Contraception in Chronic Medical Conditions

Pelin Batur, MD, FACP, NCMP

Education Director,
Primary Care Women’s Health

Deputy Editor,
Cleveland Clinic Journal of Medicine
Why do I care?

- GYNs might need our help
- Help find answers to 'annoying' questions
- You are using the most teratogenic meds
- Might need info in your personal life!

Why wouldn’t you use it!??
Some fun facts…

- 50% of pregnancies unintended
  - 4/10 of these lead to abortion
    - 54% of those who had abortions had used a contraceptive that month
- 1/3 US servicewomen can’t access before deployment
  - Most effective methods discouraged or unavailable
  - 41% hard time getting refills

Finer et al. Contraception 2011; 84:478–485
Grindlay et al. Contraception 2013; 87:162-169
Conditions that may make unintended pregnancy an unacceptable health risk

- Breast cancer
- Complicated valvular heart disease
- Diabetes with vascular complications
- Endometrial or ovarian cancer
- Epilepsy
- Bariatric surgery within 2 years
- HIV/AIDS
- Ischemic heart disease
- Malignant liver tumors
- Peripartum cardiomyopathy
- Schistosomiasis with liver fibrosis
- Severe cirrhosis
- Sickle cell disease
- Solid organ transplant within 2 years
- Stroke
- SLE
- Thrombogenic mutations
- Tuberculosis
Long Acting Reversible Contraceptives (LARCs)

- The contraceptive CHOICE project
- Prospective study: *what happens if cost is not an issue?*
  - LARCs chosen by 75% of women
  - LARCs 20x more effective than CHC
  - 2008-2010 abortions ↓ by 20.6%
  - Teen birth-rate ↓ 6.3/1000 (national av is 34.3)

Peipert JF et al. Obs Gynecol Oct 2012
Winner B, et al. NEJM May 2012
“Ashley wanted to play doctor, but I’m trying to stay out of the health care debate.”
ACA Women’s Preventive Services: Contraception

- Health Plans must cover:
  - FDA-approved contraception methods
  - Sterilization
  - Patient ed and counseling
- No deductibles and co-pays.

State Exchange Status
as of 1-4-13
Kaiser

Artia Advisor 2-7-13
Does it save us money?

- **Cost of unintended pregnancy in the US = 4.6 billion/yr**

- Including LARCs:
  - If 10% of women age 20-29 changed to LARCs, savings $288 million/year

- Extending coverage to low income Americans for 5 yrs
  - 72 prevented pregnancies per 1000 women
  - Saves $489 per woman enrolled
  - Doesn’t include cost of
    - Decreased productivity
    - Ob complications
    - Health of children
    - Undocumented immigrants

Trussel et al. Contraception 2013; 87:154
Burlone et al. Contraception 2013; 87:143
Is there really an access issue?

Counterfeit and illegal sales

- Can buy contraception without rx
  - Facebook, Twitter, Slideshare, Flickr

Martinez G. Vital Health Stat 2011; 23:1
Is there really an access issue?

**Counterfeit and illegal sales**

- Health care providers buying from these sites!

Martinez G. Vital Health Stat 2011; 23:1
Intrauterine Contraception: IUD

ParaGard
- Copper, 10 yrs
- No hormones

Mirena
- 5 yrs
- Both with local progestin

Skyla
- 3 yrs

Silver identifier
Progestin Only Contraception: *Implanon* *Nexplanon*

- Lasts 3 yrs
- 99% effective unless
  - meds that induce liver enzymes
- 30-40% amenorrhea at 1 yr
Arm pain and numbness in a Nexplanon user

Intrauterine Contraception: \textit{Essure}

- Local anesthesia, 10 minutes
- Back-up method needed for first 3 months
"WE'RE ALMOST THERE. HAPPY ANNIVERSARY, DEAR!"
MRI Safety

- **MR Safe**
  - Mirena
  - Nexplanon

- **MR Conditional**
  - Safe if scanner <3 T
    - Essure
    - Copper IUD
    - Skyla

