Contraception in Medical Disorders

Stephanie Teal, MD, MPH
Professor of Obstetrics and Gynecology
University of Colorado School of Medicine
Stephanie.Teal@ucdenver.edu
Disclosures

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Learning Objectives

Following this presentation the learner will:

- **Effectively use** the WHO Medical Eligibility Criteria for Contraceptive Use
- **Provide evidence-based counseling** on the risks and benefits of various contraceptive options for obese women
- **Utilize the appropriate options** for contraception in women with headache syndromes
Is unplanned pregnancy a problem?

- Pregnancy may worsen medical issues
  - Increased demand on compromised systems
- Medical conditions may threaten fetus
  - Hostile intrauterine environment
- Therapies may threaten fetus
  - Teratogenic medications
Considerations for contraception

- Safety with baseline disease
  - Increases risk of disease progression or occurrence of complications
- Drug interactions
  - Increased toxicity of medications
  - Efficacy of contraceptive
- Sufficient efficacy
- Ease of use
Medical conditions that impact contraceptive use

- Hematologic disorders
  - Thrombophilic
  - Hemophilic
- Endocrine
  - Obesity
  - diabetes
- Neurologic
  - Seizure disorder
  - migraine
- Psychiatric
  - Depression
  - Bipolar
  - Developmental delay
- Rheumatologic
  - Lupus
  - RA
- Infectious
  - HIV
- Neoplastic
  - Breast cancer
  - Melanoma
- GI
  - Cystic fibrosis
  - Bariatric surgery
US Medical Eligibility Criteria for Contraceptive Use

- 5th edition published June 1, 2015
- Over 1800 recommendations
- balances risks and advantages of contraceptive method with medical state or condition
- Phone app
WHO Medical Eligibility Criteria

- **Category 1**: A condition for which there is no restriction for the use of the contraceptive method

- **Category 2**: A condition where the advantages of using the method generally outweigh the theoretical or proven risks

- **Category 3**: A condition where the theoretical or proven risks usually outweigh the advantages of using the method

- **Category 4**: A condition which represents an unacceptable health risk if the contraceptive method is used.
Obesity & contraception

- Efficacy
- Synergistic health effects
  - Co-morbidities
- Worsening obesity
- Technical issues
  - Injectables
  - Intrauterine
  - Surgical
Possible Mechanism of Obesity effect on HC efficacy

- Increased basal metabolic rate
- Increased hepatic enzyme metabolism
- Increased drug sequestration
- Blunted central sensitivity
  - Early FSH activation, delayed suppression
“typical use” retrospective studies: overweight and obese women may be at an increased risk of contraceptive failure

Physiologic factors

Behavioral factors
  - Decreased compliance

Brunner Huber LR et al, Matern Child Health J. 2005
### COC efficacy: epidemiology

<table>
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<tr>
<th>Study</th>
<th>Year</th>
<th>Study Design</th>
<th>RR</th>
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What does it mean?

- Epidemiologic studies inconclusive
  - Absolute risk is likely to be small:
    - 60% increase in risk = increase from 7% to 11% in the first year of typical use of OCs
- Need for prospective studies
  - designed specifically to examine an association between body weight and contraceptive failure
EURAS

- prospective cohort
- active surveillance
  - 59,510 OC users
- effectiveness of OCs overall
  - by BMI, weight, age, duration of use, EE dose, regimen type, starting/switching status, parity
  - unplanned pregnancies during OC use
    - confirmed by interview
- OC effectiveness analysis
  - 112,659 women-years of exposure
  - 545 unplanned pregnancies
  - little variation in effectiveness by BMI/weight.

