“Repeal & Replace”
AHA under a Trump Administration
Post-Election Outlook

Health Care is Back on the Agenda

“We’re not going to have a two-year period where there’s nothing. It will be repealed and replaced….And it’ll be great care for much less”

President-elect Donald Trump

Health Care is Back on the Agenda

“The one thing we have to do is repeal and replace Obamacare. It is a disaster.”

BUT........

Everybody’s got to be covered. This is an un-
Republican thing for me to say….I would make a deal with existing hospitals to take care of people. The government is going to pay for it....”
The Debate

Critics
- Premiums have increased on avg. 25% nationally
- 50% of the Exchange plans have deductibles > $3,000
- 2/3 of the exchange plans lost over $2.2B in 2014
- Families are going without care because they can’t afford it

Supporters
- ACA increased efforts to reduce waste, fraud and abuse; slowing the rate of increase in payments to providers
- ACA has resulted in extending the solvency of Part A by more than a decade
- ACA has lowered Part B out-of-pocket costs for beneficiaries

A New Wave of Uncertainty

Options for Repeal and Replace?
“Healthcare Reform to Make America Great Again”

- Eliminate the individual mandate
- Modify existing law that inhibits the sale of health insurance across state lines
- Allow individuals to fully deduct health insurance premium payments
- Allow individuals to use Health Savings Accounts
- Require price transparency from all providers
- Block-grant Medicaid to the states
- Remove barriers to entry into the free market for drug providers that offer safe, reliable and cheaper products

Early Signals

HHS
Nominated for Secretary:
Rep. Tom Price

Dr. Price is an orthopedic surgeon who joined Congress in 2004. Voting record establishing him as a staunch conservative:
- Has introduced comprehensive ACA replacement bills in every congress since 2009, and has consistently voted to repeal and defund the ACA
- Supports work requirements for welfare recipients
- Consistently voted pro-life
- Sponsored "Empowering Patients First Act"

CMS
Nominated for Administrator:
Seema Verma

Ms. Verma and her consulting company, SVC Inc., have been involved in the development of Medicaid expansion and waiver programs across the country:
- Credited as the architect of Indiana’s Healthy Indiana Plan (HIP) and Gov. Pence’s HIP 2.0 waiver
- Assisted in development of waivers for Iowa, Ohio, and Kentucky
- Assisted in Tennessee’s coverage expansion program

“Empowering Patients First Act”

- Repeal Obamacare and replace it with a 401(k)-like plan
- Keep the basic structure of the exchanges, but replace the existing income-based subsidy with age-based credits
- Insurers could charge more if individuals lapse in coverage (up to 150% of the standard premium)
- Repeal the expansion of Medicaid
- Create incentives to contribute to HSAs
- Offer grants to states to subsidize insurance for high-risk populations
- Allow "cross-state" insurance policies
GOP Convergence
All Roads lead to “A Better Way”

Freedom and Empowerment Plan (Gov. Jindal)
Empowering Patients First Act (Rep. Price)
Improving Health and Health Care (American Enterprise Institute)
A Better Way (House Republicans)
Transcending Obamacare (Avik Roy)
Patient Freedom Act of 2015 (Sen. Cassidy)

Ryan’s Plan Adheres to Traditional Conservative Aims

“A Better Way” Plan Likely to Form Basis of Republican Negotiations
Comparison of Ryan Plan to ACA Provisions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Ryan Proposes</th>
<th>Change from ACA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insurance Market Regulation</td>
<td>Preserve pre-existing coverage protections for individual plans, mandates, and subsidies</td>
<td>Legally mandates ACA-based reforms</td>
</tr>
<tr>
<td>Medicaid Reform</td>
<td>Alter states to choose between two funding options: 1. Per capita allocation to states similar to managed care plans 2. Block grant to states if replacement program is implemented before 2020</td>
<td>Significant shift from status quo with ACA’s health insurance market reforms</td>
</tr>
<tr>
<td>Medicare Reform</td>
<td>Combine Medicare Parts A and B, increase eligibility age to 65, and create “Medicare Exchange” with traditional and private plans</td>
<td>Shift from delivery system reforms to encourage purchasing in Medicare population</td>
</tr>
<tr>
<td>Affordability</td>
<td>Expand availability of HSAs, provide tax credits toward purchase of insurance, and eliminate employer-provided health benefits</td>
<td>Supports tax incentives for individuals through tax credits rather than penalizing those who purchase insurance through the ACA</td>
</tr>
<tr>
<td>Innovation</td>
<td>Reform ACA processes, block grant funding, and exchange interoperability</td>
<td>Legally consistent with Obamacare initiatives</td>
</tr>
</tbody>
</table>

Unclear how Medicaid will be Addressed

- Medicaid not included in a repeal and replace legislation—
  - Possible that Congress chooses to focus on Marketplaces only and does not attempt to address Medicaid through reconciliation or at all legislatively
- Option 1: Eliminate Medicaid expansion
  - Different variations possible; e.g., full elimination after a transition or grandfather states but no additional states permitted to expand with the enhanced match
- Option 2: Cap federal funding for Medicaid through block grant or per capita cap
Challenges for Eliminating Expansion

- Most individuals who have gained coverage through the ACA are enrolled in Medicaid; it is unlikely that a roll back in expansion funding could be accomplished in a way that preserves coverage.

- Currently, 16 of the 31 expansion states have Republican governors; eliminating the expansion dollars will have large and immediate budget implications on all expansion states.

- Medicaid is a complex program and much larger than the marketplace (over $500 billion in spending, 70+ million enrollees); eliminating the expansion would have significant consequences for key stakeholders including hospitals, pharma and managed care plans.

Challenges for Eliminating Medicaid

- ~60% of Medicaid spending is devoted to services for high cost and growing populations including the elderly and disabled; it will be difficult to reach consensus on whether and how to cap spending for these groups.

- Formula "fights" always arise when spending cap proposals are debated, and recent developments in Medicaid will make interstate disputes over how to size and trend the capped funding even harder.

Multiple reforms to Medicaid financing are under consideration - The goal of all mechanisms is to decrease Medicaid spending over time and increase state flexibility to manage the program.

