“Never give in. Never give in. Never, never, never, never-
in nothing great or small, large or petty-
ever give in, except to convictions of honor and good sense.”

Sir Winston Churchill
Ovarian Tumors
Who Cares?

- Surgical costs exceed $5,000,000,000 annually
- 144 million women in USA
  - 5-10% will undergo a surgical procedure for a suspected ovarian neoplasm during their lifetime
- 30 million women over age 50
  - 17% develop cystic ovarian tumors
  - 2 million have persistent tumors
Risk of Malignancy

- Management challenge is an accurate risk of malignancy assessment.
- Risk of malignancy within an ovarian neoplasm varies with age:
  - 10% in children
  - 15% in reproductive age women
  - 50% in postmenopausal women
Ovarian Tumors
Premenopausal Women

- Non-inflammatory ovarian tumors
  - 70% functional cysts
  - 20% neoplastic
  - 10% endometriomas
- 15% of ovarian neoplasms in reproductive age women are malignant
- Other
  - Inflammatory process, bowel
Ovarian Tumors
Premenopausal Women

- **Functional cysts**
  - ≤ 8 cm
  - Unilateral
  - Simple, unilocular on TVS
  - No ascites
- Initial repeat TVS 6-8 weeks
- OCPs do not increase likelihood of resolution, but may decrease risk of recurrence
# Ovarian Tumors


<table>
<thead>
<tr>
<th>Type of Cyst</th>
<th># of Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regressed under observation</td>
<td>205</td>
<td>72</td>
</tr>
<tr>
<td>Required exploratory laparotomy</td>
<td>81</td>
<td>28</td>
</tr>
<tr>
<td>Ovarian neoplasms</td>
<td>46</td>
<td>16</td>
</tr>
<tr>
<td>Benign epithelial</td>
<td>32</td>
<td>11</td>
</tr>
<tr>
<td>Benign teratoma</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>Malignant epithelial</td>
<td>4</td>
<td>1.4</td>
</tr>
<tr>
<td>Dysgerminoma</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>28</td>
<td>10</td>
</tr>
<tr>
<td>Para-ovarian cyst</td>
<td>4</td>
<td>1.4</td>
</tr>
<tr>
<td>Hydrosalpinx</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Functional cysts</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Condition</td>
<td>Count</td>
<td>Percentage</td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>-------</td>
<td>------------</td>
</tr>
<tr>
<td>Spontaneous Resolution</td>
<td>2261</td>
<td>(69%)</td>
</tr>
<tr>
<td>Cyst + Septum</td>
<td>537</td>
<td>(17%)</td>
</tr>
<tr>
<td>Persistent Cyst</td>
<td>220</td>
<td>(7%)</td>
</tr>
<tr>
<td>Cyst + Solid area</td>
<td>168</td>
<td>(5%)</td>
</tr>
<tr>
<td>Solid Mass</td>
<td>21</td>
<td>(0.6%)</td>
</tr>
<tr>
<td>Removed by unrelated surgery</td>
<td>40</td>
<td>(1.2%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>3,259</td>
<td></td>
</tr>
</tbody>
</table>
Endometrioma
Mucinous Cystadenoma
Mature Cystic Teratoma
Ovarian Dysgerminoma
Ovarian Tumors
Postmenopausal Women

- Benign epithelial tumor
- Stromal tumor
  - Granulosa cell
  - Fibroma
  - Thecoma
- Epithelial cancer
- Metastatic cancer
Ovarian Tumors
Postmenopausal Women

- 50% malignant
- Asymptomatic simple cyst < 10 cm with normal CA-125
  - serial TVS
- “Any ovarian tumor in a postmenopausal woman that does not meet the above criteria should be assumed to be malignant”
  - Antiquated?
Serous Ovarian Cancer
Who Gets Referred to a Cancer Specialist?
Benefits of Surgical Staging?

