MENOPAUSE MANAGEMENT 2011

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Common challenges

- Am I menopausal?
- Is my bleeding OK and what can I do about it?
- Something else was found on my sonogram.
- Can I do something about my hot flashes?
- What are Bio-Identical hormones anyway?

AM I MENOPAUSAL?

- Why does it matter?
  - Contraception
  - Bleeding
  - Intensity, longevity of menopausal symptoms

I have severe hot flashes. Am I menopausal?

1. Now 46, I've had a hysterectomy and one ovary removed
2. I'm 51, had periods in October and March and my FSH is 38
3. I'm 32, still have my uterus but my ovaries were removed for cysts
4. I'm 48 and haven't had a period since my endometrial ablation 2 years ago

AM I MENOPAUSAL?

- No ovaries
- 12 months no bleeding (appropriate age)
- Elevated FSH >20 (as a guide) if no endometrium
  - Hysterectomy
  - Endometrial ablation
  - Mirena
  - At the end of her HFI on OC

AM I MENOPAUSAL?

- Role of FSH in the ovulation cycle
  - Rises and falls between 2 and 15 in the ovulation cycle
  - Will rise higher as aging follicles are resistant (negative feedback loop)
  - Irregular perimenopausal bleeding may/may not be preceded by ovulation
  - FSH>20, LH>30 suggests few remaining receptive follicles but does not define menopause
  - Menopause defined by 12 months amenorrhea (w/o endometrial suppression by OC, DMPA, Mirena, ablation, hysterectomy)

AM I MENOPAUSAL? Nomenclature

Perimenopause/menopause transition

From a few years prior to 12 months after FMP.

Menopause

Confirmed 12 months after the FMP

Early menopause

Spontaneous or induced age 40-45

Premature menopause

Under age 40

AM I MENOPAUSAL?

Nomenclature

Abnormal uterine bleeding -- AUB

Dysfunctional Uterine Bleeding -- DUB -- Anovulatory

Post menopausal bleeding

Cyclic hormone withdrawal bleeding

AUB
Work up

- Perimenopausal DUB vs postmenopausal
- Ultrasound
- EMBx
- Hysteroscopy

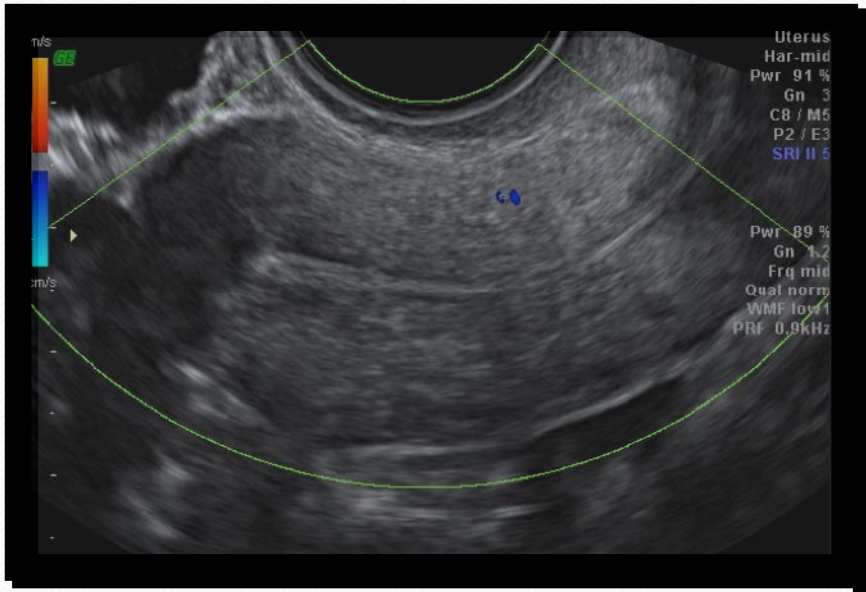
AUB
Work up- Ultrasound

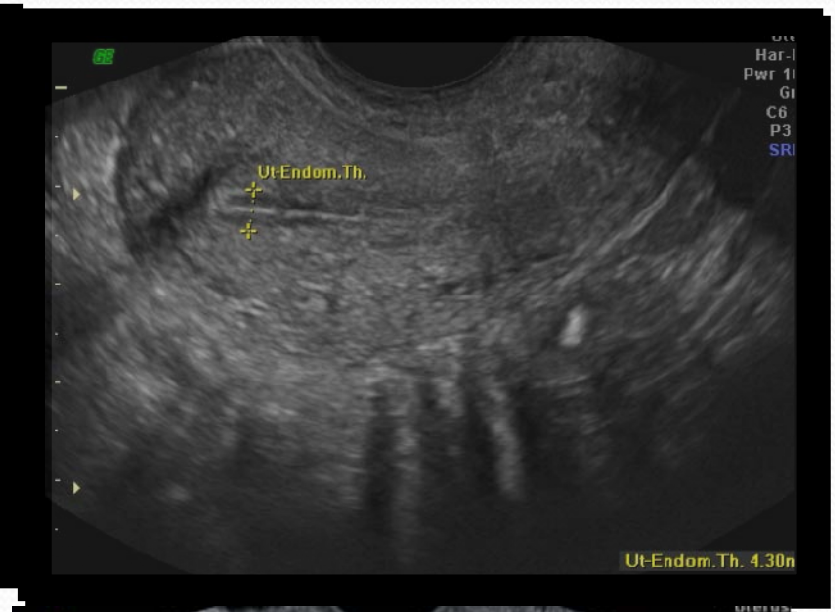
- What's the appropriate thinness for the endometrium to exclude endometrial pathology?
  - Data all based on:
    - Postmenopausal
    - Bleeding
  - Therefore may not be appropriate w/o PMB
    - Discuss "incidental findings" later