<table>
<thead>
<tr>
<th>Block Grants</th>
<th>Per Capita Caps</th>
<th>Capped Allotments</th>
<th>Shared Savings/Shared</th>
</tr>
</thead>
<tbody>
<tr>
<td>- States receive a lump sum to fund their Medicaid program</td>
<td>- Imposes per enrollee limit on federal match for Medicaid</td>
<td>- Imposes limit on total federal match for Medicaid</td>
<td>- Federal per enrollee spending target established</td>
</tr>
<tr>
<td>- Amount set by formula, may be trended to grow over time</td>
<td>- Allow for Medicaid spending to increase as enrollment increases (e.g. with program expansion, population growth, economic recession)</td>
<td>- State continues to contribute non-federal share</td>
<td>- States share in savings and risk for spending below or above target</td>
</tr>
<tr>
<td>- States may spend grants on specific activities – greater flexibility</td>
<td>- May be paired with additional flexibility for states</td>
<td>- States exceeding cap must cut costs or supplement with state dollars</td>
<td>-</td>
</tr>
<tr>
<td>- Generally states are not required to provide a match</td>
<td>- States exceeding grant must cut costs or supplement the block grant with state dollars</td>
<td>- States continue to contribute non-federal share</td>
<td>-</td>
</tr>
</tbody>
</table>
No Debate on MACRA

MACRA Continues to Enjoy Bipartisan Support

Legislation to boost MACRA:
- Legislation passed in April 2015 requiring the Medicare payment formula (GPCI)
- MIPS, which includes both Medicare Physician Fee Schedule adjustments and EHR incentive payments
- Established a payment model
  - Value-based Modifier Payment System (VMP)
  - Advanced Alternative Payment Model (APM)

Legislation to hold Bipartisan Support

<table>
<thead>
<tr>
<th>Year</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>-1.9</td>
</tr>
<tr>
<td>2015</td>
<td>0.2</td>
</tr>
<tr>
<td>2016</td>
<td>0.5</td>
</tr>
<tr>
<td>2017</td>
<td>-1.8</td>
</tr>
<tr>
<td>2018</td>
<td>-2.3</td>
</tr>
</tbody>
</table>

Setting the stage for MACRA...

Actual Updates Compared to Required Updates, 1998-2015

Track 1: MIPs

Budget-neutral P4P program -- rewards high performers with payment adjustments by penalizes the low performers, based on specific quality metrics.

Year Categories That Generation MIPS Score
Relative Weight Over Time

- Quality
- Cost Resource Use
- Clinical Practice Improvement
- Enhancing Care Alternative

Maximum Provider Penalties and Bonuses

<table>
<thead>
<tr>
<th>Year</th>
<th>High Performance</th>
<th>Low Performance</th>
</tr>
</thead>
<tbody>
<tr>
<td>2019</td>
<td>20%</td>
<td>-10%</td>
</tr>
<tr>
<td>2020</td>
<td>20%</td>
<td>-10%</td>
</tr>
<tr>
<td>2021</td>
<td>20%</td>
<td>-10%</td>
</tr>
<tr>
<td>2022</td>
<td>20%</td>
<td>-10%</td>
</tr>
</tbody>
</table>

Budget neutrality adjustment: scaling factor up to 2x may be applied to prevent
- High performers from earning pay increases
- Low performers from being penalized significantly more
Track 2: APMs

- Alternative plan to MIPS, involves much more stringent qualifications but offers higher annual bonuses and growth rates for increased risk
- Participants who qualify for APM payment track awarded 5% bonus payment during “frozen” period
- Two qualifications:
  - Participation in Advanced Alternative Payment Models
  - Required to have pre-determined percent of revenue or percent of patient volume attached to Advanced APMs
- Much more difficult to qualify for than MIPS.

APM Qualifications

- Two criteria to qualify:
  - Participation in an advanced APM as defined by CMS
  - Qualifying Payment Models for 2017
    - Medicare Payment Appeals Program Tracks 1 and 2
    - Clinical Laboratories Evaluation Program (CLUE)
    - The Star (e.g., a Medicare Access and Clinical Trials)
    - Participating in the Medicare Innovation Model (IHI)
    - Medicare Care Improvement Program (MIIP) Track 1 and 2

- Much more difficult to qualify for than MIPS.

MACRA: Overview

Baseline Medicare Provider Payment Adjustments Under Each Track

- Advanced Alternative Payment Models (APMs): 2019 and 2020, 5% annual update
- The Medical Improvement System (MIPS): 2019 and 2020, 0.25% annual update

Annual Bonus for APM Participation

- Remains awarded each year from 2019-2014 for participants who meet criteria for the APM payment track.
Now What?

The next several months are likely to be marked by continued uncertainty – but there are some sure bets:

- Be prepared to live under further rate cuts
- Develop an intentional Medicare risk strategy
- Review/update physician alignment goals
- Invest in consumer-oriented care delivery
Economics of Cancer Care in 2017 and in the Future

Edward E. Partridge, MD
Director, UAB Comprehensive Cancer Center
Professor of Gynecologic Oncology
Evalina B. Spencer Chair in Oncology
University of Alabama at Birmingham

edpartridge@uab.edu

Dr. Partridge has no financial interest or other conflict of interest in relation to this presentation.
Educational Objectives

- To understand how patient navigation can improve care and reduce costs in cancer care
- To understand MACRA and its implications in health care delivery
- To understand Alternative Payment Models such as Oncology Care Model from CMS
- To have a vision for what cancer care will look like in the future

Select References


Late-Breaking Issues in Reproduction and Fertility

Deidre D. Gunn, MD
Fellow/Instructor, Division of Reproductive Endocrinology and Infertility
Department of Obstetrics and Gynecology
University of Alabama-Birmingham Medical Center
ddowns@uabmc.edu

Objectives

After this session, the participant will be able to:

1. Define preimplantation genetic screening and describe its benefits and limitations.
2. Describe clinical management and patient counseling in pregnancies resulting from IVF-PGS.
3. Describe the benefits of chromosomal microarray of products of conception after pregnancy loss.
4. Describe the advances in endometrial receptivity testing for implantation failure.

Outline

I. Preimplantation genetic screening
   • Indications for and benefits of PGS
   • Consideration of error rates associated with different genomic techniques for screening
   • Limitations and interpretation of results
     o Mosaicism and segmental aneuploidy
   • Management of first- and second-trimester screening in pregnancies resulting from IVF-PGS

II. Chromosomal microarray for pregnancy loss
   • Advantages over traditional cytogenetic testing (karyotyping)
   • Indications and patient selection
   • Practical considerations for tissue collection and commercial testing

III. Endometrial receptivity
   • Physiology of the implantation window
   • Genetic markers for endometrial receptivity
   • Endometrial receptivity assays for patients with recurrent implantation failure
Selected References


Interstitial Cystitis/Bladder Pain Syndrome
Current Guidelines and Evidence Based Management

Isuzu Meyer, MD
Assistant Professor
Division of Urogynecology and Pelvic Reconstructive Surgery
Department of Obstetrics and Gynecology
University of Alabama at Birmingham
imeyer@uabmc.edu
Interstitial Cystitis/Bladder Pain Syndrome

Educational Objectives
At the end of the lecture, participants will be able to describe the following:
- Basic pathogenesis/mechanisms pertinent to diagnosis and treatment of interstitial cystitis/bladder pain syndrome (IC/BPS)
- Clinical features and symptoms of IC/BPS
- Current guidelines for diagnostic evaluation of IC/BPS
- Current guidelines for evidence based treatment of IC/BPS

Outline
1. Pathogenesis
   - Urothelial abnormality
   - Neurologic upregulation of pain sensation
2. Clinical Features
   - Symptoms
   - Coexisting conditions
3. Current Guidelines for Diagnostic Evaluation
   - Definition
   - Differential diagnosis
   - History and physical exam
   - Diagnostic Tests
4. Evidence Based Treatment – Stepwise Approach
   - First-line: Behavioral modification, avoidance of bladder irritants, bladder training
   - Second-line: Oral medications, physical therapy
   - Third-line: Hydrodistention, intravesical medications
   - Fourth-line: Botulinum toxin A and sacral neuromodulation

Select References
Hereditary Cancers in Women
You can choose your friends but not your kinfolks!

