


8:45 – 9:30 am

Advances and Options in Female Contraception

SPEAKER
Pelin Batur, MD, FACP, NCMP, CCD



Presenter Disclosure Information

The following relationships exist related to this presentation:

- ▶ Pelin Batur, MD, FACP, NCMP, CCD: No financial relationships to disclose.

Off-Label/Investigational Discussion

- ▶ In accordance with pmICME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Advances & Options in Female Contraception
Pelin Batur, MD, FACP, NCMP, CCD

Education Director,
Primary Care Women's Health

Deputy Editor,
Cleveland Clinic Journal of Medicine

Learning objectives

- Become familiar with the newest contraceptive options available
- Understand how a patient's medical background affects recommended choice of contraceptive

NOT SO FUNNY
~~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

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

CDC. MMWR. 2010 Jun 18;59(RR-4):1-86.

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 combined hormonal contraceptives (pill, patch, ring)
 - ◆ 2008-2013 pregnancy and birth rate 1/5 the national rate
 - ◆ Abortion rates less than 1/4 national rate

Peipert JF et al. Obs Gynecol Oct 2012
Winner B, et al. NEJM May 2012
Secura GM et al. NEJM Oct 2 2014




Etonorgestrel subdermal implant: *Implanon Nexplanon*

- Lasts 3 yrs
- 99+ % effective
- 30-40% amenorrhea at 1 yr
 - ◆ ↑ bleeding often occurs in first year

Intrauterine Permanent Contraception: *Essure*

- Local anesthesia, 10 minutes
- Back-up method needed for first 3 months

MRI Safety

- MR Safe 
 - ◆ Mirena (5 yr LNG IUD)
 - ◆ Nexplanon (3 yr arm implant)
- MR Conditional 
 - ◆ Safe if scanner <3 T
 - ◆ Essure (hysteroscopic coils)
 - ◆ ParaGard (copper IUD)
 - ◆ Skyla (3 yr LNG IUD)
- MR Unsafe 
 - ◆ No contraceptives

What's new with Depot medroxyprogesterone acetate

- Failure rate "0.0-0.7%" ~~6%~~
- Side Effects:
 - ◆ Weight gain (1-3 kg)
 - ◆ Hypoestrogenic
 - ◆ Higher insulin and FBS
 - ◆ ↓ HDL
- Uncontrolled HTN/Vascular Dz
 - ◆ Progestin only pill and Implant: category 2
 - ◆ Depo: category 3

Bone Health: DMPA

- **Black box warning: Osteopenia**
 - ◆ Studies on bone mineral density (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: DMPA

- Use of DMPA and incidence of bone fracture
 - ◆ 312,395 women in UK, retrospectively followed 5 yrs
 - ◆ Fx incidence in 1000 women: 9.1 (DMPA) vs 7.3 (non-DMPA)
 - ◆ 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)

Lanza L, et al. Obs Gynecol March 2013; 121 (3), 593

Bone Health: Depo-Provera Take home points

- Use it if patient needs it
- Consider LARC method instead
- Perimenopausal women have less time to recover BMD after discontinuation
- DXA scan not needed to monitor

Progestin only pill "mini-pill"

- For those who cannot tolerate estrogen
 - ◆ CAD, VTE, stroke
 - ◆ Migraine w/ aura
 - ◆ <6 wks postpartum
 - ◆ Uncontrolled hypertension
- Often used in lactating women
 - ◆ Higher rates of breakthrough bleeding
 - ◆ Back up method for 2 days if > 3hrs late w/ dose
 - ◆ Concern re: lower contraceptive efficacy

Combined Hormonal Contraceptives (CHC)

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

Combined Oral Contraceptives (the pill, COC)	vaginal ring (NuvaRing)	skin patch (Ortho Evra)
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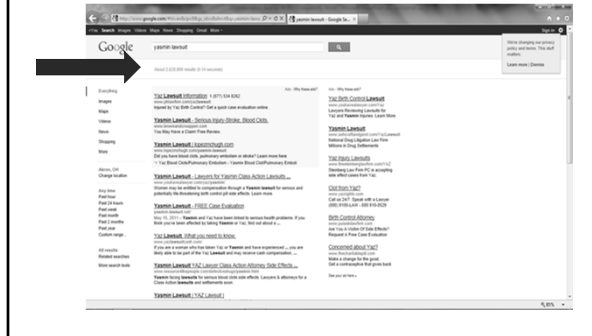
Combined Oral Contraceptives: *Progestin Formulations*

