Disclosure

I have no financial disclosures to report
Contraception: The real scoop

• Number of reproductive aged women in the US
  – 75,000,000

• Number of whom are sexually active
  – 50,000,000

• If a woman is sexually active from age 18-49 and wants 2 children, the number of lifetime monthly ovulations she must prevent is
  – 360 monthly ovulations

• If all 50 million women perfectly used OCPs
  – 150,000 women would become pregnant each year
Half of All Pregnancies in the US Each Year Are Unintended

Pregnancies (6.3 million)

Intended Pregnancies

Unintended Pregnancies

More than 1/3 of all U.S. women will have had an induced abortion by age 45.*

The Alan Guttmacher Institute: *Fulfilling the Promise*, 2006.
WHO / CDC list of conditions associated with increased risk for adverse health events as a result of unintended pregnancy

- IDDM with nephro/retino/neuropathy or other vascular disease; or >20 yr
- Hypertension (SBP >160 or DBP >100)
- Complicated valvular heart disease
- Ischemic heart disease
- Peripartum cardiomyopathy
- Stroke
- Systemic lupus erythematosus
- Thrombogenic mutations
- Epilepsy
- Bariatric surgery within the past 2 years
- Breast cancer
- Endometrial or ovarian cancer
- Malignant gestational trophoblastic disease
- Malignant liver tumors
- Severe (decompensated) cirrhosis
- Sickle cell disease
- Solid organ transplantation within the past 2 years
- HIV/AIDS
- Tuberculosis
Contraception in Women with Chronic Disease

• Impact of unintended pregnancy
• Effectiveness of contraceptive method
• Impact of contraceptive method on disease
• Impact of disease or medications/treatments on effectiveness of method
Outline

• Overview of current contraceptive methods

• Overview of WHO & CDC guidelines
  – Medical Eligibility Criteria

• Contraception for women with
  – Epilepsy
  – MS
  – Migraine headaches
<table>
<thead>
<tr>
<th>Method</th>
<th>Typical use</th>
<th>Perfect use</th>
<th>Discontinuation</th>
</tr>
</thead>
<tbody>
<tr>
<td>No method</td>
<td>85</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Diaphragm</td>
<td>16</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td>Condom (male)</td>
<td>15</td>
<td>2</td>
<td>57</td>
</tr>
<tr>
<td>OCP, patch, ring</td>
<td>8</td>
<td>0.3</td>
<td>33</td>
</tr>
<tr>
<td>DMPA (Depo)</td>
<td>3</td>
<td>0.3</td>
<td>44</td>
</tr>
<tr>
<td>IUD: Copper T</td>
<td>0.8</td>
<td>0.6</td>
<td>22</td>
</tr>
<tr>
<td>IUD: LNG-IUS</td>
<td>0.1</td>
<td>0.1</td>
<td>20</td>
</tr>
<tr>
<td>Subdermal implant</td>
<td>0.05</td>
<td>0.05</td>
<td>16</td>
</tr>
<tr>
<td>Female sterilization</td>
<td>0.5</td>
<td>0.5</td>
<td>0</td>
</tr>
<tr>
<td>Male sterilization</td>
<td>0.15</td>
<td>0.10</td>
<td>0</td>
</tr>
</tbody>
</table>

Contraceptive Use in the U.S.

- 36% of all U.S. women will have had an induced abortion by age 45
- 20% of women selecting sterilization at age 30 or younger later express regret

Mosher, Vital and Health Statistics 2010
3.1 million unintended pregnancies, by women's contraceptive use during month of conception

Consistent use, method failed, 5%

Inconsistent or incorrect use, 43%

Nonuse, 52%

Guttmacher Institute: Improving Contraceptive Use in the U.S., 2009
Thirty-eight percent of women use the pill inconsistently

% of pill users according to use during the past 3 months

- 62% None missed
- 19% 1 missed
- 11% 2 missed
- 8% 3+ missed

Guttmacher Institute: *Improving Contraceptive Use in the U.S.*, 2009
The Case for Long-Acting Reversible Contraception (LARC)

- Highly effective
- Safe, particularly in women with chronic disease
- Long-term protection
- Single motivational act for insertion
- Not related to coitus
- Immediately effective
- Rapid return to fertility upon removal
- Highest satisfaction among methods
Intrauterine Contraceptive Devices
Available in the United States