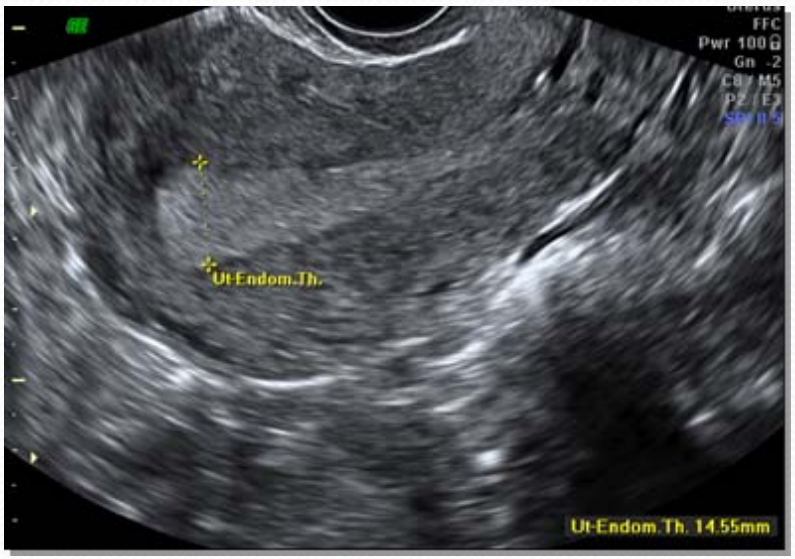
AUB
Work up- Ultrasound

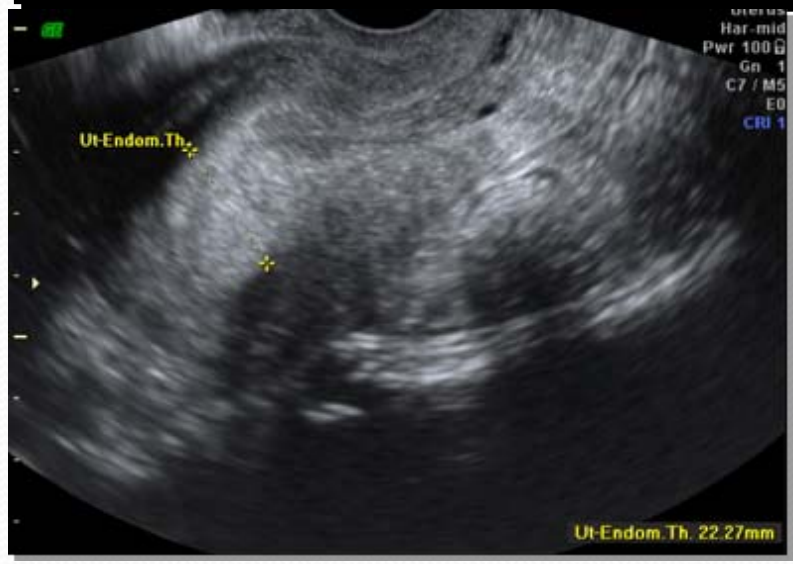
- What's the appropriate thinness for the endometrium to exclude endometrial pathology?
- <=5mm?
  - Many studies
- <=4mm?
  - ACOG Committee Opinion 8/09