The RCT

- BMI 19-25 vs. 30-40
- 2 pill formulations
- Compliance
  - Serum LNG levels
  - **Highly significant difference between BMI arms**
- Ovarian suppression
  - twice weekly ultrasound
  - Progesterone
  - Rare ovulations
  - **no difference among consistent users**

VTE risk

Mild synergistic effect between COC and BMI category

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<td>(3.1-11.7)</td>
<td>(4.0-17)</td>
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Bottom line

- LNG and copper IUDs
  - do not promote VTE
  - Have no efficacy difference
  - Do not promote weight gain
  - May be protective against hyperplasia
  - May be technically difficult to place
- ENG implant highly effective
- CHCs: still more effective than barrier methods and safer than pregnancy
Family history of breast cancer

- 23 yo G0
- Mother recently dx’d with breast CA at age 50
COCs and Breast Cancer

- Oxford pooled analysis (Lancet 1996)
  - 54 epidemiologic studies
  - 50,000 breast cancer, 100,000 controls
- US historical cohort (JAMA 2000)
  - breast CA 1944-1952
  - F/U 40-50 yrs later with 1st and 2nd degree relatives
- Women’s CARE study (NEJM 2002)
  - 4575 cases, 4682 controls
Increased risk of breast cancer with COCs?

- Oxford
  - RR 1.24 with current use, less with recent use, no increase with use >10 yrs prior
  - Extremely small increased absolute risk
  - No difference by family history
- US cohort
  - Incr risk only for OCs pre-1975
- Women’s CARE
  - No increased risk among current or former users, by length of use, age of initiation, or dose
  - No difference by family history
BRCA mutations and COCs

- Risk of primary breast CA
- Risk of asynchronous second breast CA
- No change for
  - BRCA1
  - BRCA2

Figueiredo et al, Breast Cancer Res Treat, 2009
Narod et al, J Natl Cancer Inst 2002
Haile et al, Cancer Epidemiol Biomarkers Prev 2006
Brohet et al J Clin Oncol 2007
Breast cancer and LNG-IUS

- LNG-IUS vs all population (Finland)
- LNG-IUS vs Cu-IUD (Finland, Germany)
  - Retrospective, population-based, case-control cancer registries
  - No increased risk of breast Ca with LNG-IUS
- No increased risk of recurrence
  - Controlled cohort, Belgium

Headache 1

- 21 yo new patient
  - Severe dysmenorrhea
  - Desires contraception
  - History of migraine
    - Bilateral
    - “tightening” sensation
    - Photophobia
    - No ↑ with activity
    - Respond to NSAIDS
    - Mom and sister with migraines

- Recommended COCs by her best friend

- Is a CHC appropriate for her?
What is a migraine?

- Headaches
  - Unilateral, pulsating, mod-severe
  - At least 5, lasting 4-72 hrs
- Phonophobia/photophobia OR
- Nausea/vomiting
- Common vs. classic
- Tension HA does not increase stroke risk
Headache 2

- 26 yo G1P1, non-smoker
- Has used COCs x 2 yrs.
- Severe HA 4-5x/year
  - Unilateral, pulsating, photophobia
  - Worse with activity
  - Preceded by flashing zigzag line that migrates from the center of visual field to periphery
  - No change since starting COCs
  - No assoc. with menses
- Should she continue OCs?
Migraine and stroke risk

- Migraine and stroke
  - RR 2.2-3.5 (general)
  - RR 1.6-3.0 (no aura)
  - RR 2.9-6.2 (with aura)

- COC and stroke
  - RR 1.0-3.5
Migraine, COC, and stroke

- Synergistic effect
- RR 6.6-13.9
  - Compared to women without migraine or COC use
- RR 2-4
  - Compared to migraineurs without COC

- How robust are the data?
  - No prospective studies
  - Case-control studies subject to recall, selection, ascertainment, observation bias
  - Not controlled for smoking, gender

Probable increased risk, size of risk is in dispute
CHCs and Migraine

- Synergistic effect of CHC and migraine
  - RR 6.6-13.9 compared to women without migraine or COC use
  - RR=2-4 Compared to migraineurs without COC
- How robust are the data?
  - No prospective studies
  - Case-control studies subject to recall, selection, ascertainment, observation bias
  - Not controlled for smoking, gender
- Probable increased risk, size of risk is in dispute
Headache 3