- **MR Unsafe**
Progestin Only Contraception: 
*Depo-Provera*

- Failure rate 0.0-0.7%
- Side Effects:
  - Menorrhagia, amenorrhea
  - Weight gain (1-3 kg)
  - Hypoestrogenic
  - Higher insulin and FBS
  - ↓ HDL
Bone Health: Depo-Provera

- **Black box warning: Osteopenia**
  - Studies on BMD mixed
  - BMD ↓ at 5 yrs vs controls
    - -5.38% in LS ( -3.13% 2 yrs after dc)
    - -5.16% in TH ( -1.34%)
    - -6.12% in FN ( -5.38%)
  - Decline is more pronounced in first 2 yrs

- **ACOG & WHO: Advantages of DMPA > risks**
  - Can continue for decades!

Batur P, Joy S. Clinical Reviews of Bone and Mineral Metabolism; 3(2): 103-113, 2005
Bone Health: Depo-Provera

Use of DMPA and incidence of bone fracture
- 312,395 women in UK, retrospectively followed 5 yrs

- Fx incidence in 1000 women: 9.1 (Depo) vs 7.3 (non-Depo)
  - Incidence RR 1.23 (95% CI 1.16-1.130)

Overall “message”: no significant increase
- DMPA cohort higher risk of fx at baseline
- Risk did not increase further after DMPA initiated
- Longer term users had lower fx risk than short term
- No excess risk of axial fx (hip, pelvis, vertebral)

Is a DXA scan needed?

- Use clinical judgment, depends on:
  - Length of use
  - Risk factors
  - Insurance coverage
  - Try dx code 256.39
Progestin only pill "mini-pill"

- For those who cannot tolerate estrogen
  - CAD, VTE, stroke
  - Migraine w/ aura
  - DM w/ vascular complication
  - <6 wks postpartum
  - Uncontrolled hypertension

- Main use in lactating women
  - Higher rates of breakthrough bleeding
  - Lower contraceptive efficacy
  - Back up method for 2 days if > 3hrs late w/ dose
Combined Oral Contraceptives (COC)

- Have been used ~ 50 years in the US
- Most popular contraceptive choice along with sterilization

NuvaRing

Ortho Evra
COC Metabolism

- Contraceptive effectiveness *may be reduced* when co-administered with:
  - rifampin
  - anticonvulsants (phenytoin, carbamazepine, topiramate, barbiturates)
  - anti-HIV protease inhibitors
  - non-prescription/herbal products (St. John's wort)
COC Metabolism

- EE increased when co-administered with:
  - atorvastatin (Lipitor), ↑20%
    - rosuvastatin ok
  - erythromycin/clarithromycin
  - acetaminophen
  - ascorbic acid
  - itraconazole, ketoconazole
  - grapefruit juice
Combined Oral Contraceptives: Progestin Formulations

- **First Generation**:  
  - norethindrone  
  - ethynodiol diacetate

- **Seconds Generation**:  
  - norgestrel  
  - levonorgestrel

- **Third Generation**:  
  - norgestimate  
  - desogestrel (RR VTE 1.7-19x)

- **Fourth Generation**:  
  - drospirenone (RR VTE 0.9-3x)  
  - dienogest
Why are they so mean to Yasmin/Yaz?
Letter to patients from Aetna…

- Did you suffer any cardiovascular - or gallbladder - related injury or injuries during or after [the period when you used Yaz, Yasmin, or Ocella]?
- Have you pursued, are you pursuing, or do you intend to pursue a personal injury claim related to your use of Yaz, Yasmin, or Ocella?
- Have you hired or do you plan to hire an attorney to represent you in this claim?
The aftermath...

- ~12,000 lawsuits to Bayer
- settled 1,977 cases for $402.6 million, for an average of $212,000 per case, while setting aside $610.5 million to settle the others

Source: Bloomberg.com
What does the data *really* show?