Larry C Kilgore, M.D.
Professor and Chairman
Department of Obstetrics and Gynecology
The University of Tennessee Knoxville
lkilgore@utmck.edu
Reproductive Health and Obesity

Educational Objectives

- Participant will be able to describe how obesity alters reproductive function
- Participant will be able to describe the impact of obesity on fertility treatments
- Participant will be able to describe the maternal and neonatal morbidities associated with obesity
- Participant will be able to list five Interventions to achieve weight loss
- Participant will be able to describe four goals for weight loss

Outline

1. Obesity and reproductive function
   - Menstrual cycle
     i. Follicular recruitment
     ii. Oocyte quality
   - Implantation
     i. Endometrium
2. Obesity and fertility treatments
   - Ovulation induction
   - ART
3. Obesity and maternal and neonatal morbidities
   - Maternal outcomes
   - Neonatal outcomes
     i. Prenatal programming
4. Interventions to achieve weight loss
   - Lifestyle modifications
   - Medications
   - Bariatric Surgery
5. Goals for Weight loss
   - Menstrual function
   - Fertility
   - Pregnancy outcomes
Select References
- Moragianni. The Effects of body mass index on the outcomes of first assisted reproductive technology cycles. Fertility and Sterility, 2012; 98 (1) 102-108.
Hereditary Cancers in Women

You can choose your friends but not your kinfolks!!

Larry C. Kilgore, M.D.
Professor and Chairman
UTMC Obstetrics and Gynecology

Learning Objectives

› Understand risk factors for hereditary cancer
› Define risks related to BSO in young women
› Adopt family history screening in practice
› Review results of Nurses Health Study
› Assess impact of personal and family history of cancer
› Learn management options for BRCA patients
› Learn management options for Lynch patients
› Consider role of risk reduction strategies

Pelvic Serous Cancer (PSC)

› Ovary Cancer
› Fallopian Tube Cancer
› Primary Peritoneal Cancer
Hereditary Cancer?

- Multiple cases within the family
- Autosomal dominant transmission
- Early age of onset; earlier in successive generations
- Bilateral cancers
- Synchronous cancers (> 2 at once)
- Metachronous cancers (more than one, diagnosed at different times)

Red Flags for Hereditary Cancers

- Obtaining a Family History of Cancer
  - 3-generation family history
    - 1st Generation: Parents, siblings, children
      - 50% genetic link
    - 2nd Generation: Grandparents, grandchildren, aunts, uncles, nieces, nephews, ½ siblings
      - 25% genetic link
    - 3rd Generation: Great-grandparents, great-grandchildren, great aunts/uncles, grand nieces/nephews, first cousins
      - 12.5% genetic link
Obtaining a Family History of Cancer

- Maternal and paternal data
- Include race, ethnic background, current age, all types of cancers, age at diagnosis, age at death
- Update at each visit
- Confirm with medical records and pathology reports when possible

Patient Cancer Hx Form

Identifying Individuals at Risk

- Personal and Family History
  - The most important and cost-effective tool in risk assessment
- Risk Factors for BRCA1 and BRCA2
- Amsterdam Criteria or Bethesda Criteria for HNPCC
- Gail Model for Breast Cancer Risk
Case study

- 71 yo referred. Ascites, pelvic mass
- PMH – Breast cancer age 32
- Fam hx – Sister breast cancer age 34 alive
- Surgery IIic Fallopian tube primary (PSC)
- “You and your sister both are BRCA +”
- “I have 6 brothers and 3 sisters”
- “Send them all in”
- To date…..8 family members are BRCA +

Early History

- 1895 – Aldred Scott Warthin
  - Michigan Chair of Pathology
  - Studied pedigree of German seamstress who first developed colon cancer but ultimately died of endometrial cancer
  - Published history of Family G in 1925
    - “there is some heredity to cancer”
- 1971 – Henry Lynch
  - Studied Family G
    - 2 additional families (M and N)
    - Extended the range of malignancies to include ovary renal pelvis, stomach, small bowel, pancreatic
    - Determined autosomal dominant inheritance
    - Solidified early age of onset of cancers

Mary–Claire King
Geneticist. U Washington

- Discovered Gene for BRCA 1
The Angelina Jolie Effect:
Risk Reducing Surgery for Breast and Ovarian Cancer

MAY 2013

Old Paradigms/New Paradigms

- Remove tubes/ovaries after 40 yo
  - Prevent ovary cancer?
- Remove tubes/ovaries after 50 yo
  - Prevent ovary cancer?
- Keep normal tubes/ovaries till early 60s
  - Nurses Health Study!!
- Opportunistic salpingectomy???
Bilateral oophorectomy is associated with increased mortality in women aged younger than 50 years who never used estrogen therapy and—

at no age is oophorectomy associated with increased survival.

(general population)

Parker, et al. (Obstet Gynecol 2013)

You Have a Better Chance of Living Until You are 80 – If You Keep Your Ovaries Until You are 65 Years Old!!!!!!
BSO AT WHAT COST?

- WITH NO HRT
  Higher rate of premature death, cancer heart disease and neurological disease

- HRT ???
  Duration?
  Compliance?

**Why leave the tube in women at average risk?**

In US 30% women undergo hysterectomy, 50% have ovaries and fallopian tube left in situ

~20% of women who develop ovarian cancer have had a prior hysterectomy

Up to 20% of ovarian cancer patients have had a tubal ligation

Most women with inherited risk are unidentified.

**Hereditary Cancers in Women**

- Hereditary Breast and Ovary Syndrome
  - Genes: BRCA1, BRCA2

- Lynch Syndrome
  - Nonpolyposis colorectal cancer (HNPCC)
  - Genes: MSH2, MLH1, MSH6, PMS2, EPCAM

- Li–Fraumeni Syndrome
  - Gene: TP53

- Cowden Syndrome
  - Gene: PTEN
Hereditary Cancers in Women

- Hereditary Breast and Ovary Syndrome
  - Breast, Ovary, Pancreatic, Prostate, Melanoma, Male Breast
- Lynch Syndrome
  - Colorectal, Endometrial, Ovary, Renal pelvis, small bowel, biliary tract
- Li–Fraumeni Syndrome
  - Breast, sarcoma, leukemia, brain, adrenal
- Cowden Syndrome
  - Breast, Endometrial, thyroid

---

The Status of Genetic Testing

- 0.2–0.3% BRCA mutation carrier rate in US population
  - This means 322,000–483,000 US women carry mutations.