Endometrium

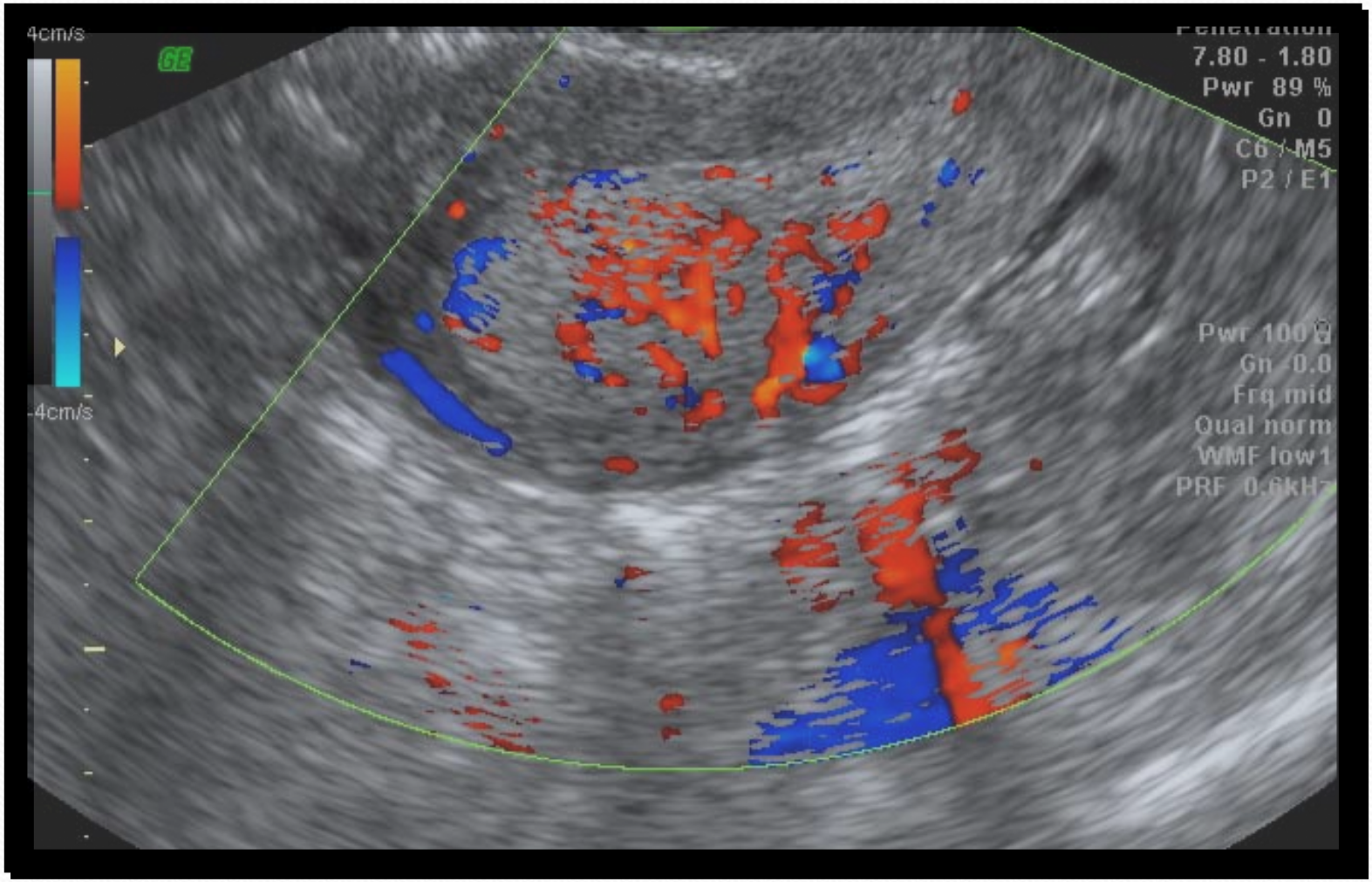




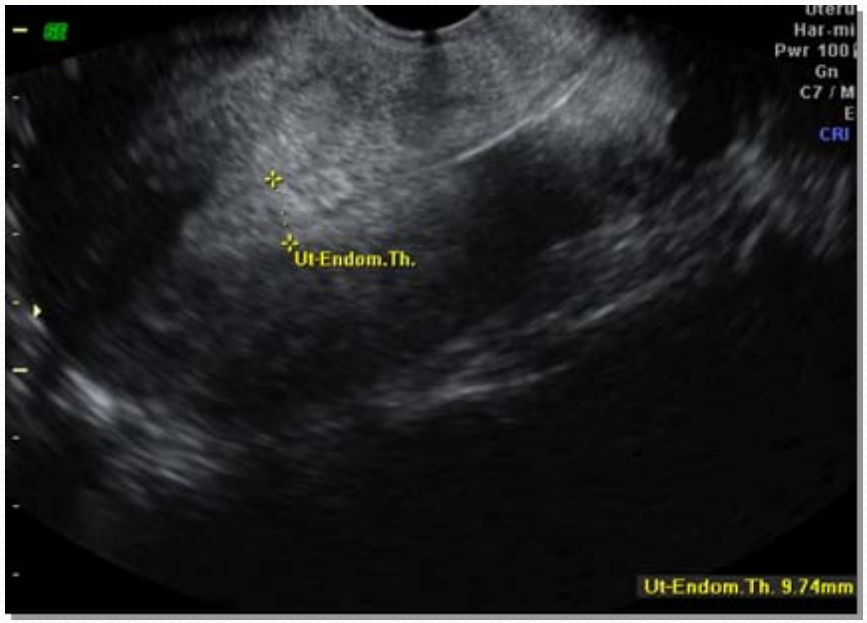


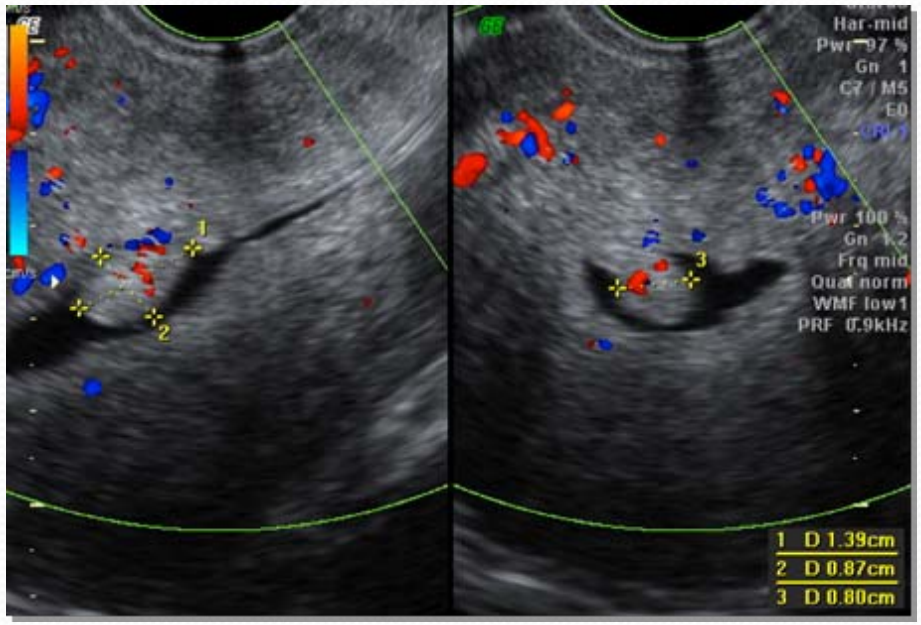


Endometrial Cancer - thickened w/ Doppler flow



Polyp (saline infusion sono)





AUB
Work up-- EMBx

- Pipelle samples only 5% of the endometrium
- Pipelle bx may be satisfactory if:
  - Endometrium is fairly thin
  - Endometrium is homogeneous by ultrasound
    - Do the sono first to avoid iatrogenic heterogeneity
- In advance of further work-up
  - Hysteroscopy if negative
  - Hysterectomy with GynOnc if positive
    - (cancel the hysteroscopy)

AUB - Perimenopausal

- Goals
  - Bleeding control
  - Contraception