CuT380A (Paragard®)
Local copper ions
10 yrs of use

LNG IUS (Mirena®)
20 mcg levonorgestrel /day
5 yrs of use

Liletta™
(levonorgestrel-releasing intrauterine system) 52 mg
Currently approved for 3 years
Generic pricing

Smaller frame
14 mcg levonorgestrel /day
3 yrs of use
Implantable Contraceptive Devices
Available in the United States

- Etonogestrel Implant (Nexplanon™)
  - Approved for 3 years use
  - 60 mcg etonogestrel / day initially
  - 30 mcg etonogestrel / day by end of year 3
Levonorgestrel Plasma Concentrations When Using Different Hormonal Methods

Contraceptive Eligibility

Which patients are eligible for which methods?
CDC adaptation of WHO guidelines
CDC

Medical Eligibility Criteria 2010

• Recommendation Grading System
  – Category 1: No restrictions
  – Category 2: Generally use (Benefits usually outweigh risks)
  – Category 3: Not recommended, unless other methods not available or appropriate. (Risks usually outweigh benefits use requires careful clinical judgment and access to clinical services)
  – Category 4: Absolute contraindication
### CDC adaptation of WHO guidelines

**Key:**
1. No restriction (method can be used)
2. Advantages generally outweigh theoretical or proven risks
3. Theoretical or proven risks usually outweigh the advantages
4. Unacceptable health risk (method not to be used)

---

**Summary Chart of U.S. Medical Eligibility Criteria for Contraceptive Use, 2019**

The summary chart only contains selected user recommendations from the U.S.MEC. For complete guidelines, see www.cdc.gov/reproductivehealth.
Contraception for Women with Migraine Headaches
Headache in Women

- The one year prevalence of migraine by age and gender
- Almost 25% of reproductive age women have regular migraines
- Peak prevalence is in women of childbearing years

Two Practical Questions

• Is combined hormonal contraception (CHC) or HRT safe for women with migraine?
  – Major concern is stroke

• Do CHC or HRT affect the clinical course of migraine?
  – Altered frequency or severity of headache
  – Altered frequency or severity of non-headache symptoms of migraine
Risk of stroke in women

Incidence of stroke per 100,000 woman-years

- General population: 7.5
- Women with all migraine types: 18
- 20 year olds: 2
- 40 year olds: 70

Beck, *Neurology*
Oral contraceptives: risks

- General
  - OC use associated with increased risk of ischemic stroke and other thromboembolic events
  - Risk lessened by use of OCs with < 50 mcg estrogen

MacGregor, J Fam Plann Reprod Health Care. 2007
# Migraines and Combined Hormonal Contraception

<table>
<thead>
<tr>
<th>Category</th>
<th>Migraine-specific recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non-migrainous headache</td>
</tr>
</tbody>
</table>
| 2        | Migraine w/out aura, age <35 y, nonsmoker  
Non-migrainous HA develops after initiating CC |
| 3        | Migraine w/out aura, age ≥35 y  
Migraine w/out aura develops after initiating CC |
| 4        | Migraines with aura, any age  
Migraines with aura develop after initiating CC |
How do OCs affect the clinical course of migraine?

- Cross-sectional survey of endogenous hormones
  - Pt’s with migraine more likely to experience headache related to the cyclic monthly hormonal changes (OR 2.79, 95% CI 1.33-5.85)
  - OCP use primarily worsened headache symptoms in patients with migraine (39 vs. 3.6%, p<0.001)
  - More participants with migraine had improvement in HA symptoms at menopause (15.8 vs. 2.4%, p=0.46)

How do OCs affect the clinical course of migraine?

- Retrospective studies in headache clinics: COCs worsen severity and frequency of headaches, cause new onset headache
  - One study noted new onset aura in 8 women on OC\textsuperscript{1}
  - Only a subset of women
  - Majority have no change in headache
  - Some report improvement
  - MA patients much more likely to worsen on OC\textsuperscript{2}

Observations: Headache and COC use

• More common in women 35 and older

• Character of OC headaches poorly studied

• “HA-susceptible group” poorly characterized

• No effect from type or dose of progesterone

• Switching to lower dose OC may not improve headaches
  – 30 vs 20 EE: No diff in dropout due to HA.¹
  – 50 mestranol vs 35 EE. No diff in headache at 1st f/u visit²
  – Significant increase in headache, patients switched from 50 to 35 mcg pill. ³, ⁴