Figure 1: VTE Risk with Yasmin Relative to LNG-Containing COCs (adjusted risk^a)

- Ingenix (Hazard Ratio^b,c,d)^a
- EURAS (Hazard Ratio^e,f,g,h)^a
- LASS (Hazard Ratio^e,f,g,h)^a
- FDA-funded study (Hazard Ratio^i,j,l)^a
- Danish (Rate Ratio^i,l,k,j)^a
- Danish re-analysis (Rate Ratio^i,l,k,j)^a
- MEGA study (Odds Ratio^a,l)^a
- German case-control (Odds Ratio^f,g,h,i,k,l,m,n,o,p)^a
- PharMetrics (Odds Ratio)^a
- GPRD study (Odds Ratio)^a

Prospective Cohort Studies

Retrospective Cohort Studies

Case-Control Studies

Non-fatal idiopathic cases only
## Summary of VTE: absolute risks

<table>
<thead>
<tr>
<th>Condition</th>
<th>Rate of VTE (per 10,000 women per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reproductive Aged (baseline-no pill)</td>
<td>1-5</td>
</tr>
<tr>
<td>Pill users</td>
<td>3-10</td>
</tr>
<tr>
<td></td>
<td>(*rates vary by progestins)</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>10-29</td>
</tr>
<tr>
<td>Postpartum</td>
<td>65-400</td>
</tr>
</tbody>
</table>
COC Risks

- Coronary artery disease
- Hypertension
- Stroke
- Breast cancer
- Lung cancer
COC Risks

- **Coronary artery disease**
- Hypertension
- Stroke
- Breast cancer
- Lung cancer

**COC Risks**

- **Coronary artery disease**
- Hypertension
- Stroke
- Breast cancer
- Lung cancer

Fertil Steril 2006; 85(5):1425

? Protective effect

NEJM 2012; 366:2257

- 30-40 mcg EE RR ↑ 1.3-2.3
- 20 mcg EE RR ↑ 0.0-1.6
- Ortho Evra  RR 0.0
- Nuvaring ↑ 2.1
COC Risks

- **Coronary artery disease**

  Fertil Steril 2006; 85(5):1425
  ? Protective effect

  NEJM 2012; 366:2257
  30-40 mcg EE RR ↑ 1.3-2.3
  20 mcg EE RR ↑ 0.0-1.6
  Ortho Evra RR 0.0
  Nuvaring ↑ 2.1
COC Risks

- Coronary artery disease
- **Hypertension**
- Stroke
- Breast cancer
- Lung cancer
COC Risks

- Coronary artery disease
- Hypertension
- **Stroke**
  - Stroke 2009; 40(4):1050
  - No increased risk
- Breast cancer
- Lung cancer
  - NEJM 2012; 366:2257
  - 30-40 mcg EE RR ↑ 1.5-2.2
  - 20 mcg EE RR ↑ 0.9-1.7
  - Ortho Evra ↑ 3.2
  - Nuvaring ↑ 2.5

**ACOG**
Risk is small but catastrophic
COC Risks

- **Stroke**
  - Stroke 2009; 40(4):1050
  - No increased risk

  - NEJM 2012; 366:2257
    - 30-40 mcg EE RR ↑ 1.5-2.2
    - 20 mcg EE RR ↑ **0.9**-1.7
    - Ortho Evra ↑ 3.2
    - Nuvaring ↑ 2.5

  - ACOG
    - Risk is small but catastrophic
COC Risks

- Coronary artery disease
- Hypertension
- Stroke
- Breast cancer
- Lung cancer

**No ↑ risk**
- Contraception 2012; 85: p342
- NEJM 1986; 315:p405
- JAMA 2000;284: p1791
- NEJM 2002; 346: p2025

**↑ risk**
- Lancet 1996; 347: p1713
- Br J Cancer 2003;88: p50
- Can Epid Prev 2010; 19: p2496
COC Risks

- **Breast cancer**

  **BRCA carriers:**
  - ↓ ovarian cancer RR 0.50 (CI 0.33-0.75)
  - No association with breast cancer
    - Formulations before 1975 ↑ risk
    - RR 1.47 (1.06-2.04)

