HOT TOPICS IN OBGYN 2018
WHAT’S NEW?

▸ Contraception: Long Acting reversible contraception
▸ Contraception: Birth control pills
▸ Vaginal dryness: Treatments
▸ Breast density: Diagnosis and plans
CONTRACEPTION

- Long active reversible contraceptives (LARCs) are the focus of new contraceptive options
- New information on the “oldest” method, the birth control pill
- Medical conditions and birth control: migraines, moods and epilepsy
“Most accidents are caused by humans and most humans are caused by accidents”

Professor John Guillebaud, Emeritus Professor of Family Planning at University College London
WHY SHOULD OUR PATIENTS USE BIRTH CONTROL?

COMPARATIVE RISK OF VENOUS THROMBOEMBOLISM:

<table>
<thead>
<tr>
<th></th>
<th>Pregnancy</th>
<th>High dose OC</th>
<th>Low Dose OC</th>
<th>General Population</th>
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</thead>
<tbody>
<tr>
<td>VTE per 100,000 Woman-</td>
<td>60</td>
<td>40</td>
<td>20</td>
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<td>Years</td>
<td>0</td>
<td>20</td>
<td>10</td>
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Schulman, LP J Reprod Med 2003
LARC METHODS

CONTRACEPTIVE IMPLANT

Progestin-only (etonogestrel) subdermal implant (Nexplanon or Implanon)- approved for 3 years

Method of action:
- inhibits pituitary gonadotropin release, inhibiting ovulation
- thickens cervical mucous, thins Endometrial lining

UNINTENDED PREGNANCY: perfect use: .05%
typical use: .05%
SUBDERMAL IMPLANT—NEXPLANON

Side effects: Irregular spotting or bleeding

Acne

Mood changes

Weight gain

Bloating

Effectiveness of the etonogestrel implant in women who weigh more than 130% of their ideal body weight has not been defined because these women were NOT studied in clinical trials.
Intrauterine devices are underutilized in the United States.

Not enough trained professionals willing to insert devices

Negative publicity and misconceptions

Fear of litigation, cost, lack of awareness
**IUD’S/ IUC’S**

Intrauterine contraceptive devices:

- Do **NOT** cause abortions
- Do **NOT** cause ectopic pregnancies
- Do **NOT** cause pelvic infections
- Do not decrease the likelihood of a future pregnancy
- Can be used by nulliparous women
- Do **NOT** need to be removed to treat PID
- Need **NOT** be removed if actinomyces-like organisms are noted on a Pap
IUD'S /IUC'S:

Copper T IUD: Brand name: PARAGARD

- Copper ions
- Approved for 10 years
- Can be used as emergency contraception

Mechanism of action: PREVENTS FERTILIZATION

- reduces motility and viability of sperm
- inhibits development of ova
- inhibition of implantation is secondary

ACOG statement on Contraceptive Methods, 1998
IUD’S/ IUC’S:

LEVONORGESTREL INTRAUTERINE SYSTEM

BRAND NAMES: Mirena, Skyla, Kyleena, Lilleta

DAILY PROGESTERONE RELEASE: 20mcg, 14mcg, 17.5mcg, 20 mcg

APPROVED FOR: 5 yrs, 3 yrs, 5 yrs, 3 yrs
(much data on longer-lasting effects)

Amenorrhea or shorter lighter periods for all

Great choice for taking your patient through the perimenopausal transition and into menopause
LARC METHODS

IUD’S/IUC’S:

AUB: Abnormal uterine bleeding, not related to anatomic problems

GOALS: stop the bleeding, avoid future irregular bleeding
Provide contraception if needed

Levonorgestrel: second generation Progestin (mildly Androgenic)

IUD: Has a Progesterone (Steroid) reservoir in the device and MIRENA excretes 20 mcg/day

Thickens cervical mucous, suppresses the endometrium, &

Lethabay et al, Cochran database Syst Rev 2015 April
WHAT'S NEW IN BIRTH CONTROL PILLS?