• Multivitamin or Vit B6 do not modify HA risk

• If HA occurs in 1ˢᵗ cycle on OC, only 1/3 chance it will occur in 2ⁿᵈ cycle ⁵

¹ Bassol, Cephalalgia, 2000
² Basnayake, Stud Fam Plann, 2004
³ Gerais, Int J Gynaecol Obstet, 1983
⁴ 5 Berger, Contraception, 1979
Design flaws with prior studies about hormones and headache

- Generally of low quality (rarely prospective)
- Studied older COC regimens with higher estrogen doses
- Did not distinguish migraine from other HA types
- Did not measure or compare to baseline migraine prevalence in non-users

Migraine and the menstrual cycle

MacGregor et al. *Cephalalgia* 1996
Hormonal contraception to treat menstrual migraine

- Continuous use of hormonal contraception to eliminate the culprit—estrogen drop
- Aura symptoms also reduced\(^1\)
  - Monophasic pill, vaginal ring, subdermal implant
  - Patch cannot be used continuous
  - LNG-IUD may not work due to break through ovulation
- Gradual estrogen drop through the use of tetraphasic OCP—estradiol valerate/dienogest (Natazia\(^\text{TM}\))\(^2,3\)

CHCs and Migraine: the bottom line

- Consensus: benefits of CHCs often outweigh drawbacks in women with migraine without aura
- Use discouraged in women who have migraine with aura
- If headache occurs or worsens in early cycles, it is likely to improve.
- If severe headaches develop or neurologic accompaniments to headache develop or worsen use should be discontinued
- 30 or 35 mcg, non-varying estrogen dose best
  - Evidence points to additional advantages from continuous administration
  - Less clear that lowering dose or switching methods helps
Contraception for women with Epilepsy
Unintended pregnancy and Epilepsy

• Increased risk to woman
  – Increased seizure frequency around delivery

• Increased risk to fetus from teratogenic AEDs:
  – Phenytoin
  – Valproate
  – Carbemazepine
  – Barbiturates
  – Lamotrigine
  – Topiramate
  – Zonisamide

• Risk of major congenital malformations\(^1\)
  – Epilepsy alone (no AED) 2.8% vs. 2.2% healthy controls
  – Monotherapy: 3.7%, Polytherapy 6.0%

• Need for effective contraception
  – Ideal to plan pregnancy, optimize AED preconception

1. Hill et. al., *Expert Rev Neurother* 2010
Contraception use and Epilepsy

• Survey 148 women with Epilepsy
  – Ethnically diverse sample, about half: prior pregnancy

• 50% of pregnancies were unplanned
  – Similar to general population in U.S.

• Of those sexually active in past month:
  – 74% used contraception
    • 53% used more effective methods
      – sterilization, IUD, pill, patch, injection
    • 47% used less effective methods
      – condoms, withdrawal, rhythm, spermicides

Davis et. al, Contraception 2008
Hormones and Seizures

• Estrogen pro-convulsant
• Progesterone and progestins anti-convulsant
• Catamenial seizure patterns are common (20-70%)\(^1\)
  – Increased seizure frequency often perimenstrual or around ovulation
• Does progesterone or progestin Tx impact seizure frequency?
  – Direct effect of progesterone/progestin?
  – Effect of ovulation suppression?

Pennell, Neurol Clin 2009
Treatment of Seizures with Medroxyprogesterone

• 14 patients treated with MPA (case series)
  – All started with oral-MPA (10 mg BID-QID)
  – 6 patients w/o amenorrhea, switched to Depot-Medroxyprogesterone Acetate (contraceptive)
  – Amenorrhea more common after DMPA
  – 11/14 women achieved amenorrhea
    • 39% reduction in seizure frequency
    • 7 women with definite improvement
  – No change in AED levels

Mattson RH et. al., Neurology 1984
Treatment of Seizures with Cyclic Progesterone

- Double blind, placebo controlled RCT (N=294)
- 200 mg PO progesterone TID, days 14-28 vs. placebo
- Women not taking other hormones
- Stratified by catamenial vs. noncatamenial
- No difference in response to progesterone vs. placebo in either strata
  - Level of perimenstrual seizure exacerbation (C1), predictor of response to progesterone
    - 21% with C1 level ≥3, significant response to progesterone
    - Cyclic progesterone may help this subset
- Better ovulation suppression may be more effective