  - Long or short term
  - Other issues
    - FH ovarian or breast cancer
    - Fibroid related pain
    - Urologic sxs

AUB - Perimenopausal
Treatment – short term

- Progestin withdrawal
  - MPA, Megestrol, Norethindrone
- OC withdrawal
- Mirena
- Out patient procedure
  - Hysteroscopy w/ D&C, polypectomy, myomectomy, endometrial ablation. UFE
- Inpatient surgery
  - Hysterectomy, abdominal myomectomy

AUB
Treatment – short term

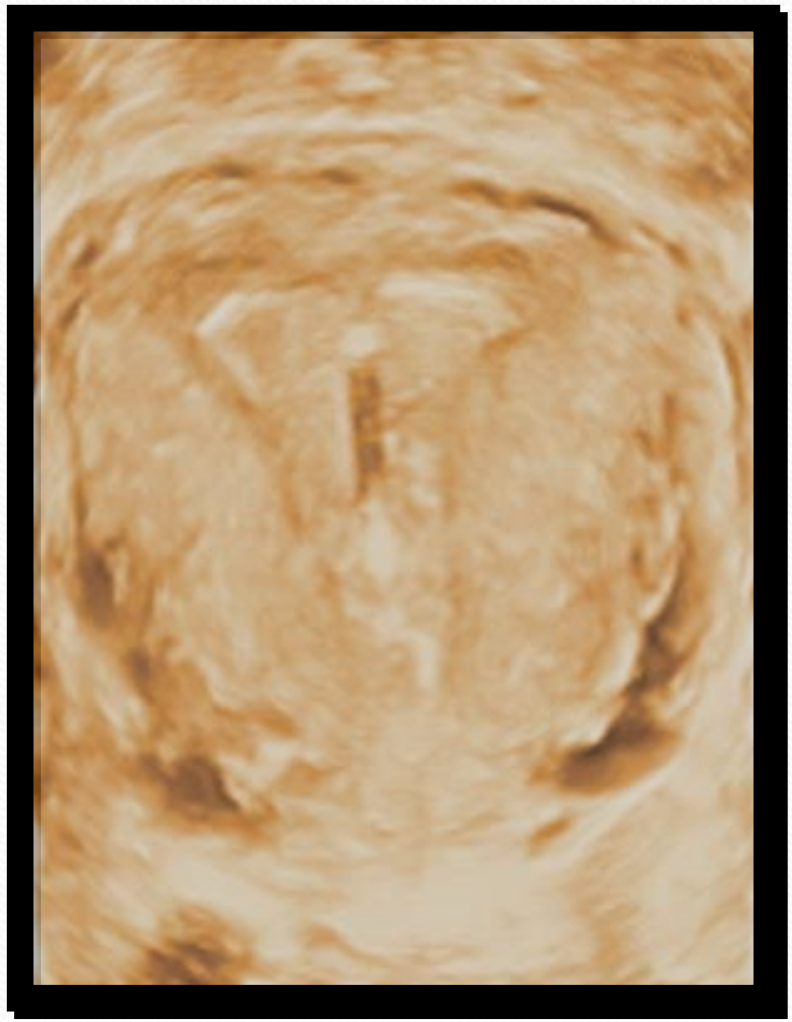
- Progestin, OC withdrawal
  - MPA 20mg or OC* tid x 7 days followed by MPA 20mg or OC daily x 21 days
  - Most stop bleeding in a few days
  - Expect withdrawal bleeding at end of therapy
- How about next month?