VARIOUS REGIMENS:

**High Dose** (50 mcg EE)

**Medium Dose** (30-35mcg EE)

**Low Dose** (20 mcg EE)

**Lowest Dose** (10 mcg EE)

**21/7 Regimen/ 24/4 Regimen/TriCyclic**

**Continuous Dosing** (no inactive)
COMBINED ORAL CONTRACEPTIVES:

- Work for heavy and irregular bleeding
- Improve quality of life
- 24/4 Regimen extends the active pills, and decreases the number of non-hormonal pills, reducing the possibility of follicular recruitment; fewer pregnancies

Most likely missed pill is the first in the new pack
EPILEPSY/MIGRAINES/MOOD CHANGES

- Oral contraceptives increase the Clearance of Lamictal.
- Anti-epileptic medication can decrease the effectiveness of oral contraceptives by 60%.
- For the OC to still be effective, it has to have at least as much Progesterone as what is in the mini-pill (Progesterone-only birth control pill) which is 35mcg daily.
- Can calculate whether their OC is still effective.
MIGRAINES

- Almost 50% of women experience migraines at some point in their lives
- 30% have migraine with aura
- 30% of reproductive age women are on a combined hormonal contraceptive
- Women who have migraine with aura and use combined hormonal contraception are 6 times more likely to have an ischemic stroke
- Determining the type of migraine is critical when assessing the safety of combined hormonal contraceptives

Champaloux et al, Use of Combined Hormonal Contraceptives Among Women With Migraines and risk Of Ischemic Stroke /Am J Obstetrics & Gyn doi:10.1016
ORAL CONTRACEPTIVES

MOODS

- Nationwide, prospective cohort study
- More than one million women in Denmark
- Age 15-34, from 2000 to 2013
- Compared with non-users, users of combined oral contraceptives had a relative risk of first anti-depressant use of 1.23 (95% confidence interval 1.22-1.25)
- CONCLUSION: use of hormonal contraception was associated with subsequent use of anti-depressants

ORAL CONTRACEPTION IN THE NEWS:

- A word on the recent study that was published: Dec 2017
- New England Journal of Medicine
- Slightly elevated breast cancer risk among hormonal contraceptive users
- 1.9 million Danish women over 10 years
- Using hormonal birth control for more than a year may lead to an additional 13 breast cancers among 100,000 women, or one extra case for every 7,690 women
ORAL CONTRACEPTION IN THE NEWS:

- Compare this with the risk of drinking alcohol on breast cancer risk:

- Drinking 3-6 drinks a week is associated with 22 extra cases of breast cancer per 100,000 women

- Compare this with the risk of overweight/obesity:

- Women who gained 20-30 pounds after age 18 are 40% more likely to develop breast cancer after menopause than women who had only gained 5 pounds
GENITO-URINARY SYNDROME OF MENOPAUSE

- **Old terminology:** VAGINAL ATROPHY
- **New terminology:** Genitourinary syndrome of Menopause (GSM)
- Dryness, itching, burning, painful intercourse, loss of elasticity, bladder irritability, leakage
- Symptom of menopause that does not improve with time
GENITO-URINARY SYNDROME OF MENOPAUSE

- **TEMPORARY solutions.** (lubricants)
- Longer term local non-hormonal solutions (moisturizers)
- **Local hormonal solutions** (Estrogen, DHEA)
- Oral medication (hormonal or non-hormonal)
- Procedural solutions (laser)
GENITO-URINARY SYNDROME OF MENOPAUSE:

- LUBRICANTS:
  - Temporary
  - Water, oil or silicone

- MOISTURIZERS:
  - Last for 3 days
  - Replens, RePhresh, Luvena, KY Liquibeads: correct the vaginal pH
GENITO-URINARY SYNDROME OF MENOPAUSE

- Treatment should address:
  - Superficial cells—should increase
  - Parabasal cells—should decrease
  - Vaginal pH—should decrease
  - MBS—“most bothersome symptom”; on a scale of 0-3—should go down
GENITOURINARY SYNDROME OF MENOPAUSE:

- Local hormonal solutions:
  - ESTROGEN- local low dose solution for local symptoms
  - Cream, pill, ring
  - Brand names: Estrace or Premarin cream (.5gm 2 x per week vaginally- can also use on the external tissue) Vagifem or Yuvafem (10 mcg 2 x per week vaginally- melts at body temp) E-string- vaginal ring that gets replaced Q 90 days (reservoir of 2mg Estradiol, releases 7.5mcg over 24 hours)
Recent 12-week randomized multi center clinical trial