Herzog AG et. al, Neurology 2012
# Contraception and Epilepsy (CDC)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Combined pill, patch, ring</th>
<th>Progestin-only</th>
<th>LNG-IUD</th>
<th>Cu-IUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy‡</td>
<td>1*</td>
<td>1*</td>
<td>1*</td>
<td>1</td>
</tr>
<tr>
<td>Anticonvulsant therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Certain anticonvulsants</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>(phenytoin, carbemazepine, barbiturates, primidone, topiramate, oxcarbazepine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Lamotrigine</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

‡ Condition that exposes woman to increased risk from unintended pregnancy
* See drug interactions below
## Interaction of CHC and Anticonvulsants

<table>
<thead>
<tr>
<th>Decrease CHC steroid levels</th>
<th>Do not decrease CHC steroid levels</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name</strong></td>
<td><strong>Trade Name</strong></td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Ethosuximide</td>
</tr>
<tr>
<td>Primidone</td>
<td>Mysoline</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Dilantin</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Tegretol</td>
</tr>
<tr>
<td>Felbamate</td>
<td>Febatol</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>Trileptal</td>
</tr>
<tr>
<td>Topiramate</td>
<td>Topamax</td>
</tr>
</tbody>
</table>

**CHC decreases anticonvulsant levels**

Lamotrigine

Gaffield et. al, *Contraception* 2011
Contraception for women with Multiple Sclerosis
Hormones and the Immune System

• Influence of gender on immunity
  – Gender influences susceptibility to autoimmune diseases
  – Alterations in autoimmune diseases in pregnancy
  – MS relapse and exacerbations during pregnancy and post partum

• Immune function fluctuations throughout the menstrual cycle
  – RA, MS, SLE all fluctuate with monthly cycles and in menopause
  – Estrogen suppresses T-cell dependent inflammation in MS and RA
Contraception and Multiple Sclerosis

• Does hormonal contraception affect risk of MS development or disease severity?

• Do hormonal contraceptives interact with MS treatment medications?

• Are women with MS at higher risk for complications of hormonal contraception?
Hormonal Contraception and MS

• Villard-Mackintosh and Vessey
  – Women using CHC had a lower incidence of MS onset
  – No associations between MS onset, duration of CHC use, or elapsed time since CHC use ended

• Thorogood and Hannaford
  – Prospective study of 46,000 CHC users
  – Found no effect on MS incidence or survival

  – Conclusion: Women with MS can use CHC
  – Results did not reach statistical significance
    • 177 MS cases between the two studies
Hormonal Contraception and MS

• N=315
  – Trend toward decreased incidence of MS in CHC users, but not significant
  – No lasting protective affect of CHC use or parity on risk of MS development
  – Concern about MS development or disease severity should not affect contraceptive choice

Other Disease Concerns That May Affect Contraceptive Choice

• Immobility and VTE risk
  – Lower extremity paraparesis or parathesias
  – Risk of VTE increases with increasing immobility
  – Patients with immobility should be steered away from estrogen containing contraceptives.

• Sexual dysfunction
  – Affects 50-90% of individuals with MS
  – Vaginal dryness, changes in sensation at the thighs or genital region, reduced libido, difficulty achieving orgasm, incontinence, muscle weakness
Hormonal Contraception and Sexual Dysfunction

• COCs suppress ovarian testosterone and increase SHBG levels

• Unclear if anti-androgenic effect of COCs impacts sexual function
  – Exogenous androgen treatment does not improve desire
  – Higher doses of estrogen do not increase sexual side effects

• Variations in COC formulations do not influence sexual effects

• Non-oral delivery of CHC (patch, ring) have shown no negative effects on sexual function

• Progestin-only methods are not associated with sexual SEs
Summary of MS and Contraception Choice

• All contraceptive methods are acceptable for patients with MS

• Estrogens and progestins do not increase MS risk, disease severity or progression

• MS patients with increased VTE risk from impaired mobility may not be ideal for estrogen-containing methods

• Some medications for symptom control (i.e. anticonvulsants) may affect hormonal contraceptive efficacy

• Some therapies are FDA Category D or X and a highly effective contraceptive method should be strongly encouraged

• Tailor contraceptive plan to each patient
Thank you

Questions?