- **1st Generation:** (cycle control problems)
 - norethindrone
 - ethynodiol diacetate
- **2nd Generation:** (androgenic problems)
 - norgestrel
 - levonorgestrel
- **3rd Generation:** (RR VTE 1.7-6x)
 - desogestrel
 - etonogestrel
 - norgestimate
 - norelgestromin
- **4th Generation:** (RR VTE 0.9-3x)
 - drospirenone
 - dienogest

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 - ➔ drospirenone (RR VTE 0.9-3x)
 - dienogest

Why are they so mean to drospirenone?



The aftermath...

- \$1.575 billion settlements in the U.S.¹
 - 7,660 claimants (mostly VTE)
 - average claim per case = \$ 212,000
- Bayer agreed to settle ~ 8800 gallbladder injuries = \$24 million

Litigation not directed towards providers

¹ Bayer HealthCare stockholder newsletter, financial report as of September 30, 2013. Page 65 product related litigations. <http://www.stockholders-newsletter-q3-2013.bayer.com/en/bayer-stockholders-newsletter-3q-2013.pdf>

Summary of VTE: absolute risks

Condition	Rate of VTE (per 10,000 women per year)
Reproductive Aged (baseline-no pill)	1-5
Pill users	3-10 (*rates vary by progestins)
Pregnancy	5-20
Postpartum	40-65

ACOG Committee Opinion No 540: Risk of venous thromboembolism among users of DRSP-containing oral contraceptive pills. *Obstet Gynecol.* 2012 Nov;120(5):1239-42

What's new with CHC Risks?

- Breast cancer
 - Stroke
 - Coronary artery disease
 - VTE
- No ↑ risk**
- Contraception 2012; 85: p342
 - Contraception 2009; 80: p 372
 - NEJM 1986; 315:p405
 - NEJM 2002; 346: p2025

(c) Family history of cancer	1	1	1	1	1	1

• JAMA 2000;284: p1791
• Br J Cancer 2003;88: p50
• Can Epid Biomark 2010; 19: p2496
• Mayo Clin Proc 2006;81: p1287

What's new with CHC BENEFITS?

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

Ovarian Cancer Prevention
NNT 185 x 5 yrs
Longer use is better
Protection attenuates after d/c
Consider using in 40s

Eur J Cancer 2010;46(12): 2275

Obstet Gynecol July 2013; 122(1):139

What's new with CHC Risks?

- Breast cancer
 - Stroke
 - Coronary artery disease
 - VTE
- Obstet Gynecol Aug 2013; 122(2):380**
OR Ischemic stroke = 1.90 (95% CI 1.24-2.91)
Very few with EE <35mcg dose
Insufficient data to stratify by progestin
- NEJM 2012; 366:2257**
30-40 mcg EE RR ↑ 1.5-2.2
20 mcg EE RR ↑ 0.9-1.7
Patch ? ↑ 3.2 [CI 0.8-2.6]
Vaginal ring ↑ 2.5 [CI 1.4-4.4]
- Obstet Gynecol Oct 2013; 122(4): 800**
Vaginal ring not increased compared to oral

What's new with CHC Risks?

- Breast cancer Obstet Gynecol Aug 2013; 122:380
OR= 1.34 (CI 0.87-2.08)
Insufficient data to stratify by EE dose
- Stroke NEJM 2012; 366:2257
30-40 mcg EE RR ↑ 1.3-2.3
20 mcg EE RR ↑ 0.0-1.6
Patch RR 0.0
Vaginal ring ?↑ 2.1 [CI 0.7-6.5]
- MI Obstet Gynecol Oct 2013; 122(4): 800
Vaginal ring not increased compared to oral
- VTE