Patients with moderate to severe vulvovaginal symptoms

Received either 10 mcg Estradiol vaginal tablet + placebo gel, Placebo tablet plus vaginal moisturizer or dual placebos

Primary outcome = decrease in MBS

Secondary outcomes = Vaginal maturation index, vaginal pH and scores on a Female Sexual Function scoring tool

JAMA Int Med, 2018
GENITO-URINARY SYNDROME OF MENOPAUSE:

RESULTS:

- Data collected from 302 women
- Most commonly reported MBS=60% Pain w/penetration
- ALL treatment groups had similar reductions in MBS, with no significant differences among the groups
- Neither prescribed vaginal Estradiol tablet nor OTC moisturizer reduced symptoms compared to placebo
GENITO-URINARY SYNDROME OF MENOPAUSE

► CONCLUSIONS: *abandon local estrogen? NO*

► The use of OTC lubricants and moisturizers represents appropriate first line therapy for women with symptomatic GSM. *(NAMS)*

► Numerous longer-term (>12 months) studies have consistently demonstrated vaginal estrogen’s superiority to placebo at managing symptoms of GSM, as well as its safety.

Lethaby et al.: Local Estrogen for Vaginal Atrophy in Postmenopausal Women /Cochrane database 2016
GENITO-URINARY SYNDROME OF MENOPAUSE:

- RECENTLY FDA APPROVED
- Vaginal DHEA—brand name Intrarosa
- Suppository for Daily use
- Inserted QHS vaginally
- Melts within 45 minutes at body temp
- Metabolized to small local amounts of Estrogen and Testosterone w/out raising systemic levels
GENITO-URINARY SYNDROME OF MENOPAUSE:

- INTRAROSA (Prasterone)
- Evaluated in 2 12-week randomized placebo controlled studies where painful intercourse was their MBS
- Both studies showed a significant reduction in scores on MBS, as well as an increase in superficial cells, decrease in parabasal cells, and a decrease in the vaginal pH
- No increase in systemic levels of Estrogen or Testosterone

JAMA. 2017;318(16):1607-1608
GENITO-URINARY SYNDROME OF MENOPAUSE:

▶ ORAL MEDICATIONS:

▶ Oral HRT (Estrogen, or Estrogen + Progesterone): Has a beneficial effect on symptoms of vaginal and vulvar dryness and pain, but if the symptoms are only vaginal, should not use systemic HRT

▶ Oral SERM: Selective Estrogen Receptor Modulator- Ospemifene. (Brand name=OSPHENA)
GENITO-URINARY SYNDROME OF MENOPAUSE:

› OSPHENA

› Oral, daily SERM, 60 mg daily

› Taken with food for better bioavailability

› May take up to 12 weeks to see the effects

› Has been shown to increase superficial cells, decrease parabasal cells and decrease vaginal pH in pivotal double blind randomized placebo controlled trials

› Works at the Estrogen receptor in the vaginal mucosa

Archer DF, Carr BR, Pinkerton JV et al, Effects of Ospemifene on female Reproductive Tract Menopause 2015:22(7)1-11
**GENITO-URINARY SYNDROME OF MENOPAUSE:**

- OSPHENA
- *Not* tested in breast cancer patients
- *Not* to be used with irregular or undiagnosed bleeding
- Indicated for menopausal women who may *not* want to use vaginal products
- *Agonist at the vaginal receptors,* antagonist —??
GENITO-URINARY SYNDROME OF MENOPAUSE:

- PROCEDURES:
  - Fractionated CO2 laser
  - RAF- Radiofrequency
  - Surgical procedures- vaginoplasty/labiaplasty
GENITO-URINARY SYNDROME OF MENOPAUSE

- Fractionated CO2 laser- brand name: MonaLisa Touch

- 6-7 years of experience in Europe

- 4 years in the US

- Studies have shown increase in superficial cells, decrease in pH; increase in collagen and fibroblasts in the vaginal mucosa, decrease in discomfort

- Office procedure, 3 treatments, 6 weeks apart

*Int J Womens Dermatolv 2(3); 2016 Sep* PMC5418869
Currently, 34 states require some type of notification after a mammogram where dense breasts are diagnosed.

