Updates in Gynecology

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Presentation Goals

• Review Cervical Cancer screening guidelines and changes

• Review Breast Cancer screening recommendations and controversy

• Discuss newest evidence / controversies in Hormone Replacement Therapy

• Summarize current recommendations
Cervical Cancer Screening
Cervical Cancer

- 2 Main Types
  - Squamous Cell (most common - 70% of cases)
    - Contiguous lesions
    - Usually less aggressive
  - Adenocarcinoma
    - “Skip lesions” make it hard to resect
    - Margins mean less
    - More aggressive
Human Papillomavirus (HPV)

- Most commonly diagnosed sexually transmitted infection in the US
- At least half of all sexually active individuals will acquire HPV at least once by age 50
- 80-90% lifetime exposure rate
- Most women clear cellular damage from the infection between 8-24 months and become HPV negative at a cellular level
- Can reactivate later in life (usually during time of immunocompromise)
- Progression to cancer requires persistent infection (usually over years)
HPV

Over 100 different types identified

• 114 subtypes; 40 of which cause anogenital infections
  ▪ Low-risk types - NOT associated with cervical cancer
    - Types 6 and 11 cause 90% of condyloma
  ▪ High-risk types have potential to cause cancer
    - Associated with cervical, anal, vaginal, vulvar, penile, and head/neck cancers
    - Types 16 and 18 cause 80% of cervical cancer
Utility of HPV screening

- Option to perform test of High Risk HPV subtypes at time of pap (“HPV regardless”)

- No utility in checking for Low Risk subtypes; options to test does not exist

- Limit to women over age 30

- Neg HR HPV with normal pap is more sensitive than pap alone in detecting low and high grade dysplasia
  - Sensitivity of single pap to detect high grade lesion is only 60-80%
  - False neg rate for pap when pt has invasive cancer is 11-33%
Current Recommendations

- 2001, ASCCP initiates process to develop a comprehensive, evidence based consensus for screening
- 2006, updated
- 2008, updated but not nationally validated
- 2012, Consensus update which finally acknowledged advancing science and understanding of HPV
Current Recommendations*

• Begin screening at age 21
  • Regardless of when patient became sexually active
  • Still offer other STD screening once sexually active

• Necessary to get pap smears even if completes HPV vaccination series

• After hysterectomy
  • No further paps if no cervix AND no h/o CIN 2, CIN 3, or adenocarcinoma in-situ within last 20 yrs

*From Am College of Ob and Gyn, Am Cancer Soc, Am Soc for Colposcopy and Cervical Pathology, and Am Soc for Clinical Pathology
Current Recommendations*

- **Age 21-29**
  - Pap cytology alone *every 3 years*
  - Use HR HPV testing ONLY as reflex if ASC-US pap

- **Ages 30-65**
  - Pap cytology WITH HR HPV co-testing *every 5 years*

- **Age 65 and up**
  - Okay to stop pap screening
  - Continue age based screening in anyone with h/o CIN 2, CIN 3, or adenocarcinoma in-situ within last 20 yrs

*From Am College of Ob and Gyn, Am Cancer Soc, Am Soc for Colposcopy and Cervical Pathology, and Am Soc for Clinical Pathology*
Breast Cancer Screening
Breast Cancer Statistics

- Most common cause of cancer in women in US
- 2nd leading cause of cancer death of women in US for most ethnicities
- 1:8 women, 75% of which have no family history

- Mortality has decreased by 1/3 over last 25 yrs
  - Screening contributed to over 1/2 that reduction
  - Decreased use of HRT after WHI trial
  - Improved treatment
Breast Cancer Screening: Mammography

- Imaging of the breasts can detect lesions between 0.1-1 cm in size before would be palpable
- Earlier detection leads to reduction in mortality

Average-size lump found by woman practicing occasional breast self-exam (BSE)

Average-size lump found by woman practicing regular breast self-exam (BSE)

Average-size lump found by first mammogram

Average-size lump found by getting regular mammograms
Breast Cancer Screening: Digital 2D Mammography

- Less radiation with better image quality
- Images can be viewed on computer, magnified
- Increased accuracy in women under age of 50
- Downsides:
  - Less sensitivity with dense breasts
  - Callbacks associated with overlapping tissue
Breast Cancer Screening: Breast Tomosynthesis ("3D Mammography")

- Camera moves over the breast taking images from multiple angels
- Images are then combined into a 3-dimensional rendering of the breast tissue
- Takes less than 10 seconds
- Images produced in 1 mm slices
- Most centers use this in conjunction with tradition 2D mammogram
Breast Cancer Screening:
Breast Tomosynthesis (“3D Mammography”)

- **PROS**
  - No significant increase in radiation compared with 2D mammogram
  - Earlier detection of small Breast cancers that may be hidden on 2D mammograms
  - Possible reduction in callbacks for overlapping tissue

- **CONS**
  - Increase in cancers detected in prospective trials were invasive cancers (not in-situ lesions)
  - Issue of storage archives for imaging centers
Breast Cancer Screening Controversy: When to Initiate Screening

- **USPSTF** recommends beginning biennial screening at age 50 unless women have risk factors
  - No screening after age 75
  - Recommends against the Breast Self Exam (BSE)
  - Number of women who needed to be “invited to screen” to prevent 1 cancer death
    - Age 39-49: 1904
    - Age 50-59: 1339
    - Age 60-69: 377
  - Increased # of call-backs and biopsies in women < age 50

- **All other organizations** recommend beginning mammograms at age 40

- Screening mammograms in women age 40-49 continues to demonstrate a 15% reduction in Breast cancer-related mortality (similar to reduction seen in women age 50-59)
Breast Cancer Screening Controversy