- *Norethindrone 1 mg and ethinyl estradiol 35 mg

AUB
Treatment – long term

- Systemic
  - OC
    - Risks: age, smoker, HTN, MI, stroke, VTE, GB, Ca
    - Benefits: BC, Menopausal sxs, PMS, Menstrual HA
  - DMPA
    - Benefits: BC, Menopausal sxs, PMS, Menstrual HA
  - Oral suppressive Progestin
- Local
  - Mirena. Contraception and cycle control only
  - Surgeries already discussed
    - ablation not contraceptive

Mirena



AUB
Treatment – long term

- Medical Eligibility Criteria
  - www.who.int/reproductivehealth
- **1. A condition for which there is no restriction for the use of the contraceptive method.**
- **2. A condition where the advantages of using the method generally outweigh the theoretical or proven risks.**
- **3. A condition where the theoretical or proven risks usually outweigh the advantages of using the method.**
- **4. A condition which represents an unacceptable health risk if the contraceptive method is used.**

Incidental Imaging Findings

- “Thick endometrial echo”
  - Endometrial thickness algorithm is based on PMB
  - If she’s not PM or bleeding, the findings are incidental and may or may not be meaningful
- Fibroids
- “Ovarian cyst”

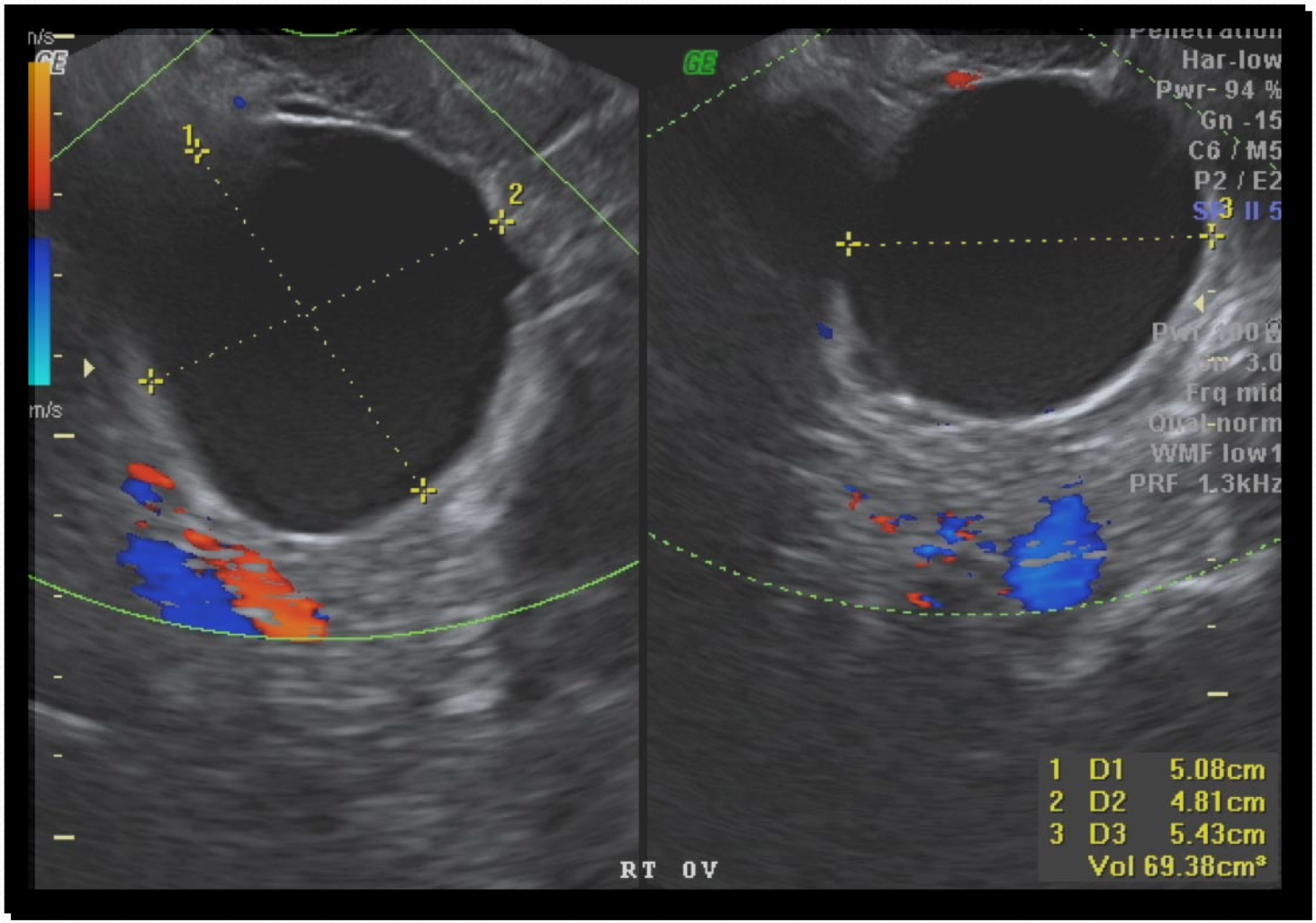
Incidental Imaging Findings Endometrial echo