In 2014 only 26% of women with ovarian cancer were tested for BRCA Mutations among patients who meet guidelines for BRCA testing.
Ovarian Cancer Risk Factors: Increased Risk

<table>
<thead>
<tr>
<th>Factor</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hx of Breast Cancer</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.0</td>
</tr>
<tr>
<td>1st Degree Relative</td>
<td>2.1</td>
</tr>
<tr>
<td>Personal History</td>
<td>10</td>
</tr>
<tr>
<td>Hx of Ovarian Cancer</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>1.0</td>
</tr>
<tr>
<td>One 1st Degree Relative</td>
<td>3.1</td>
</tr>
<tr>
<td>&gt;2 1st Degree Relatives</td>
<td>4-15</td>
</tr>
<tr>
<td>Hereditary Cancer Syndrome</td>
<td>12-40</td>
</tr>
</tbody>
</table>

(SEER) National Cancer Institute
Risk Factors for Ovarian Cancer

- General Population: 1.0
- BRCA 1 Mutation: 35-46
- BRCA 2 Mutation: 13-23
- Lynch Syndrome: 3-14
- + FHx Ov Ca/ - Gene Mut.: Uncert.
- Infertility: 2.7
- PCO: 2.5
- Endometriosis (Clear Cell, Muc, LG Serous): 2-3
- + Cigs (Muc): 2
- IUD: 1.8

http://seer.cancer.gov/
BRCA 1 and BRCA 2 Function

- Tumor suppressor genes
  - Regulate normal cell growth and proliferation
  - Counteract stimulatory effects of oncogenes

- Play a role in DNA repair
  - Interact with RAD51, a known DNA repair protein
  - “Caretaker genes”

Prevalence of BRCA

- BRCA 1 general population 1:400–1:800
- BRCA 2 lower
- Ashkanazi Jewish Descent 1:40

BRCA Risk of Ovarian Cancer

<table>
<thead>
<tr>
<th>AGE</th>
<th>BRCA1</th>
<th>BRCA2</th>
</tr>
</thead>
<tbody>
<tr>
<td>40</td>
<td>2.2%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>50</td>
<td>8.7%</td>
<td>1.9%</td>
</tr>
<tr>
<td>60</td>
<td>22%</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

Chen et al, JCO 2007
### Breast Cancer

<table>
<thead>
<tr>
<th>Age at Diagnosis</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dx &lt; 50 years</td>
<td>20%</td>
</tr>
<tr>
<td>Dx &gt; 50 years</td>
<td>7%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian Cancer</td>
<td>10–20%</td>
</tr>
<tr>
<td>Both Breast and Ovarian Cancer</td>
<td>90%</td>
</tr>
</tbody>
</table>

### Breast Cancer

**Family Cancer History**

<table>
<thead>
<tr>
<th>Relative Count</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>One 1st degree relative</td>
<td>3.8%</td>
</tr>
<tr>
<td>≥ 3 relatives</td>
<td>20%</td>
</tr>
<tr>
<td>Bilateral</td>
<td>18%</td>
</tr>
<tr>
<td>Breast + ovarian cancer</td>
<td>40%</td>
</tr>
</tbody>
</table>

### BRCA and BRCA2-Associated Cancers: Lifetime Risks

- **Breast cancer:** 40%–85% (often early age at onset)
- **Contralateral breast cancer:** 40%–60%
- **Ovarian cancer:** 15%–40%

In men, risk of breast cancer is elevated, and some studies suggest that the risks of prostate and pancreatic cancer are also elevated.
BRCA testing in patients unaffected by cancer

- 2 relatives with breast cancer, 1 < 50 yo
- 1 relative with Pelvic Serous Cancer (PSC)
- 1 relative with breast ca and 1 with PSC
- Breast Cancer in 1 male first degree relative

OPTIONS WITH BRCA or Family History

- SURVEILLANCE
- RISK AVOIDANCE
- PROPHYLACTIC SURGERY

NCCN guidelines for BRCA mutation carriers

- Remove the tubes and ovaries when between the age of 35–40 or when completed childbearing.
- Screening with CA 125 and ultrasound q 6 months.
All guidelines recommend: Risk Reducing salpingo–oophorectomy for BRCA mutation carriers

- 90% effective in reducing ovarian cancer
- 50% reduction in breast cancer if performed before age 50
- Increase life expectancy 6.6–11.7 years for combined BSO, mastectomy.

Oophorectomy reduces Breast Cancer Risk in BRCA mutation carriers

Risk reduction if performed by age 40
- BRCA 1: 56% (OR= 0.44; 95% CI 0.29, 0.66)
- BRCA 2: 46% (OR=0.57; 95% CI 0.28, 1.15), Domchek JAMA, 2010
- Eisen et al., J Clin Oncol, 2005

Salpingectomy in mutation carriers

- Some cancer risk reduction
- Avoid premature menopause
- Maintain option for IVF pregnancy
- Option for those unwilling to have BSO
- Pros
- Cons
- Two stages to surgery
- Delay of removing the ovaries
- May not be as effective
- No Breast cancer risk reduction
SURVEILLANCE

- BREAST CANCER
  - self examination
  - mammograms
  - MRI

- OVARIAN CANCER
  - clinical examinations
  - vaginal ultrasound
  - Ca 125 level

Follow Up Studies BRCA + Pts.

HNPCC or Lynch Syndrome

- ~7% of hereditary ovarian cancer cases
- 5% of all colorectal cancer cases
- Most common cancers: COLON and ENDOMETRIAL
- Increased incidence of other adenocarcinomas, including stomach, small bowel, and bile duct malignancies (not breast)
Lynch Syndrome

- Autosomal dominant inheritable cancer syndrome
- Formerly Known as Hereditary Nonpolyposis Colorectal Cancer (HNPCC)
- Responsible for most common form of hereditary colorectal cancer AND endometrial cancer

HNPCC

- Responsible genes: Mismatch repair genes (MMR) including MLH1, MSH2, and MSH6
- Autosomal dominant
- Prevalence in the general population: 0.1% (1/400 to 1/1000)

Lynch Associated Cancers

- Colorectal
- Endometrial
- Ovarian
- Renal Pelvis
- Ureter
- Stomach
- Small bowel
- Sebaceous adenocarcinoma
- Hepatobiliary
- Pancreas
- Brain (glioma)
- Prostate?
- Breast?
- Laryngeal??
- Hematologic?
Clinical Significance

- 50–80% risk of malignancy by age 70
- 7–15% will have synchronous tumors at diagnosis
- 20–65% chance of metachronous tumors
- Significantly under-recognized

Case presentation

- 40 yo G4P4 (wife of obgyn)
- Father colon cancer at 33 yo
- Sister colon cancer
- Tested for Lynch----Positive
- Advised Risk Reduction TLH, BSO
- At surgery
  - Synchronous primary cancer (uterus and ovary)
  - Colonoscopy negative
- Currently NED after surgery/chemotherapy