- Patients in whom comprehensive surgical staging confirms early-stage disease have a *better prognosis* than those who were thought to have early stage disease but were unstaged.
- Accurate identification of women who require adjuvant chemotherapy.
Appropriate Staging

- Women with *early stage* ovarian cancer
  - N=291
- Complete surgical staging:
  - 97% gynecologic oncologists
  - 52% general obstetrician/gynecologists
  - 35% general surgeons

MEMO TO THE MEDIA

Press Release

Studies Examine Ass Volume, Surgeon Spec in Ovarian Cancer

Ariel Whitworth

In addition to hospital or surgeon volume, a surgeon’s area of specialty may also affect patient outcomes. Previous studies have found that patients are more likely to receive the recommended surgery and treatment for ovarian cancer if they are treated by highly specialized surgeons such as gynecologic oncologists. To examine the association between surgeon specialty and patient outcome, Craig C. Earle, M.D., of the Dana-Farber Cancer Institute in Boston, and colleagues identified 3067 ovarian cancer patients in the SEER database who underwent a surgical procedure to remove ovarian cancer.

Of those patients, 45% were treated by a gynecologic oncologist, 45% by a general gynecologist, and 22% by a general surgeon. Outcomes among these patients were marginally superior to those of patients treated by general oncologists, and much better than those of patients treated by general surgeons. Gynecologic oncologists were most likely to perform sufficiently extensive surgery, and were most likely to provide patients with post-operative chemotherapy when needed.

Past studies have suggested that patients treated at hospitals with higher case loads or by more experienced surgeons have higher survival rates after surgery for certain types of cancer, including colorectal cancer and lung cancer. Patients may take such factors into account when making decisions about where and from whom to seek medical care.
Referral Patterns

- Only 39% were ever seen by a Gyn Onc
- Patients with advanced disease had significant survival advantage when managed by Gyn Onc (median survival 26 mo vs. 15 mo, p < 0.01)
- Age < 40, age > 70, and residence in a rural area were not seen by a gynecologic oncologist

Value of Specialists

- Meta-analysis (18 studies) concluded marked benefit with Gynecologic Oncologist (Giede 2005)
  - Complete surgical staging with early stage disease
  - Optimal cytoreductive surgery with advanced disease
  - Improved median and overall survival
- Others supporting GO involvement:
  - NCCN guidelines
  - SGO, ACOG
  - SOGC clinical practice guidelines
  - NIH consensus statement
  - London Medical Advisory statement
Suggestive of Malignancy
ACOG, SGO

- Examination
  - Fixed or nodular
- Imaging study
  - Mostly solid tumor or distant mets
  - Ascites
- CA-125
  - premenopausal  > 200
  - postmenopausal > 35

Im et. al. Obstet Gynecol, 2005
So How Do I Know Who Gets Referred and Who Doesn’t?

- Examination
- Imaging
- Serum
Pelvic Examination
Pelvic Examination

Inaccuracy

- Patient age $\geq 55$
  - 30%
- Patient weight $\geq 200$ lb
  - 9%
- Uterine weight $\geq 200$ g
  - 16%

Ueland et al, Gyn Oncol 2005
So How Do I Know Who Gets Referred and Who Doesn’t?

- Examination
- Imaging
- Serum
## Pelvic Exam vs. Ultrasound

<table>
<thead>
<tr>
<th></th>
<th>Pelvic Exam</th>
<th>Ultrasound</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient age</strong></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient wt</strong></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 200 lb</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Uterine wt</strong></td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>≥ 200 g</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ueland et al, Gyn Oncol 2005
## Ultrasound