- **ACOG**
  - Age 40-49 - every 1-2 yrs
  - Age 50 and older - every 1 yr
  - Annual Clinical Breast Exam
  - Monthly Self Exm
Breast Cancer Screening: BIRADS terminology

- Category 0: Additional Imaging Eval Needed
  - Spot compression views
  - Ultrasound

- Category 1: Negative

- Category 2: Benign Finding

- Category 3: Probably Benign Finding
  - Needs some sort of short term follow up (as indicated by Radiologist)

- Category 4: Suspicious Finding
  - 4A: low suspicion
  - 4B: Intermediate Suscipicion
  - 4C: Moderate concern

- Category 5: Highly Suscipient

- Category 6: Biopsy Proven Malignancy
Breast Cancer Screening: BIRADS Density Reporting

- BIRADS 1: < 25% glandular, mostly fat
- BIRADS 2: 25-50% glandular, scattered fibroglandular densities
- BIRADS 3: 51-75%, heterogeneous tissue
- BIRADS 4: > 75%, extremely dense fibrous and glandular
don this
- Some states mandate reporting of category 3 and 4 to the patient
- NC IS ONE OF THOSE STATES
Hormone Replacement Therapy
History of HRT

- Huge increase in estrogen use between 1960 and 1975 after research and best-selling book indicating estrogen prevented many age-related diseases
  - Idea of hormone therapy as a “fountain of youth”

- Decrease in estrogen prescriptions around 1975 when link between estrogen and endometrial cancer found

- Increase again mid-80s with addition of progestins to estrogen therapy

- Second fall in HRT prescriptions with release of WHI trial results in 2002
  - Largest and longest trial of postmenopausal women using hormone therapy
### WHI Trial
**Major Initial Findings**

<table>
<thead>
<tr>
<th>Estrogen + Progestin (Prempro)</th>
<th>Estrogen only (Premarin)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Increased risk of cardiac events</td>
<td>• No difference in risk of cardiac events</td>
</tr>
<tr>
<td>• Increased risk of stroke</td>
<td>• Increased risk of stroke</td>
</tr>
<tr>
<td>• Increased risk of breast cancer</td>
<td>• No increased risk of breast cancer</td>
</tr>
<tr>
<td>• Increased risk of blood clots</td>
<td>• Increased risk of blood clots</td>
</tr>
<tr>
<td>• Decreased risk of colorectal cancer</td>
<td>• No difference in risk of colorectal cancer</td>
</tr>
<tr>
<td>• Decreased risk of fractures</td>
<td>• Reduced risk of fracture</td>
</tr>
<tr>
<td>• No impact on cognitive impairment</td>
<td></td>
</tr>
</tbody>
</table>

• **Surprise Finding:**
  - Increase risk of cardiac events

• **Surprise Finding:**
  - No increased risk of breast cancer
Subsequent analysis / Expert agreement
“Lowest dose for shortest duration necessary”

- HRT indicated for treatment of moderate to severe menopausal symptoms in “relatively young” healthy women (up to age 59 or within 10 yrs of menopause)
  - Individualization is key
  - Counseling on risks
  - Use of lowest necessary dose for shortest duration necessary

- If predominant symptom is vaginal dryness, use low dose vaginal estrogen not systemic estrogen
  - tablet, ring, cream
  - For dyspareunia only, new ospemifene
  - OTC Replens

2012 Kronos Early Estrogen Prevention Study and 2013 JAMA published WHI f/u subsequent analysis
Subsequent analysis / Expert agreement

- Progesterone is required if women has uterus
  - Note: women without a uterus can still take progestin if they might benefit from it or can’t take estrogen

- For osteoporosis, recommend diet, exercise, Vit D, Calcium, bisphosphonates or SERMS first-line unless contraindicated

- In general, Hormone Therapy not recommended for disease prevention

- For symptoms only!

2012 Kronos Early Estrogen Prevention Study and 2013 JAMA published WHI f/u subsequent analysis
Surgical Menopause / Timing Hypothesis

- Increased risk in cognitive decline with surgical menopause at earlier age (if not placed on HRT)*

- NAMS Consensus Statement- “In women with premature ovarian insufficiency, systemic hormone therapy is recommended at least until the average age of natural menopause”

- 2009 study showed that prophylactic oophorectomy at time of hysterectomy increased risk of all-cause mortality and coronary artery disease (Obstet Gynecol. 2009;113:1027-1037)
  - Change in how patients counseled on oophorectomy prior to surgery

- Concern that failure to replace hormones immediately at time of surgical menopause will lead to increased risk of heart events

*NIH study; Amer Acad Neur 65th Ann Mtg; Harvard Medical Center
Appendix
Websites / Journal Articles

- **Pap Guidelines**
  - American Society for Colposcopy and Cervical Pathology (ASCCP)
    - [www.asccp.org/Guidelines](http://www.asccp.org/Guidelines)
  - American College of Obstetrics and Gynecology (ACOG)
    - [www.acog.org](http://www.acog.org)

- **Breast Cancer Screening**
  - Recommendations on screening intervals
    - [www.acog.org](http://www.acog.org)
    - [www.cancer.org](http://www.cancer.org)
    - [www.uspreventiveservicestaskforce.org/uspsbrca.htm](http://www.uspreventiveservicestaskforce.org/uspsbrca.htm)
  - 3-D Tomosynthesis
    - [www.acrin.org](http://www.acrin.org)
    - [www.hologic.com](http://www.hologic.com)

- **Hormone Therapy**
  - North American Menopause Society (NAMS)
    - [www.menopause.org](http://www.menopause.org)
Thank you

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