- Not meaningful
  - Internal fluid with thin walls (<2mm apiece)
- Meaningful
  - Internal fluid with thick endometrium
    - May represent internal bleeding w/ cervical stenosis
- Questionably meaningful
  - Heterogeneous
  - Polyp
  - “thick”

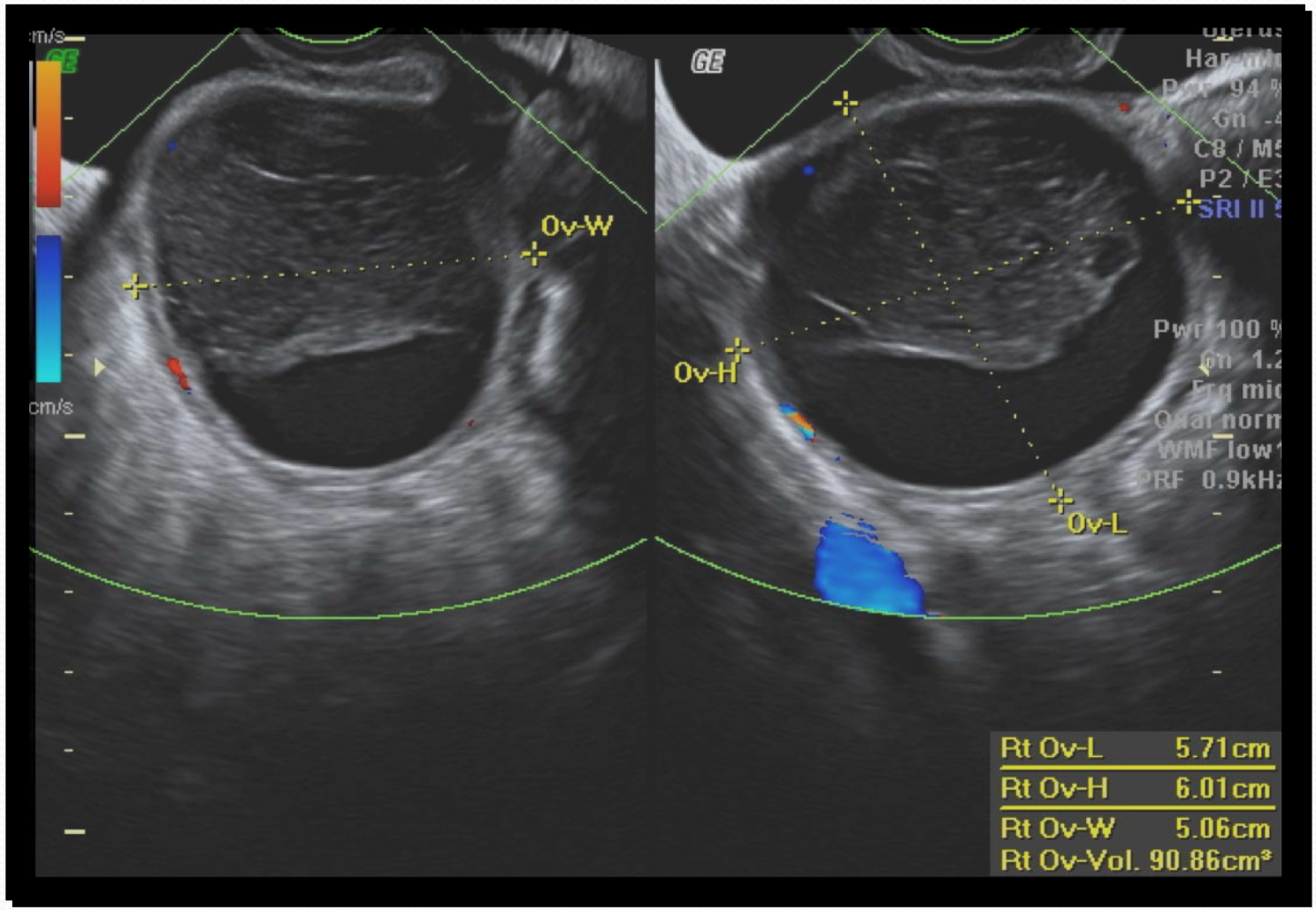
Incidental Imaging Findings

- Ovarian cysts
  - Follicles and corpora lutea are the normal ovarian functional process
  - “Simple” cysts have almost no cancer potential
    - <10cm, thin border, unilocular, anechoic
    - CA125
    - repeat sono 2 months for stability
  - Every thing else is “complex” and deserves referral