### Differentiating Ovarian Tumors

<table>
<thead>
<tr>
<th>Author</th>
<th>Number</th>
<th>Prevalence</th>
<th>Sens(%)</th>
<th>Spec (%)</th>
<th>PPV(%)</th>
<th>PPV (at 20%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kobayashi, 1976</td>
<td>406</td>
<td>15</td>
<td>70</td>
<td>73</td>
<td>31</td>
<td>39</td>
</tr>
<tr>
<td>Hermann, 1987</td>
<td>241</td>
<td>21</td>
<td>82</td>
<td>93</td>
<td>75</td>
<td>73</td>
</tr>
<tr>
<td>Finkler, 1988</td>
<td>102</td>
<td>36</td>
<td>62</td>
<td>95</td>
<td>88</td>
<td>75</td>
</tr>
<tr>
<td>Benacerraf, 1990</td>
<td>100</td>
<td>30</td>
<td>80</td>
<td>87</td>
<td>72</td>
<td>62</td>
</tr>
<tr>
<td>Granberg, 1990</td>
<td>180</td>
<td>22</td>
<td>82</td>
<td>92</td>
<td>74</td>
<td>73</td>
</tr>
<tr>
<td>Sassone, 1991</td>
<td>143</td>
<td>10</td>
<td>100</td>
<td>83</td>
<td>37</td>
<td>59</td>
</tr>
<tr>
<td>Ueland, 2003</td>
<td>442</td>
<td>12</td>
<td>98</td>
<td>81</td>
<td>41</td>
<td>56</td>
</tr>
</tbody>
</table>

*Definition of (+) US varied with each author*
## Sonographic Characteristics

### Ovarian Tumors

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral</td>
<td>Bilateral</td>
</tr>
<tr>
<td>Simple (MI &lt; 5)</td>
<td>Complex (MI $\geq$ 5)</td>
</tr>
<tr>
<td>Doppler</td>
<td>Partly solid</td>
</tr>
<tr>
<td></td>
<td>Internal papillations</td>
</tr>
<tr>
<td>Peripheral flow</td>
<td>Central flow</td>
</tr>
<tr>
<td>No ascites</td>
<td>Ascites</td>
</tr>
<tr>
<td>Resolution</td>
<td>Persistence or growth</td>
</tr>
</tbody>
</table>
Kentucky Morphology Index
Ueland et al Gyn Oncol 2003

- UK gynecologic ultrasound database
- 442 women with confirmed ovarian tumor
  - Morphology Indexing
  - Color Flow Doppler
  - Surgery
# MORPHOLOGY INDEX

<table>
<thead>
<tr>
<th>TUMOR VOLUME</th>
<th>TUMOR STRUCTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0  &lt;10 cm$^3$</td>
<td><img src="image" alt="Diagram" /></td>
</tr>
<tr>
<td>1  10-50 cm$^3$</td>
<td><img src="image" alt="Diagram" /></td>
</tr>
<tr>
<td>2  &gt;50-100 cm$^3$</td>
<td><img src="image" alt="Diagram" /></td>
</tr>
<tr>
<td>3  &gt;100-200 cm$^3$</td>
<td><img src="image" alt="Diagram" /></td>
</tr>
<tr>
<td>4  &gt;200-500 cm$^3$</td>
<td><img src="image" alt="Diagram" /></td>
</tr>
<tr>
<td>5  &gt;500 cm$^3$</td>
<td><img src="image" alt="Diagram" /></td>
</tr>
</tbody>
</table>
Tumor Structure
Score = 0

MORPHOLOGY INDEX

<table>
<thead>
<tr>
<th>TUMOR VOLUME</th>
<th>TUMOR STRUCTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10 cm³</td>
<td>![Image]</td>
</tr>
<tr>
<td>10-50 cm³</td>
<td>![Image]</td>
</tr>
<tr>
<td>&gt;50-100 cm³</td>
<td>![Image]</td>
</tr>
<tr>
<td>&gt;100-200 cm³</td>
<td>![Image]</td>
</tr>
<tr>
<td>&gt;200-500 cm³</td>
<td>![Image]</td>
</tr>
<tr>
<td>&gt;500 cm³</td>
<td>![Image]</td>
</tr>
</tbody>
</table>
Tumor Structure
Score = 3

MORPHOLOGY INDEX

<table>
<thead>
<tr>
<th>TUMOR VOLUME</th>
<th>TUMOR STRUCTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;10 cm³</td>
</tr>
<tr>
<td>1</td>
<td>10-50 cm³</td>
</tr>
<tr>
<td>2</td>
<td>&gt;50-100 cm³</td>
</tr>
<tr>
<td><strong>3</strong></td>
<td>&gt;100-200 cm³</td>
</tr>
<tr>
<td>4</td>
<td>&gt;200-500 cm³</td>
</tr>
<tr>
<td>5</td>
<td>&gt;500 cm³</td>
</tr>
</tbody>
</table>
**Tumor Structure**