Does the type of progestin used affect the arterial risk ? **No**

Type of Progestin/ Hormonal Contraception	CVA		MI	
	# of events/ 100,000 person- years	Adjusted RR (30 mcg EE dose)	# of events/ 100,000 person-years	Adjusted RR (30 mcg EE dose)
Norethindrone	22.1	1.17 (1.49-3.15)	11.0	2.28 (1.34-3.87)
Levonorgestrel	31.3	1.65 (1.39-1.95)	19.8	2.02 (1.63-2.50)
Norgestimate	17.2	1.52 (1.21-1.91)	6.2	1.33(0.91-1.94)
Desogestrel*	31.6	2.20 (1.79-2.69)	13.7	2.09 (1.54-2.84)
Gestodene*	21.6	1.80 (1.58-2.04)	10.1	1.94 (1.03-2.63)
Drospirone*	18.1	1.64 (1.24-2.18)	6.3	1.65 (1.03-2.63)
Patch	42.1	3.15 (0.79-12.60)	0	0
Vaginal ring	31.4	2.49 (1.41-4.41)	3	7.8 (0.67-6.48)

Lidegaard et al. *N Engl J Med* 2012; 366:2257-66.

What's new with COC Risks?

- Breast cancer
- Stroke
- Coronary artery disease
- VTE

Does the VTE risk vary based on the progestin formulation? **Probably yes**

risk vary based on the progestin formulation? No

	Relative Risk of VTE According to Generation of Progestin			
	Non-use	First	Second	Third
Non-use	1			
First generation	3.2 (2.0-5.1)	1		
Second generation	2.8 (2.0-4.1)	0.9 (0.6-1.4)	1	
Third generation	3.8 (2.7-5.4)	1.2 (0.8-1.9)	1.3 (1.0-1.8)	1

Stegemen BH et al. *Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis. BMJ* 2013;347.

Medical Considerations: Bariatric Surgery

- ◆ Gastric bypass
 - ◆ Oral pills are category 3
 - ◆ All other methods category 1
- ◆ Restrictive (lap band)
 - ◆ All category 1

Seizure Disorder

- ◆ Decreased contraceptive efficacy, consider IUD
- ◆ Use estrogen doses >50 mcg EE with:
 - ◆ Barbiturates, carbamazepine, oxcarbazepine, felbamate, topiramate levels reduced
 - ◆ Levetiracetam, valproic acid ok
- ◆ lamotrigine levels ↓ 50% with COC pills
 - ◆ May need higher doses of lamotrigine to control seizure
 - ◆ Can get toxic levels in placebo week
 - ◆ Use continuous regimen if COC must be used

Medical Considerations: Organ Transplant

- Amenorrhea/infertility common with hepato- renal disease
 - ◆ Up to 1/20 transplant patients have become pregnant
- Pregnancy risks post transplant:
 - ◆ Graft rejection
 - ◆ Pregnancy complications
 - ◆ Most antirejection agents are pregnancy class D
- IUD, hormonal options are category 2
 - ◆ Unless graft failure, rejection, allograft vasculopathy
 - COC category 4
 - IUD category 3
 - Depo, POP category 2

Medical Considerations: Rheumatoid arthritis

- DMARDs: methotrexate & leflunomide are pregnancy category X
 - ◆ Stop MTX 3 months & leflunomide 2 yrs prior to conception

Ann Rheum Dis. 1996 February; 55(2): 94-98.
J of Rheumatology. Vol 31: Supplement 69, March 2004

Emergency Contraception

Method	Dose	Efficacy
high dose estrogen	5 mg EE qd x 5	75-80%
estrogen + progestin	100 ug EE + 0.5 mg levonorgestrel po q12 hr x 2	56-89 %
levonorgestrel	(Plan B) 0.75 mg q12 x 2 (Plan B One-Step) 1.5 mg x1	60-94 %
ulipristal (ella™)	30 mg	85-98.6%
copper IUD	Insert within 5 days	99%

Cleland K, et al. Hum Reprod. 2012 Jul;27(7):1994-2000.

Emergency Contraception

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levonorgestrel	(Plan B) 0.75 mg q12 x 2 (Plan B One-Step) 1.5 mg x1	60-94 %
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Emergency Contraception

Method	Dose	Efficacy
	EC Hotline: <u>1-888-NOT-2-LATE</u>	

Take home points

- Long acting reversible contraceptives (LARCs) are preferred due to better efficacy
- Use CDC 2010 guidelines help to decide *which* method is appropriate
- Use CDC 2013 guidelines help to decide *how to* use the method
- Only a BP and PMHx is needed to initiate CHC
- Ulipristal and copper IUD are more effective forms of emergency contraception than the OTC products