Women with Lynch Syndrome:

- Colon cancer:
  - 50–80% lifetime risk
- Endometrial cancer:
  - 40–70% lifetime risk
- Ovarian cancer:
  - 10–14% lifetime risk
Endometrial Cancer in Lynch Syndrome

- Similar lifetime risk to colorectal cancer
- Survival similar to sporadic
- Endometrioid common but all cell types documented
- Similar hormonal/reproductive risk modifiers to sporadic cancer
- More often lower uterine segment

Characteristics of Lynch CRC

- Predominantly right colon
- Evolve from flat large adenoma
- Rapid progression (months rather than years)
- Higher 5 year OS than sporadic tumors

Ovarian Cancer in Lynch Syndrome

- 2–14% lifetime risk
- Pathology and survival similar to sporadic
  - More likely to be diagnosed as stage I or II
- Significantly younger age than sporadic
- BRCA larger portion of familial ov cancer
Identifying Individuals at Risk

- History based
  - Amsterdam
  - Bethesda
- Prediction models
- Tumor based
  - IHC
  - MSI
- Genetic evaluation

Targeted Surveillance?

- Transvaginal Ultrasound
  - Endometrial stripe measurement (difficult premenopausal
  - Ovarian imaging
- Annual endometrial biopsy
  - Starting at age 30–35 or five years prior to earliest diagnosed LS malignancy
- CA125
- NO surveillance in this (or any other) patient population has shown improved overall survival…..but many still recommend

Clinical Management of Women with HNPCC: Screening

- Annual ultrasound or endometrial biopsy beginning at age 25–35
- Hysterectomy and BSO when childbearing complete
  - Reduces risk of endometrial cancer
  - Reduces risk of ovarian cancer
Intervention

- Risk Reducing Surgery
  - Hysterectomy/ BSO

Prophylactic Surgery to Reduce the Risk of Gynecologic Cancers in the Lynch Syndrome

- When completed child baring
- Supracervical inappropriate
- Surgeon should be prepared for complete staging procedure
- Occult cancer not uncommon at time of “prophylactic” surgery
- Frozen/intraoperative pathologic evaluation usually indicated.
- Serial sectioning of ovaries
- TAH/BSO should be offered at time of prophylactic or therapeutic colectomy
- Estrogen replacement probably acceptable in the absence of endometrioid cancer
- Primary peritoneal cancer risk still 0.5–1.5%

Elevated HNPCC Risk: Amsterdam Criteria

- 1. At least two successive generations with colorectal cancer
- 2. Diagnosis of at least one individual before age 50
- 3. Colon cancer in at least 3 relatives
- 4. Family history of other cancers including ovarian, endometrial, stomach, urinary tract, small bowel, and bile duct
When might genetic testing be considered?
- Personal or family hx of pre-menopausal breast cancer OR ovarian cancer (any age)
- 1st-degree relative with BRCA1 or 2 mutation
- Family hx of ≥ 2 cases of pre-menopausal breast cancer
- Family hx of ≥ 1 cases of ovarian cancer

Genetic Testing (con’t)
- Personal or family hx of bilateral breast cancer
- Family hx of male breast cancer
- Ashkenazi Jewish ancestry in the setting of a personal or family hx of breast or ovarian cancer

Clinical Management
- Now that you’ve got it, what do you do with it?!
  - Genetic counseling/testing
  - Screening
  - Prophylactic measures/chemoprevention
  - Consider clinical trials
References

- Parker. (Obstet Gynecol 2013)
- Kuran AW, Curr Opin Obstet Gynecol 2015
- Chen. JCO 2007.
- Domchek JAMA 2010.
Abnormal Uterine Bleeding (AUB)

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Division of Women's Reproductive Healthcare
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AUB: Learning Objectives

• Review the physiology and characteristics of the normal menstrual cycle
• Discuss the components of the appropriate evaluation of AUB
• Discuss the best treatments for AUB and the rationale behind their usage

AUB: Faculty Disclosures

• None
THE “NORMAL” MENSTRUAL CYCLE

MENSTRUAL CYCLE

Normal Menstrual Cycle
Normal Menstrual Cycle

AUB: Components of History

<table>
<thead>
<tr>
<th>Clinical Dimensions of Menses</th>
<th>Descriptive Terms</th>
<th>Normal limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of menses (days)</td>
<td>Frequent</td>
<td>&lt;24 days</td>
</tr>
<tr>
<td></td>
<td>Normal Infrequent</td>
<td>24 – 38 days</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>&gt; 38</td>
</tr>
<tr>
<td>Regularity of menses</td>
<td>Regular</td>
<td>±2 to 20 days</td>
</tr>
<tr>
<td></td>
<td>Irregular</td>
<td>&gt; 20 days</td>
</tr>
<tr>
<td>(Cycle to Cycle variation in days)</td>
<td>Prolonged</td>
<td>&gt;8 days</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td>4.5 – 8 days</td>
</tr>
<tr>
<td></td>
<td>Shortened</td>
<td>&lt;4.5 days</td>
</tr>
<tr>
<td>Duration of flow (days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Volume of monthly blood loss (mL)</td>
<td>Heavy</td>
<td>&gt;80 mL</td>
</tr>
<tr>
<td></td>
<td>Normal Light</td>
<td>5 – 80 mL</td>
</tr>
<tr>
<td></td>
<td>Light</td>
<td>&lt;5 mL</td>
</tr>
</tbody>
</table>

Normal Menstrual Cycle

• Follicular Phase
  – Duration is highly variable
  – 10.3 – 16.3 days

• Luteal Phase
  – Duration is fairly constant
  – 24 ± 1.4 days
Normal Menstrual Cycle

- “Synchronous rise and fall in estrogen and progesterone levels throughout the cycle is the most important determinant of normal menses”

CLASSIFICATION OF AUB

"ABNORMAL" MENSTRUAL CYCLES

- AUB
  - HMB
  - Acute AUB
  - Chronic AUB
- IMB
AUB: Terminology

- AUB – Abnormal uterine bleeding
- HMB – Heavy menstrual bleeding
- IMB – Intermenstrual bleeding

Munro et al. Int J Gynecol Obstet. 2011;113:3-13

AUB: Validated Terminology

- Acute AUB
- Chronic AUB

Munro et al. Int J Gynecol Obstet. 2011;113:3-13

AUB: Terminology

- Discarded terms
  - Menorrhagia
  - Metrorrhagia
  - Menometrorrhagia
  - Dysfunctional uterine bleeding
EVALUATION OF AUB

FIGO AUB Classification System

- Key:
  - Amenorrhea
  - Polypedony
  - Leiomyoma
  - Malignancy & Hyperplasia
  - Structural Abnormality

- Dysfunctional Uterine Bleeding
- No Structural Abnormality

Munro et al. Int J Gynecol Obstet 2011;113:3-13

EVALUATION OF AUB

- FIGO Recommendations
  1. General Assessment
  2. Determination of Ovulatory Status
  3. Screening for Systemic Disorders of Hemostasis
  4. Evaluation of the Endometrium
  5. Evaluation of the Structure of the Endometrial Cavity
  6. Myometrial Assessment
AUB Evaluation: History

- General Assessment: History
  - Bleeding pattern
  - Symptoms of anemia
  - Sexual and reproductive history
  - Associated symptoms
  - Systemic cause of AUB
  - Chronic medical illness
  - Medications
  - Family history

AUB Evaluation: History

- General Assessment: Ovulatory Status
  - Regular cycles
  - Mittleschmerz
  - Pre-ovulatory mucus
  - Moliminal symptoms
  - Predictable bleeding

AUB Evaluation: History

Screening for Systemic Disorders of Hemostasis
Has the patient suffered from excessive or heavy bleeding in any of the following situations?