Score = 5

**MORPHOLOGY INDEX**

<table>
<thead>
<tr>
<th>TUMOR VOLUME</th>
<th>TUMOR STRUCTURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt;10 cm³</td>
</tr>
<tr>
<td>1</td>
<td>10-50 cm³</td>
</tr>
<tr>
<td>2</td>
<td>&gt;50-100 cm³</td>
</tr>
<tr>
<td>3</td>
<td>&gt;100-200 cm³</td>
</tr>
<tr>
<td>4</td>
<td>&gt;200-500 cm³</td>
</tr>
<tr>
<td>5</td>
<td>&gt;500 cm³</td>
</tr>
</tbody>
</table>
Morphology Index
Total Score (5-10)
Kentucky Morphology Index

- MI < 5  benign
- MI ≥ 5  malignant
Kentucky Morphology Index

- Sensitivity: 0.981
- Specificity: 0.807
- Positive predictive value: 0.409
- Negative predictive value: 0.997
- Accuracy: 0.828

Disease Prevalence = 12%
What about Doppler?
<table>
<thead>
<tr>
<th></th>
<th>Sens</th>
<th>Spec</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>0.981</td>
<td>0.807</td>
<td>0.409</td>
<td>0.997</td>
</tr>
<tr>
<td>PI &lt; 1.00</td>
<td>0.528</td>
<td>0.776</td>
<td>0.288</td>
<td>0.905</td>
</tr>
<tr>
<td>RI &lt; 0.4</td>
<td>0.222</td>
<td>0.867</td>
<td>0.222</td>
<td>0.867</td>
</tr>
<tr>
<td>No flow</td>
<td>0.163</td>
<td>0.640</td>
<td>0.056</td>
<td>0.854</td>
</tr>
</tbody>
</table>
\( f_0 = \text{transmitted US frequency} \)

\( v \cos \theta = \text{target velocity} \)

\( c = \text{velocity of surrounding medium} \)

\( \Delta f = 2f_0 \frac{v}{c} \cos \theta \)
Doppler Reproducibility

\[ \Delta f = 2f_0v \cos(\theta) / c \]

- Is the angle of insonation constant \((\theta)\)?
  - 2 to 3 fold change for \(\Delta \theta\) (from 30°-80°)*
  - Optimal angle and frequency depends on depth of vessel

- Is each Doppler measurement of the same vessel? Are these vessels straight?

Ultrasound Conclusions

1. $MI \geq 5$
   - 40% malignant
2. $MI < 5$
   - 0.3% malignant
3. Doppler adds little
Other Imaging

- CT scan abdomen and pelvis
  - IV and PO contrast
  - CT-guided biopsy
    - Accuracy exceeds 90% for solid tumors
    - What about high risk cystic tumors?

- MRI
- PET
CT Scan

Omental cake

Ovarian tumor
So How Do I Know Who Gets Referred and Who Doesn’t?

- Examination
- Imaging
- Serum
CA-125

- Antigen derived from:
  - coelomic epithelium (pericardium, pleura, peritoneum)
  - mullerian epithelium (tubal, endometrial, endocervical)
- Two different assays
  - Assay I ≤ 35 U/ml
  - Assay II < 20 U/ml
- Expressed by 80% non-mucinous EOC
- FDA-approved to follow the progress of cancer treatment
  - Neither a screening nor a diagnostic test
- Normal CA-125 values (low sensitivity)
  - 50% of early stage ovarian cancers
  - 20-25% of advanced stage ovarian cancers
  - Mixed mullerian tumors, clear cell cancers
CA-125
Non-specific

- Benign ovarian cysts
- Uterine leiomyomata
- Pelvic inflammatory disease
- Endometriosis
- Adenomyosis
- Pregnancy
- Menstruation
- Ascites
- Heart failure
- Liver failure
- Renal failure
- Peritoneal tuberculosis
- Diverticulitis
- Pancreatitis
- Recent abdominal or thoracic surgery
- Other malignancies
So Again, What Should I Do?