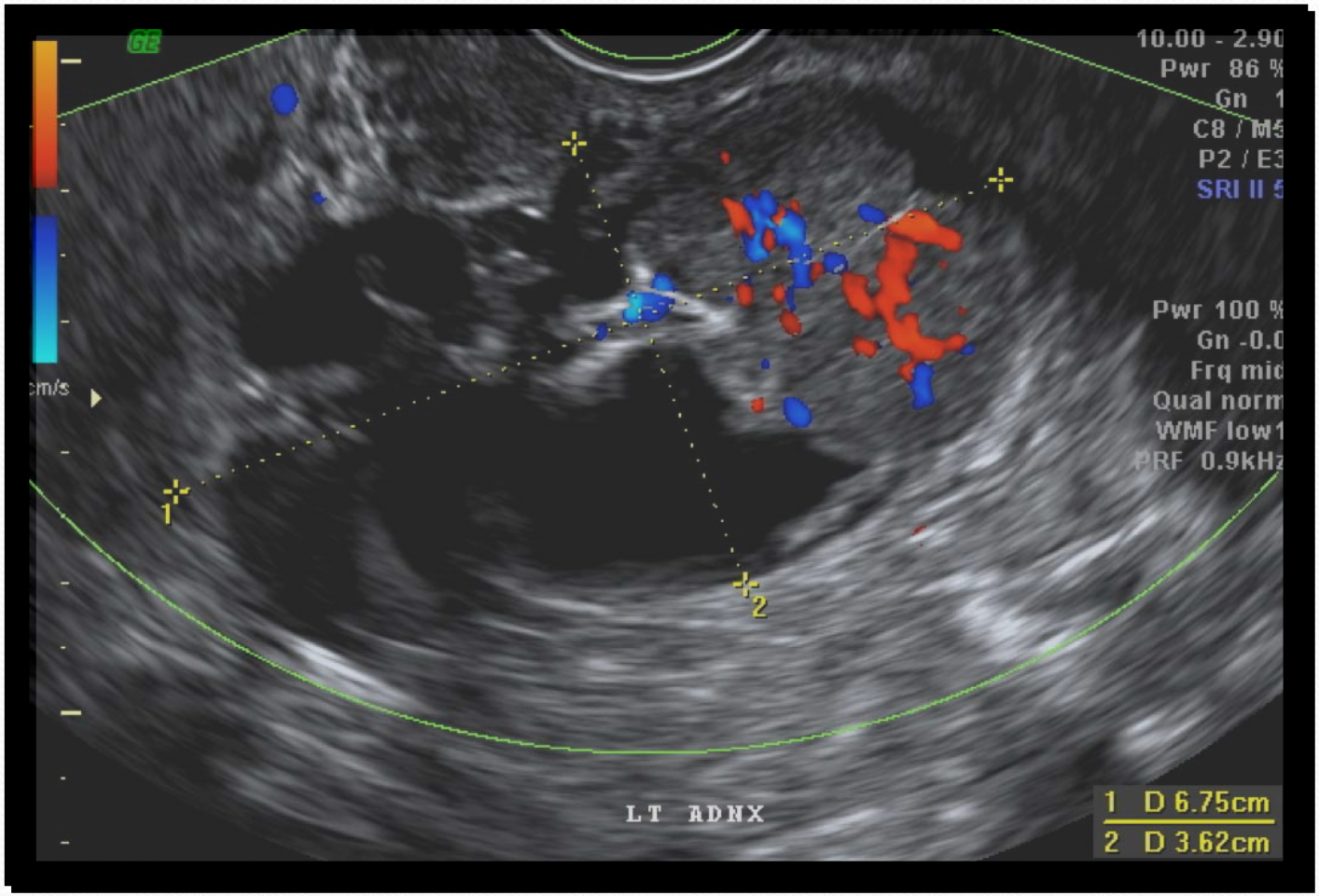
Ovarian cyst - simple



Ovarian cyst – Complex hemorrhagic with retracting clot



Ovarian Cancer



Hormone therapy Nomenclature

- Gone is “HRT” ☹
- HT, ET, EPT, Vaginal ET, Systemic HT, Progestin
  - Say what you mean
    - Combined, daily E+P
    - Cyclic E+P
    - Estrogen therapy (no uterus)
    - Unopposed estrogen therapy (with uterus)

How many postmenopausal women are using HT?

1. >50%
2. 25-50%
3. 15-25%
4. <15%
5. "No one in MY practice"

Barbaglia G, et al. Trends in hormone therapy use before and after publication of the WHI: 10 years of follow-up. Menopause 2009;16:1061-4

Shetty KD, Vogt WB, Bhattacharya J. Hormone replacement therapy and cardiovascular health in the US. Med Care 2009;47:600-6

HT

#1. Are they hormone related sxs?