- Heavy menstrual bleeding since menarche
- One of the following
  - Postpartum hemorrhage
  - Surgical-related bleeding
  - Bleeding associated with dental work
- Two of the following
  - Bruising 1-2x per month
  - Epistaxis 1-2x per month
  - Frequent gum bleeding
  - Family history of bleeding symptoms

Munro et al. Int J Gynecol Obstet 2011;113:3-13
AUB Evaluation: Exam

- General Assessment – Exam
  - Vital signs – BP, pulse, BMI, orthostatics
  - Neck exam - thyroid
  - Abdominal exam – tenderness, distension, mass
  - Bimanual exam
  - Rectal exam – as indicated
  - Testing – Pap and STI screening, as indicated
  - Labs – CBC, urine pregnancy
    - TSH, PRL, Coags, VW panel, Free testosterone – as indicated

Bradley et al. AJOG 2015

AUB Evaluation: Exam

General Assessment

- Rule out other location for bleeding
  - Rectal bleeding
  - Hematuria
  - Trauma

Munro et al. Int J Gynecol Obstet. 2011;113:3-13

AUB: Evaluation Guidelines

Evaluation of the Endometrium (FIGO)

- Endometrial biopsy
  - “Endometrial sampling should be considered for all women over a certain age, usually 45 years”
  - “Persistent AUB that is unexplained or not adequately treated requires endometrial sampling-if possible, in association with hysteroscopic evaluation of the uterine cavity”
- Screen for chlamydia, if symptomatic

Munro et al. Int J Gynecol Obstet. 2011;113:3-13
AUB: Evaluation Guidelines

Evaluation of the Endometrium (ACOG)

- Endometrial biopsy
  - “Endometrial tissue sampling should be performed in patients with AUB who are older than 45 years as a first line test”
  - “Endometrial sampling also should be performed in patients younger than 45 years with a history of unopposed estrogen exposure (such as obesity or PCOS), failed medical management, and persistent AUB.”


AUB: Evaluation Guidelines

Evaluation of the Structure of the Endometrial Cavity (FIGO)

- Transvaginal ultrasound
  - “should be performed first or early in the course of the investigation.”
- Indications for SIS or office hysteroscopy
  - Features indicative of an endometrial polyp (AUB-P)
  - Myomas that may be encroaching on the endometrial cavity (AUB-L)
  - The exam is suboptimal


AUB: Evaluation Guidelines

Evaluation of the Structure of the Endometrial Cavity (ACOG)

- Transvaginal ultrasound
  - “Any patient with an abnormal physical examination...should undergo transvaginal ultrasound.”
  - “When symptoms persist despite treatment in the setting of a normal pelvic exam.”
- Indications for SIS or office hysteroscopy
  - When there is clinical suspicion for endometrial polyps or submucosal leiomyomas

AUB: Evaluation Guidelines

Evaluation of the Structure of the Endometrial Cavity (ACOG)

- Transvaginal ultrasound
  - "Measurement of endometrial thickness in premenopausal women is NOT helpful in the evaluation of AUB."


AUB: Evaluation Guidelines

Myometrial Assessment

- Transvaginal ultrasound
  - Assess presence and location of myomas (AUB-L)
  - Assess for adenomyosis (AUB-A)
    - At least 3 criteria must be present for diagnosis
- MRI
  - Helpful in delineating fibroid location prior to myomectomy
  - Not required in most situations.

Munro et al. Int J Gynecol Obstet. 2011;113:3-13
TREATMENT OPTIONS

AUB Treatment

• Options for Treatment of Acute AUB
  – IV conjugated equine estrogen (CEE)
  – Oral transexamic acid
  – Multi-dose combined monophasic OCP
  – Multidose oral progestin
  – GnRH agonist with aromatase inhibitor

AUB Treatment – Acute AUB

• Conjugated equine estrogen (CEE)
  – Rapid growth of the endometrial epithelium and stroma
  – Stimulating vasospasm of uterine arteries
  – Promotes platelet aggregation and capillary clotting
  – Increasing fibrinogen, factor V, and factor XI
  – Increases the production of estrogen and progesterone receptors
AUB Treatment – Acute AUB

• Conjugated equine estrogen (CEE)
  – 25 mg dose of IV CEE q4-6 hrs.
  – Transition to progesterone alone or combination OCP’s for 10-14 days
  – If still bleeding at 24 hours, consider hysteroscopy, dilation and curettage

AUB Treatment

• HMB
  – Levonorgestrel intrauterine system (LNG-IUS)
  – Tranexamic acid
  – Combined OCP
  – Cyclic or continuous progestin
  – Injectable progestin (DMPA)
  – GnRH agonist
  – Danazol
AUB Treatment

- Nonsteroidal anti-inflammatory drugs (NSAIDS)
  - Suppress prostaglandin synthetase by inhibiting cyclooxygenase
  - Alter the equilibrium between:
    - Thromboxane A2 – vasoconstriction/platelet aggregation
    - Prostacyclin – vasodilation and prevents platelet aggregation
  - Reduces blood loss by as much as 40%

AUB Treatments

**Combination hormonal contraceptive**

- Pills, vaginal rings, and the transdermal patch have all been shown to afford:
  - Cycle control
  - Reduce menstrual blood loss
  - Reduce the incidence of irregular bleeding

AUB Treatment

**Estrogen**

- Prevents FSH secretion
- Prevents development of a dominant follicle
- Provides endometrial stability
- Enhances the progestational impact

**Progesterone**

- Prevents the LH surge and ovulation
- Creates an atrophic endometrial lining
- Reduces overall blood loss at the time of withdrawal bleeding
AUB Treatment

- Progestogen-only Formulations
  - Medroxyprogesterone acetate (MPA) 2.5-10mg daily
  - Norethindrone 2.5-5mg daily
  - Megestrol acetate 40-320mg daily
  - Micronized progesterone 200-400mg daily
- Dosing options
  - Cyclically – begin on day 5 for 21 days
  - Continuous dosing

AUB Treatment

- Progestogen-only Formulations
  - Endometrial effects
    - Stabilizes endometrial fragility
    - Inhibits the growth of the endometrium by triggering apoptosis
    - Inhibits angiogenesis
    - Stimulates conversion of estradiol to estrone

AUB Treatment

- Progestogen-only Formulations
  - Ovarian effects
    - Prevents ovulation
    - Prevents ovarian steroidogenesis
    - Intermits the production of estrogen receptors
    - Intermits the estrogen-dependent stimulation of the endometrium
AUB Treatment

- Progestogen-only Formulations
  - “The use of a luteal phase progestin alone has not proved to be successful in the treatment of ovulatory HMB”.
  - “In women with anovulatory bleeding, a cyclic progestin given for 12-14 days each month leads to regulation of the menstrual cycle in 50% of women”.