- 32 yo G2P2
  - Migraine without aura
  - Occur ONLY in the 2 days pre-menstrual, resolve within first few days of bleeding
  - NSAIDS: minor relief
  - Smokes 2-5 cigs/day

- Is COC appropriate?
Migraine and contraception

- If menstrual only, avoid estrogen-free placebo week
- Consider non-estrogen methods IF migraine with...
  - True aura, focal neuro sx
  - Smoking
  - Over 35
- For adolescents, absolute risk is extremely low
Possible Effects of COC on migraine

- No change
- Improvement (usually without aura)
- Migraine without aura in pill-free week only
- More severe/more frequent (typically with aura)
- New onset migraine (typically with aura)
Lupus

- 27 year old G1P0 with SLE.
- She has + LA activity and + aCL-abs, and a hx of a brachial DVT for which she is on warfarin.
- Moderate lupus nephritis, rx MTX and cyclophosphamide, now quiescent x 6 mo.
- In a new sexual relationship, and wants OCPs.
Issues with SLE and contraception

- **Thrombophilia**
  - who is at risk for clots with exogenous hormones? Which hormones?

- **Immunosuppression**
  - Does hormonal contraception worsen? Can she use an IUD?

- **Disease flares**
  - Do OCs promote flares, and in who?

- **Osteopenia**
  - Concomitant use of prednisone and ovulation suppressors?
SLE and OC’s: 2 RCTs

- N=183; COC vs. placebo
  - Inactive (76%) or stable (24%) lupus
    - Excl: mod/high levels of anticardiolipin abs, LAC, or hx thrombosis
  - No diff in mild, mod or severe flares
  - No diff complications (thrombosis, infection)

- N=162; COC v IUD v POP
  - Mild/mod dz, 134 active
  - 30% with ACA
  - Global dz activity by SLEDAI score
  - No difference in global or max dz activity, clots, infxn

Anti-convulsants

- Induce p450 enzymes, Cyp3A4
- Decrease EE and P AUC and Cmax
- Increase EE clearance
- Increase SHBG
- Includes parenteral hormones
- COCs may also affect drug levels by changing bioavailability
Hormones and anti-convulsants

- Most evidence is very poor quality
- Surrogate endpoints, few assessments of breakthrough ovulation
- No studies with pregnancy as outcome
- Correlation of BTB and ovulation unclear
- No evidence to support 50 mcg EE pill
Sample of drug interactions

<table>
<thead>
<tr>
<th>Induction of hepatic enzymes, reduction of EE or P level</th>
<th>NO Induction of hepatic enzymes, no reduction of EE or P levels</th>
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<tbody>
<tr>
<td>Carbamazepine (Tegretol)</td>
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<td>Oxcarbazapine (Trileptal)</td>
<td>Lamotrigine (Lamictal)*</td>
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<tr>
<td>Topiramate (Topamax)</td>
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<td>Primidone (Mysoline)</td>
<td>Vigabatin (Sabril)</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>Valproate (Depakote)</td>
</tr>
<tr>
<td>Phenytoin (Dilantin)</td>
<td>Levetiracetam (Keppra)</td>
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</table>
Anti-convulsant use

- Determine drug(s) interactions
- Recommend higher dose pill with back-up (e.g. condoms)—Level C
- Recommend DMPA, LNG-IUD, Cu-IUD—Level B
- Progestin-only pills, subdermal implant not recommended—Level B
Seizure disorder

- 22 yo G3 P1 TAB2
- Seizure disorder since childhood
- On dilantin, lamictal, and trileptal
Clinical pearls

- Progestins do not promote thrombosis.
- Anti-coagulated patients benefit from menstrual reduction.
- Patients on teratogenic medications MUST be adequately contracepted.
Questions?