- Vasomotor sxs, urogenital atrophy, sleep, libido
- Beware of the 60+ yo w/ new sxs
  - Rheumatoid issues, Carcinoid

#2. Is she a candidate for HT?

- Hx Ca, VTE, stroke, MI

#3. Does she need contraception or bleeding control?

#4. What hormone, dose, vehicle?

Combined HT single vehicle

- Oral
  - CEE+MPA
  - E2+Norethindrone acetate, drosperinone
    - 17b E2 plus synthetic progestin
  - NEA + EE 1mg/5mcg, 0.5mg/2.5mcg
    - EE 10mcg + NE 1mg now available as OC
- Transdermal
  - E2 + Norethindrone acetate or levonorgestrel
- BIH compounded

Combined HT multi-vehicle

Any combination of oral, transdermal, vaginal

- Estrogen
  - 17b estradiol, CEE, synthetic estrogens, estrone

+PLUS!!!!!

- Progestin
  - OMP 100mg, MPA 2.5mg, Mirena
    - Aygestin is 5mg NE (Activella uses 0.5mg paired with 1mg E2 and 0.1mg paired w/ 0.5mg E2)
    - Minipill is 0.35mg NE

Combined HT multi-vehicle

- Advantage:
  - mix and match different types, vehicles, doses
- Disadvantage:
  - Cost, confusion, selective use

HT

- For symptom control or osteoporosis
- Lowest dose estrogen, shortest time, corresponding progestin to prevent endometrial hyperplasia
- Timing of initiation
- Continue long term?

HT

- OMP side effect is sleepiness
- Transdermals don't increase VTE risk
- Local (vaginal) therapy for local problem
- None of the major medical societies suggests a difference between the synthetic and bio identical hormones

Bio Identical Hormones

- Which hormones are “Bio Identical”
  - 1. Generic oral estradiol (Brand name Estrace)
  - 2. Oral Micronized Progesterone (“Prometrium”)
  - 3. Brand /generic transdermal or vaginal estrogens
  - 4. Hormones from a Compounding Pharmacy
  - 5. All of the above

“Bio Identical Hormones”

- Same as those produced in humans
- If your patient is on Estrace, any transdermal or ring and Prometrium
  - She’s already on BIH thru her local pharmacy and prescription plan. There is no difference between the FDA approved bio identical hormones and those from a compounding pharmacy
- Advantage of a Compounding Pharmacy:
  - Manipulate the dose outside what’s available otherwise
  - Personalize the vehicle
  - Add testosterone (not FDA approved)
- SAME INDICATIONS, CONTRAINDICATIONS!

“Bio Identical Hormones”

- Compounding Pharmacy disadvantages:
  - Not FDA regulated
  - Not standardized FOR you
    - Easy to underdose the progesterone as the estrogen is manipulated for symptom control
    - Hormone levels are of minimal value w/ standard doses
  - Cost
  - Absorption swings may precipitate the very sxs you are trying to treat
  - Absorption may not be effective (transdermal P)

HT

- The perfect SERM?

Review

- Menopause defined as 12 months of amenorrhea
- AUB work up includes ultrasound and EMBx
- AUB treatment includes both short and long term goals
- Incidental findings on sonogram may not be meaningful
- Hormone therapy endless variety needs personalization
- Bio-identical hormones are available through regular and compounding pharmacies

Glossary
Estrogens

- CEE: (conjugated equine estrogens) Premarin
- CEE/MPA: Prempro (continuous), Premphase (sequential)
- Estradiol, 17b: “E2”. Estrace, generic oral estradiol, all patches, creams, sprays, Femring, Vagifem, Estrace cream, BIH. 1 mg equiv to 0.05mg patch, 5mcg EE, Premarin 0.625mg. Now in an OC.
- Estrogens, synthetic: Cenestin (conjugated, A), Menest (esterified), Enjuvia (conjugated B)
- Ethinyl estradiol: “EE”. In FemHRT (2.5, 5mg), OCs (10,20,25,30,35,50mg) and Nuvaring 15mg

Glossary
Progestins

- Drosperinone: 4th gen OC progestin (Yasmin, Yaz 3mg) and in Angeliq 0.5mg
- Levonorgestrel: 2nd gen OC progestin using 1mg w/ 20mcg EE. Used in ClimaraPro w/ E2
- Medroxyprogesterone acetate: MPA, Provera, Depoprovera
- Megestrol: Megace
- Mirena: levonorgestrel containing IUD
- Norethindrone/Norethindrone acetate: "NE/NEA". 1st generation progestin for OCs using 1, 0.5, 0.4mg. Aygestin is 5mg, minipills are 0.35mg. Activella contains 0.5 (w/ 1mg E2) or 0.1mg (w/ 0.5mg E2). Combipatch w/ E2.
- Progesterone: Prometrium (oral micronized progesterone), BIH
- Progestin: all synthetic progesterones

Useful References

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- Munro, MG, et al, Oral Medroxyprogesterone Acetate and Combination Oral Contraceptives for Acute Uterine Bleeding; A Randomized Controlled Trial. Obstet Gyn 2006;108:924-9
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