Bradley et al. AJOG January 2016

AUB Treatment

- Injectable progesterone (DMPA)
  - Produces amenorrhea in >50% of users after 1 year
  - DMPA Trial (3900 women)
    - 12 months – 57% experienced AUB
    - 24 months – 32% experienced AUB
    - 37% experienced weight gain of >10lbs at 24 months

Bradley et al. AJOG January 2016

AUB Treatment

- “There is a lack of clinical data on the utility of DMPA for the treatment of acute or chronic AUB”.

Bradley et al. AJOG January 2016
AUB Treatment

Levonorgestrel IUS
• Releases 20 mcg of progestin every 24 hrs.
• Reduces the endometrial thickness
• Reduces the mean uterine vascular density

Bradley et al. AJOG January 2016

AUB Treatment

Levonorgestrel IUS
• Reduction in menstrual blood loss
  – 86% after 3 months
  – 97% after 12 months

Lethaby et al. Cochrane 2005
Mansour et al Best Practice 2007
Anderson et al Obst Gynecol 1990
Kaunitz et al Obstet Gynecol 2009

Bradley et al. AOGS January 2016

AUB Treatment

Levonorgestrel IUS
• Randomized controlled trials have demonstrated the LNG-IUS to be superior to:
  – Luteal phase oral MPA
  – Norethindrone for 21 days
  – Continuous oral norethisterone
  – DMPA
  – Combination OCP’s
  – Mefenamic acid
  – Endometrial ablation

Bradley et al. AOGS January 2016
AUB Treatments

- Tranexamic Acid
  - Competitively blocking plasminogen binding sites
  - Preventing plasma formation, fibrin degradation, and clot degradation
- 1 gram PO q6-8 hrs. during menstruation
- 40% reduction in blood loss

Bradley et al. AJOG January 2016

AUB Treatments

- Tranexamic Acid
  - Proven to be superior to the following:
    - Placebo
    - Mefenamic acid
    - Luteal phase progestins

Bradley et al. AJOG January 2016

SPECIAL POPULATIONS
AUB: Obesity

- Obese women suffer from ovulatory dysfunction because:
  - Elevated estrogen levels due to increased peripheral androgen aromatization
  - Elevated free estradiol and testosterone as a result of a reduction in SHBG
  - Insulin levels are elevated secondary to insulin resistance
  - Elevated insulin levels stimulates androgen production in the ovarian stroma and disrupts normal follicular development

Bradley et al. AOGS January 2016

AUB: Leiomyoma

- Submucosal fibroids cause unpredictable and heavy uterine bleeding
  - Unsteady vasculature of the endometrium
  - Inadequate rebuilding and healing
  - Increased endometrial surface area
  - Inadequate uterine contractions to compress the vessels on the surface of the endometrium

Bradley et al. AOGS January 2016

AUB: Leiomyoma

- Medications shown to reduce bleeding in women with fibroids
  - LNG-IUS
  - Combined OCP
  - NSAIDS
  - Danazol
  - Transexamic acid
  - “Medical therapies are most successful in the absence of a submucosal myoma”.

Bradley et al. AOGS January 2016
AUB: Leiomyoma

- GnRH Agonists
  - Down-regulate GnRH receptors, thereby inhibiting gonadotropin secretion
  - Menopausal symptoms limit their usefulness
  - Uterine volume can be reduced by 30-60% after 3 months use
  - Can improve anemia
  - Know plan for what you will do after therapy before you start!

AUB: Inherited bleeding disorders

- Prevalence
  - 84% of women with von Willebrand disease present with HMB
  - 30-20% of all women with AUB have an inherited bleeding disorder
  - 50% of adolescents with HMB will be diagnosed with a coagulopathy

AUB: Inherited bleeding disorders

- Treatment
  - Similar to women without a bleeding disorder
  - NSAIDS are contraindicated
  - Estrogen enhances von Willebrand factor and factor VIII
  - If standard treatment fails:
    - Consult Hematology
    - Desmopressin during 2-3 heavy days of cycle
AUB: Anticoagulation

- Prevalence
  - 70% experience changes in cycle
  - 50% experience a greater number of days
  - 66% experience HMB

- “LNG-IUS remains the superior method to control and significantly reduce menstrual blood loss in this group of patients”.

- Tranexamic acid and estrogen-containing contraceptives are contraindicated

Bradley et al. AOG January 2016

AUB: Anticoagulation

- “LNG-IUS remains the superior method to control and significantly reduce menstrual blood loss in this group of patients”.

- Women on progestin-only methods should be monitored very closely because they face a higher risk of thrombosis than nonusers of hormonal medications”.

Bradley et al. AOG January 2016

Additional Information

AUB PALM-COEIN
AUB: Structural Abnormalities

• AUB-P - Polyps
  – Etiology
    • Unknown
    • Clusters of anomalies in chromosomes 6 and 12, which control proliferative processes
  – Prevalence
    • 7.8 – 35%
    • Increase with age


AUB: Structural Abnormalities

• Premenopausal Polyps
  • 64 – 86% have symptoms
  • Present with HMB, AUB, IMB, or postcoital bleeding
  • Symptoms do NOT correlate with number, diameter and site
  • Stromal congestion leads to venous stasis and apical necrosis
  • Polyps caused 39% of all AUB in one study

Polyps < 1 cm are more likely to spontaneously regress


AUB: Structural Abnormalities

• Postmenopausal Polyps
  • Most are symptom free
  • Cause for 21-28% of PMP bleeding
  • Associated with cervical polyps in 24-27%
  • Incidence of carcinoma varies between 0 – 4.8%

ACOG Practice Bulletin #128 – “If the cancer occupies <50% of the surface area of the endometrial cavity, the cancer can be missed by a blind endometrial biopsy...persistent bleeding with a previous benign pathology requires further testing to rule out a nonfocal endometrial pathology.”