*Eur J Cancer 2010: 46(12): 2275*
COC Risks

- Coronary artery disease
- Hypertension
- Stroke
- Breast cancer
- **Lung cancer**
CDC: US medical eligibility criteria for contraceptive use, 2010

1 = condition with no restriction
2 = condition where advantage > risk
3 = condition where advantage < risk
4 = condition represents unacceptable health risk if that method is used

http://www.cdc.gov/mmwr/preview/mmwrhtml/rr59e0528a13.htm
Contraception for diabetics

Don’t worry about: gestational diabetes of DM
Special Considerations:
Bariatric Surgery

- Gastric bypass
  - COC category 3
  - All other methods category 1

- Restrictive (lap band)
  - All category 1
Headache...

<table>
<thead>
<tr>
<th>Condition</th>
<th>Sub-condition</th>
<th>Combined pill, patch, ring</th>
<th>Progestin-only pill</th>
<th>Injection</th>
<th>Implant</th>
<th>LNG-IUD</th>
<th>Copper-IUD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Headaches</td>
<td>a) Non-migrainous</td>
<td>1*</td>
<td>2*</td>
<td>1*</td>
<td>1*</td>
<td>1*</td>
<td>1*</td>
</tr>
<tr>
<td></td>
<td>b) Migraine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>i) without aura, age &lt;35</td>
<td>2*</td>
<td>3*</td>
<td>1*</td>
<td>2*</td>
<td>2*</td>
<td>2*</td>
</tr>
<tr>
<td></td>
<td>ii) without aura, age ≥35</td>
<td>3*</td>
<td>4*</td>
<td>1*</td>
<td>2*</td>
<td>2*</td>
<td>2*</td>
</tr>
<tr>
<td></td>
<td>iii) with aura, any age</td>
<td>4*</td>
<td>4*</td>
<td>2*</td>
<td>3*</td>
<td>2*</td>
<td>3*</td>
</tr>
</tbody>
</table>
Seizure Disorder

- Decreased contraceptive efficacy

- Use doses >50 mcg EE
  - Barbiturates, carbamazepine, oxcarbazepine, felbamate, topiramate levels reduced
  - Levetiracetam, valproic ok

- lamotrigine (*Lamictal*)
  - COCs decrease the lamotrigine levels by 50%
  - Toxic levels in placebo week

- DMPA, IUD

Cochrane Rev Abstract 2007
Sickle cell disease

- No proof COC contributes to extra VTE risk
  - No studies looking at this directly
- No effect on number of crisis
  - Fair-poor quality studies
- In CR only 1 trial met criteria to be included
  - 25 patients- Depo-Provera vs placebo
  - During DMPA use, less sickle episodes
    - OR 0.23 (95% CI 0.05-1.02)

Cochrane Rev Abstract 2007
Contraception 2012; 85: 527
Systemic Lupus Erythematosus

- Low likelihood of significant flare w/COC*
  - Thrombosis risk not increased
  - Excluded those with mod-high ab levels

- Caution w/ drospirenone, DMPA
- Severe thrombocytopenia: avoid ParaGard & DMPA
- Use of immunosuppressants does not affect choice

Rheumatoid arthritis

- COC has no negative outcomes on RA
  - COC use > 5 yrs, RR of severe dz 0.1 (95% CI 0.01-0.6)
- DMARDs: methotrexate & leflunomide are pregnancy category X
  - Stop MTX 3 months & leflunomide 2 yrs prior to conception

J of Rheumatology. Vol 31: Supplement 69, March 2004
Organ Transplant

- Amenorrhea/infertility common with hepato-renal disease
  - 1/20 transplant patients of childbearing get pregnant

