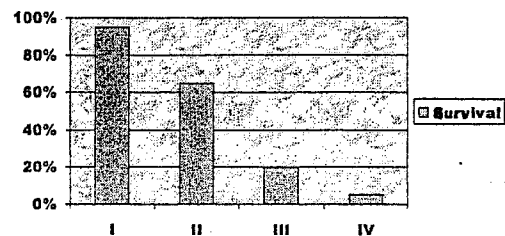
## TESTING MAY BE:

- Negative      Therefore Misleading
- Indeterminate      Therefore Confusing
- Positive      Therefore Distressing

## Distribution of Types



## Stage and Survival: Overall 50%



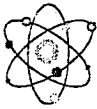
### Screening: is it possible to detect earlier?

- ⌘ Goff et al.
- ⌘ 90% of Patients noted symptoms up to 12 months ahead of diagnosis
- ⌘ Knew "something was wrong"
- ⌘ Classic error:
- ⌘ No pelvic exam
- ⌘ However, a small % have "normal" ovaries
- ⌘ And, growth and "in situ" phase unknown

### SGO: Screening Recommendations

- ⌘ **Comprehensive family history**
- ⌘ None or 1 family member: Annual exam
- ⌘ 2 or more family members:
  - ☑ Genetic counseling
  - ☑ Annual rectovaginal pelvic exam, Ca 125, transvaginal ultrasound (?)
  - ☑ Consider participation in clinical trials

### How good is Ca-125 as screening tool?



- ⌘ Elevated in 80% of epithelial
- ⌘ Only 25-50% of Stage I
- ⌘ POOR specificity, especially premenopausal
- ⌘ NOT a screening test for the GENERAL population
- ⌘ Presently no serum screening test

### What about ultrasound?

- ⌘ Screening: Not cost effective for general population
- ⌘ Example: screening of 5000 women, 65 laparotomies/ 1 case of ovarian cancer
- ⌘ 1600 women with strong family history, 12 laparotomies/ 1 case of ovarian cancer
- ⌘ ? Survival benefit?

### Can we reduce the risk?

- ⌘ OCP: RR 0.5 at 5 years, persists at least 10 years
- ⌘ Breast feeding
- ⌘ BTL/ Hysterectomy RR 0.33/ 0.67
- ⌘ Prophylactic Oophorectomy (1-3% risk)

### Retinoic Acid: Vitamin A

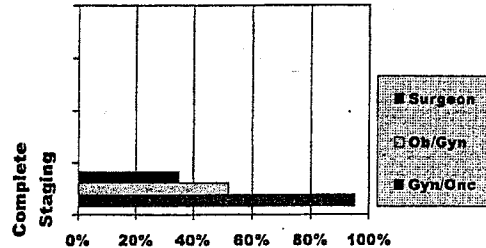
- ⌘ Needed for differentiation throughout embryogenesis and adult life
- ⌘ Evidence (Italian) fewer women with breast AND ovary cancers when added to tamoxifen
- ⌘ Present GOG trial to look at fenretidine versus none before prophylactic oophorectomy

### Making the diagnosis:

- ⌘ Requires a suspicious nature
- ⌘ Rectovaginal pelvic exam
- ⌘ Ultrasound/ CT
- ⌘ Ca-125
  
- ⌘ **REQUIRES SURGICAL EXPLORATION**



### WHO SHOULD DO THE SURGERY???????????



### Who Should Do The Surgery?

- ⌘ Junor et al. Brit J Ob/Gyn, 11/99
- ⌘ **Significant advantage for those women managed by Gyn Oncologist**
  - ☑ Optimal cytoreduction greater
  - ☑ Reduction in death by 25% (p=.005) compared to Ob/Gyn or General Surgeon

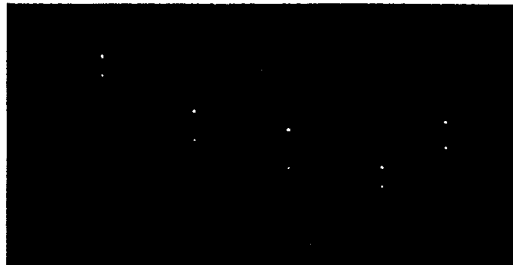
### Some bad ideas:

- ⌘ **Let's "biopsy" the mass**
- ⌘ Rupture: changing the Stage, increasing the risks of local reaction and problems
- ⌘ Potentially: spreading disease into difficult areas (muscle of abdominal wall)

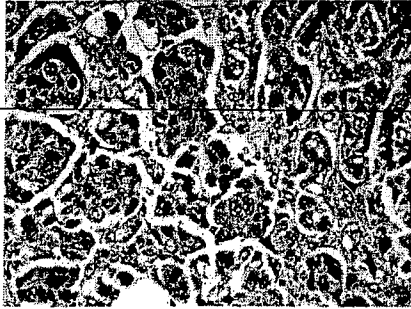
### Standard treatment: surgery

- ⌘ Laparotomy with:
  - ☑ TAH/BSO
  - ☑ Omentectomy
  - ☑ Nodes dependent on size and visible disease
  - ☑ Bowel resection
  - ☑ Removal of implants
  - ☑ Appendectomy
  - ☑ Other (bladder/ ureter/ etc)

### Survival by residual disease



## GRADE MATTERS:



## What is appropriate for EARLY cancers?

- ⌘ Staging: 30% have metastatic disease
- ⌘ Conservation: potential for young women if truly IA and lower grade
- ⌘ Optimal is still TAH/BSO/staging

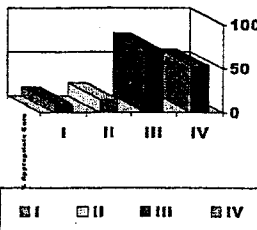
## What is appropriate for advanced stages?

- ⌘ Staging, debulking
- ⌘ All should have "standard" first line, taxane and platinum (may be on protocol if particularly high risk disease)
- ⌘ Median survival 38 months with taxane/platinum

## What is appropriate with recurrence?

- ⌘ Very high rate of recurrence, often detected only with Ca-125
- ⌘ 75% of high Stage will recur after COMPLETE response (50% after complete histologic response)
- ⌘ Options include:
  - ☑ Retreatment
  - ☑ Second line therapies
  - ☑ Second surgery

## How well are we doing? Patterns of Care



- ⌘ Correct surgical Staging of Early Stage Disease not done
- ⌘ Advanced stages: Cytoreduction and use of taxane/platinum are the failures

## Does it matter who gives care after diagnosis?

- ⌘ England.
- ⌘ Only 43% received appropriate treatment by consensus guidelines
- ⌘ **If INAPPROPRIATELY managed:**
- ⌘ Significantly increased risk of death
- ⌘ RR: 1.48 (1.34-4.78 Confidence Interval)



### **Future Directions:**

- ⌘ Screening: High priority
- ⌘ Early Detection opportunities?
- ⌘ Prevention: Including new strategies
- ⌘ Options for treatment as second line therapy with immunotherapy, potential for molecular approach/ proteomics

### **Summary:**

- ⌘ Pay attention to symptoms of women, even if vague
- ⌘ Do pelvic exam
- ⌘ Identify greater risk group
- ⌘ REFER to appropriate individual once likely diagnosis