AUB: Structural Abnormalities

### Endometrial Polyp Detection

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Acc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV U/S</td>
<td>91%</td>
<td>90%</td>
<td>86%</td>
<td>90%</td>
<td></td>
</tr>
<tr>
<td>SIS</td>
<td>95%</td>
<td>92%</td>
<td>95%</td>
<td>94%</td>
<td></td>
</tr>
<tr>
<td>Blind Bx</td>
<td>10%</td>
<td>100%</td>
<td>66%</td>
<td>33%</td>
<td></td>
</tr>
<tr>
<td>Dx HSC</td>
<td>90%</td>
<td>93%</td>
<td>96%</td>
<td>93%</td>
<td></td>
</tr>
</tbody>
</table>

ACOG Practice Bulletin #138 – “A positive test result (EMB) is more accurate for ruling in disease than a negative test result is for ruling it out.”

### Structural Abnormalities

- **AUB-A - Adenomyosis**
  - Ectopic endometrial glands and stroma within the myometrium
  - Hypertrophy and hyperplasia of surrounding myometrium
  - Prevalence varies from 0.5% - 70%

Usual presentation includes HMB, uterine enlargement, and dysmenorrhea.

### Ultrasound Criteria for Adenomyosis

<table>
<thead>
<tr>
<th>U/S findings</th>
<th>Sens.</th>
<th>Spec.</th>
<th>PPV</th>
<th>NPV</th>
<th>Acc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Globular configuration</td>
<td>69%</td>
<td>86%</td>
<td>75%</td>
<td>83%</td>
<td>80%</td>
</tr>
<tr>
<td>Myometrial A-P asymmetry</td>
<td>62%</td>
<td>64%</td>
<td>50%</td>
<td>74%</td>
<td>63%</td>
</tr>
<tr>
<td>Identification of endomyometrial junction</td>
<td>46%</td>
<td>82%</td>
<td>60%</td>
<td>72%</td>
<td>69%</td>
</tr>
<tr>
<td>Echogenic linear striations</td>
<td>31%</td>
<td>96%</td>
<td>80%</td>
<td>70%</td>
<td>71%</td>
</tr>
<tr>
<td>Myometrial cysts</td>
<td>62%</td>
<td>64%</td>
<td>67%</td>
<td>78%</td>
<td>74%</td>
</tr>
<tr>
<td>Heterogeneous myometrium</td>
<td>81%</td>
<td>61%</td>
<td>55%</td>
<td>84%</td>
<td>69%</td>
</tr>
</tbody>
</table>
AUB: Structural Abnormalities

Linear Striations
80% PPV
72% Accurate

Heterogeneous myometrium
81% PPV
69% Accurate


AUB: Structural Abnormalities

• Myometrial Cysts
  – 66.7% PPV
  – 74% Accuracy


AUB: Structural Abnormalities

Detection of Adenomyosis

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>TV U/S</td>
<td>65-89%</td>
<td>58-98%</td>
<td>50-93%</td>
<td>20-98%</td>
</tr>
<tr>
<td>MRI</td>
<td>78%</td>
<td>93%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• Transvaginal U/S and MRI have similar accuracy for the diagnosis of adenomyosis
• Limited data on the best treatment for women with adenomyosis due to:
  • Difficulty detecting adenomyosis
  • Unclear whether it is always pathologic

AUB: Structural Abnormalities

- **AUB-M - Malignancy and Hyperplasia**
  - Detected based upon results of office biopsy or curettage
  - FIGO AUB Staged only as present or absent
  - Use existing WHO and FIGO categorization
  - Up to 40% of patients with a biopsy diagnosis of complex hyperplasia with atypia will have a concomitant endometrial adenocarcinoma present

Nonstructural Abnormalities

- C – Coagulopathy
- O – Ovulatory Dysfunction
- E – Endometrial
- I – Iatrogenic
- N – Not classified.
AUB: Nonstructural Abnormalities

- **AUB-C - Coagulopathy**
  - **Prevalence**
    - 0.8 – 1.3% of the general population
    - 13% of women presenting with HMB
  - **Etiologies**
    - Von Willebrand’s disease (10%)
    - Platelet Dysfunction
    - Factor XI deficiency
    - Factor X deficiency
  - Category includes patient’s taking anti-coagulants

- **AUB-O - Ovulatory**
  - **Presentation**
    - Manifests as a combination of unpredictable timing of bleeding and variable amount of flow
    - Wide range of presentations
      - Amenorrhea
      - Extremely light and infrequent bleeding
    - Episodes of unpredictable and extreme AUB
  - **Cause**
    - Absence of predictable cyclic progesterone production from a corpus luteum

- **AUB-O – Ovulatory Dysfunction**
  - **Etiology**
    - Polycystic Ovarian Syndrome (PCOS)
    - Hypothyroidism
    - Hyperprolactinemia
    - Mental stress
    - Obesity
    - Anorexia
    - Weight loss
    - Extreme exercise
    - Adolescence
    - Menopausal transition
AUB: Nonstructural Abnormalities

• AUB-E – Endometrial
  "When AUB occurs in the context of predictable and cyclic menstrual bleeding typical of ovulatory cycles and particularly when no other definable causes are identified, the mechanism is probably a primary disorder of the endometrium."


AUB: Nonstructural Abnormalities

• AUB-E - Endometrial
  – Deficiencies of local production of vasoconstrictors
    • Endothelin-1
    • Prostaglandin E
  – Excessive production of plasminogen activator
  – Increased local production of substances that promote vasodilation
    • Prostaglandin E
    • Prostacyclin I
  – Disorders of endometrial repair (inflammation)
    • Chlamydia


AUB: Nonstructural Abnormalities

• AUB-E - Endometrial
  – Tests measuring these abnormalities are not currently available to clinicians
  – "The diagnosis of AUB-E should probably be determined by exclusion of other identifiable abnormalities in women of reproductive age who seem to have normal ovulatory function."

AUB: Nonstructural Abnormalities

- **AUB-I - Iatrogenic**
  - Breakthrough bleeding (BTB) using gonadal steroids is the major component of AUB-I.*
  - Oral contraceptives
  - Continuous or cyclic progesterone
  - IUD or implant related bleeding
- **Cigarette smoking**
  - Reduces the level of contraceptive steroids because of enhanced hepatic metabolism
- **Systemic agents that interfere with dopamine metabolism**
  - Amitriptyline
  - Serotonin uptake inhibitors

AUB: Nonstructural Abnormalities

- **AUB-N - Not Yet Classified**
  - Disorders that would be identified or defined only by biochemical or molecular biology assays
  - Arteriovenous malformations
  - Myometrial hypertrophy
  - Category for new etiologies

Classification Categorization

- Single Entity Examples
  - P0 A0 L1 (SM) M0 - C0 O0 E0 I0 N0
  - P1 A0 L0 M0 - C0 O0 E0 I0 N0
  - P0 A0 L0 M0 - C0 O0 E0 I0 N0
Classification Categorization
Multiple Entity Examples

P0 A0 L1 (SM) M1 - C0 O0 E0 I0 N0

P1 A1 L0 M0 - C0 O0 E0 I0 N0

P1 A0 L1 (O) M0 - C0 O0 E0 I0 N0

P0 A1 L1 (O) M0 - C1 O0 E0 I0 N0