- National transplantation pregnancy registry:
  - Live birth rate 50-86%

- Medicare:
  - Live birth rate 55%
  - Post transplant pregnancy 33/1000 women

- Estimates don’t include abortions
Organ Transplant

- Pregnancy risks post transplant:
  - Graft rejection
  - Pregnancy complications
  - Most antirejection agents are pregnancy class D

- Contraception should be discussed prior to transplant
  - Women should wait 18-24 months before pregnancy
  - IUD, hormonal options are category 2
    - Unless graft failure, rejection, allograft vasculopathy
      - COC category 4
      - IUD category 3
      - Depo, POP category 2
HIV

- CDC update 6/2012: All hormonal contraception may be used in those with HIV

- Increased risk of HIV acquisition
  - Depo HR 2.04 (CI 1.04-2.05)
  - COC HR 1.8 (CI 0.55-5.82)

MMWR 2012; 61(24):449
Increased HIV acquisition

- Should we shift away from DMPA to condoms or pills?
  - 600 additional unwanted births per 100 HIV infections averted
  - If no protection: 5400 unwanted births

Jain AK. Contraception 86 (2012): 645
CHC Category 1 Medical Conditions

- Family history of breast cancer
- Cirrhosis
- Endometrial cancer/hyperplasia
- Ovarian cancer
- HIV
- Malaria
- Viral hepatitis
- Varicose veins
- TB
Category 1 Medical Conditions assuming not...

- Cirrhosis ➔ *not* severe, decompensated
- HIV ➔ watch drug interactions
- Viral hepatitis ➔ *not* acute or flare
CHC Category 2 Medical Conditions

- Cervical cancer
- DVT family hx (1st degree)
- Superficial thrombophlebitis
- Gallstones (asymptomatic)
- Pregnancy related cholestasis
- HTN during pregnancy
- FNH liver
- IBD
- Valvular heart disease
Category 2 Medical Conditions assuming not...

- Preg related cholestasis $\rightarrow$ not COC related

- IBD $\rightarrow$ not extensive, dehydration, vitamin deficiency, surgery, steroid use, immobilization

- Valvular heart dz $\rightarrow$ not complicated
  
  (pulm htn, htn, afib, SBE)
CHC Category 3 Medical Conditions

- VTE/PE
- Breast cancer
- Peripartum cardiomyopathy >6 months
CHC Category 3 Medical Conditions assuming:

- **VTE/PE** → anticoagulation for 3 months, low risk for recurrence

- **Breast cancer** → disease free for 5 years

- **Peripartum cardiomyopathy** → >6 months & normal or mildly impaired cardiac function
# Emergency Contraception

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>high dose estrogen</td>
<td>5 mg EE qd x 5</td>
<td>75-80%</td>
</tr>
<tr>
<td>estrogen + progestin</td>
<td>100 ug EE + 0.5 mg levonorgestrel po q12 hr x 2</td>
<td>56-89 %</td>
</tr>
<tr>
<td>levonorgestrel</td>
<td>(Plan B) 0.75 mg q12 x 2 (Plan B One-Step) 1.5 mg x1</td>
<td>60-94 %</td>
</tr>
<tr>
<td>ulipristal (ella™)</td>
<td>30 mg</td>
<td>~98.6%</td>
</tr>
<tr>
<td>copper IUD</td>
<td>Insert within 5 days</td>
<td>99%</td>
</tr>
<tr>
<td>Method</td>
<td>Dose</td>
<td>Efficacy</td>
</tr>
<tr>
<td>-----------------</td>
<td>---------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td>levonorgestrel</td>
<td><em>(Plan B)</em> 0.75 mg q12 x 2 <em>(Plan B One-Step)</em> 1.5 mg x1</td>
<td>60-94 %</td>
</tr>
<tr>
<td>ulipristal <em>(ella™)</em></td>
<td>30 mg</td>
<td>~98.6%</td>
</tr>
</tbody>
</table>

Emergency Contraception
# Emergency Contraception

<table>
<thead>
<tr>
<th>Method</th>
<th>Dose</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EC Hotline: 1-888-NOT-2-LATE
Thank you!

baturp@ccf.org