- Surgical removal of ovarian tumor if symptomatic or high risk imaging
- Sonographic observation if asymptomatic, low risk MI
  - 6 wks, 3 mo, 6 mo
- CT scan abdomen/pelvis if suspect malignancy
High Risk Indicators

- **Ultrasound** (Ueland et al, 2003; Sassone et al, 1991)
  - Internal papillary projection
  - Cystic and solid, solid
  - Ascites

- **CT Scan/MRI** (Kurtz et al 1999)
  - Cystic and solid, solid
  - Ascites

- **CA-125** (Roman et al, 1997)
  - Premenopausal >100 U/mL
  - Postmenopausal >35 U/mL
Laparoscopy
Ovarian Tumor
Laparoscopy Guidelines

- Prepared for laparotomy
  - Informed consent
- Surgical technique
  - Abdominopelvic inspection, biopsy
  - Washings
  - Tumor removal and containment with endoscopic bag
  - No morcellation, please
  - Intraoperative frozen section
A lot of people don't have principles, but I do! I'm a highly principled person.

I live according to one principle, and I never deviate from it.

What's your principle?
Ovarian Tumor
Laparoscopy

- Be principled
  - Do not delay treatment to “confirm diagnosis” at laparoscopy
  - For high risk tumor, consider referral to specialist
  - Informed consent for surgery includes explanation of alternatives
  - “What would I do for my mother?”
Ovarian Cancer Incidence and Mortality

Data from the American Cancer Society

200 Kentucky deaths from ovarian cancer in 2006
# Stage and Outcome

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percent</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>24</td>
<td>95%</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>65%</td>
</tr>
<tr>
<td>III</td>
<td>55</td>
<td>15-30%</td>
</tr>
<tr>
<td>IV</td>
<td>15</td>
<td>0-20%</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>50%</td>
</tr>
</tbody>
</table>
Ovarian Cancer

Symptoms

- Survey distributed to 1500 women who subscribe to CONVERSATIONS!, a newsletter about ovarian carcinoma
- 1725 surveys returned
- Median age 52 years
- 70% had stage III or IV disease

Ovarian Cancer
Symptoms

- 95% of patients reported having symptoms prior to diagnosis
  - Abdominal 77%
  - Gastrointestinal 70%
  - Pain 58%
  - Constitutional 50%
  - Urinary 34%
  - Pelvic 26%
Ovarian Cancer

Symptoms

- Asymptomatic prior to diagnosis
  - Stage I/II – 11%
  - Stage III/IV – 3%

- Women who ignored their symptoms were more likely to be diagnosed with advanced stage disease
Ovarian Cancer

Symptoms

- Factors associated with delay in diagnosis
  - Omission of pelvic exam at first visit
  - Multiple symptoms
  - Missed diagnosis: no problem, depression, stress, IBS, or gastritis
  - No imaging or CA-125
  - Younger age

- Type of health care provider seen initially, insurance, and specific symptoms did not correlate with a delay in diagnosis
Cancer History

- Ovarian cancer
- Breast cancer
- Endometrial cancer
- Other
- BRCA 1,2
- HNPCC
Conclusions

- Identify patients at risk
  - Cancer history, symptoms, other
- Ovarian examination is often inaccurate
  - Age, obesity, large uterus
- Stratify risk with ultrasound, other imaging
- Informed surgical consent
- Consider laparoscopic approach if feasible
Conclusions

- Referral for an adnexal tumor depends on risk of malignancy assessment.
- When a Gyn Onc performs surgery for early stage ovarian cancer, patients are more likely to be accurately staged and receive proper adjuvant treatment.
"Let us have faith that right makes might, and in that faith, let us, to the end, dare to do our duty as we understand it."

Lincoln's Cooper Institute Address
February 27, 1860.