There are different categories of breast density seen on a mammogram:

- a: Almost entirely fatty
- b: Scattered areas of fibroglandular densities
- c: Heterogeneously dense
- d: Extremely dense

**BREAST DENSITY CAN OBSCURE CANCERS.** Breast density increases the likelihood that cancer will be...
BREAST DENSITY IS AN INDEPENDENT RISK FACTOR FOR THE DEVELOPMENT OF BREAST CANCER.

Women with the densest breasts (heterogeneously dense or extremely dense) are 4 to 6-fold more likely to develop breast cancer than women with the least dense breasts.

Need to identify the patients at highest risk and in need of additional screening.

Should have a screening system in place so that the right patients get the right screening.
3D MAMMOGRAPHY (TOMOSYNTHESIS):

Digital breast tomosynthesis (tomo), also known as 3D mammography is a revolutionary new screening and diagnostic breast imaging tool to improve the early detection of breast cancer.

During the 3D part of the exam, an x-ray arm sweeps over the breast, taking multiple images in seconds.

3D mammography uses the same amount of radiation as a regular 2D mammogram. They may avoid multiple call-backs for more images as they can see smaller areas of tissue.
SCREENING MODELS:

- Identify all patients who are eligible for genetic testing by family history. First degree relative with breast cancer before 50, any relative with ovarian cancer, or multiple family members with cancer; any male relative with breast cancer; also family ancestry Ashkenazi Jewish, (1:40 +BRCA) or a relative with a known genetic mutation.

- Guidelines may be more lax depending on insurance and other risk factors.

- Multiple, young, rare
BREAST DENSITY:

[www.densebreastinfo.org](http://www.densebreastinfo.org) has a breast cancer risk assessment that you can download, and print for patients to fill out.

Including: Do you drink >5 oz alcohol daily?, were you over 30 when you had your first pregnancy? Has your weight increased since menopause, making you overweight or obese?

Risk models: Are used to identify patients who need additional screening, patients that would benefit from risk-reducing medications, and to identify women who meet criteria for high risk screening MRI.
Breast Health

Breast Density: Flow Chart—Who Needs More Screening?

- >10 year life expectancy? NO → Breast imaging Only with abnl finding
  - YES

- Under age 75? NO → Annual mammo With 3D Tomo If available
  - YES

- High risk for Breast cancer?* NO → Over 40? NO → Screening mammo at 40 With 3D Tomo
  - YES

* by risk assessment model

YES → Screening mammo With 3D Tomo

YES

NO

YES

NO

NO
Identified a woman at high risk* for breast cancer via a risk assessment model or positive genetic screen

Recommend annual MRI at age 25-30 and annual Mammogram at age 30. If impossible, mammogram+US.

Woman not at higher risk but with dense breasts

Recommend annual mammogram with 3D tomo, and add breast ultrasound if pt accepts potential false positives.
RISK MODELS:

▸ GAIL MODEL: women at increased risk for breast cancer defined as: at least a 1.7% five-year risk for developing breast cancer

▸ TYRER-CUZICK MODEL: women at increased risk defined as >20% lifetime risk for developing breast cancer

▸ Any woman with a first degree relative who is a mutation carrier but who is untested
RISK ASSESSMENT:

- PATIENT RISK CHECKLIST: fill out the form
- History/physical
- Assessment of and discussion about modifiable risk factors
- Genetic testing for *all* who meet criteria
- 3D Mammogram as a screening with appropriate risk model analysis for heterogeneously/extremely dense
- High risk -> appropriate additional screening and f/u
GAIL MODEL: Risk-assessment model that can help determine the absolute 5 year and lifetime risk of breast cancer, DCIS or LCIS

- Includes age, first menstrual period, first live birth, and relatives with breast cancer, ethnicity

- Calculated risk >1.7% are candidates for chemoprevention or referral to a breast surgeon
BREAST CANCER PREVENTION:

- TYRER-CUZICK MODEL:
  - Includes age, height, weight, menarche, breast density, family history, and biopsy history
  - High-risk = >20% lifetime risk of breast cancer
  - As per NCCCN guidelines, entitled to annual breast MRI
  - Additional surveillance: 3D mammogram, Ultrasound, clinical breast exam
BREAST CANCER:

- FOCUS SHOULD BE ON PREVENTION
- Modifiable risk factors
- Family cancer history
- Appropriate screening & management
THANK YOU

Dr Rebecca Levy-Gantt
Premier ObGyn Napa Inc