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Contraception 2012

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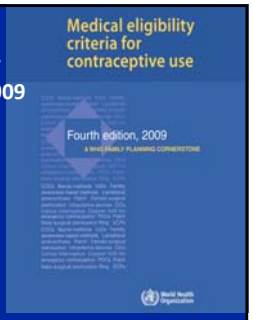
No commercial disclosures for this lecture

Do You Use the US MEC in Your Practice?

1. Every day (or more often)
2. Occasionally (a few times a week)
3. Rarely (a few times a month)
4. Never…they don't apply to my practice
5. I've never heard of them!

- WHO *Medical Eligibility Criteria* for Contraceptive Use – 3rd edition - 2009
  - www.who.int/reproductive-health/publications/mec/
  - www.reproductiveaccess.org/contraception/WHO_chart.htm



Purpose: *who* can safely use contraceptive methods

MMWR
Morbidity and Mortality Weekly Report
www.cdc.gov/mmwr
Early Release May 28, 2010 / Vol. 59

U.S. Medical Eligibility Criteria for Contraceptive Use, 2010

Adapted from the World Health Organization Medical Eligibility Criteria for Contraceptive Use, 4th edition

WHO Medical Eligibility Criteria

Categ	Definition	Recommendation
1	No restriction in contraceptive use	Use the method
2	Advantages generally outweigh theoretical or proven risks	More than usual follow-up needed
3	Theoretical or proven risks outweigh advantages	Clinical judgment that the patient can use safely
4	Unacceptable health risk if the method is used	Do not use the method

Case Study: Headaches

- Ms. K is a married 22 year old G_2 P_0 TAB_2 woman who requests a prescription for OCs
- Her first two pregnancies were at 17 and 19 years old and occurred while using condoms
- She stated that she has occasional "sick headaches"
- Recently, 2 episodes were so severe that she left work

Tension Headache

- Most common headache: 59% of reproductive aged women
- Diagnosis
  - Lasts for 30 minutes-7 days
  - At least two of
    - Bilateral location
    - Pressing/tightening in neck, scalp; non-pulsating
    - Mild-moderate intensity
    - Not made worse by physical activity
  - Both of
    - No nausea/vomiting
    - No more than 1 of photophobia, phonophobia

International Headache Society (IHS)

Tension Headache

- Improved with sleep, analgesics, relaxation
- Not associated with increased stroke risk
- No effects of menstrual cycles or exogenous hormones on frequency or severity of headaches

International Headache Society (IHS)

Migraine Headache Without Aura

aka: common or simple migraine

- Attacks last 4-72 hours (untreated or unsuccessful)
- At least 2 of the following…
  - Unilateral or bilateral temporal pain
  - Pulsating (throbbing) quality
  - Moderate or severe pain intensity
  - Aggravated by routine physical activity
- At least 1 of the following during the attack…
  - Nausea, vomiting
  - Phonophobia (sound) *and* photophobia (light)
  - Not attributed to another disorder

International Headache Society (IHS)

Migraine Headache With Aura
(aka: complex or classic migraine)

A. Meets criteria for migraine, *and* ≥2 attacks with B-D
B. Aura, with at least one fully reversible finding…
- Visual flickering lights, spots, lines *or* loss of vision
  - Flashing zig-zag line from center of visual field to periphery
- Sensory: pins and needles and/or numbness
- Dysphasic speech disturbance

International Headache Society (IHS)

Migraine Headache With Aura
(continued)

C. At least 2 other characteristics
- Homonymous visual symptoms or unilateral sensory sxs
- At least 1 aura symptom develops over ≥ 5 mins
- Each symptom lasts ≥ 5 mins and < 60 minutes

D. Headache develops during the aura or follows <60 min
- Aura without headache = "opthalmic migraine"

E. Not attributed to another disorder

International Headache Society (IHS)

Migraine Headache: Complications

- Migraine *with aura* associated with stroke risk
  - An increased relative risk
  - A low absolute risk

Condition	Odds ratio	Stroke/10,000/yr
No migraine or OCs	1.0	6
Migraine without aura	1.8	
Migraine with aura	2-4	18
Migraine + COCs	6-14	54
Migraine with smoking	7-10	
Migraine +smoking + OC	34.4	

Edlow AG, Bartz D. Rev in Obstet Gynecol, 2010; 3(2): 55-65

US MEC 2010: Headaches

	OC/P/R		POP		DMPA	Impl	LNG-IUD	Cu-IUD
Non-migrainous	1		1		1	1	1	1
Migraine	I	C	I	C	I	C		
Without aura								
– Age <35	2	3	1	2	2	2		1
– Age ≥35	3	4	1	2	2	2		1
With aura – Any age	4	4	2	3	2	3		1

I: Initiate C: Continue

Headaches and Contraception: Management

- Differentiate migraine from non-migraine headaches
  - If unclear, seek neurologist consultation
- Menstrual headaches: extended regimen OCs or NuvaRing
- CHC in women with migraines without aura
  - Use low estrogen dose product
  - Recommend frequent follow-up visits initially
  - If HA worsening frequency or severity, or new neurological symptoms, discontinue CHC
- Progestin-only methods, IUC are safe and effective

Case Study: Type 2 Diabetes

- 33 year old G_3P_3 woman with gestational diabetes diagnosed in 2nd pregnancy
- No insulin between 2nd-3rd pregnancies, required insulin during 3rd pregnancy…ended 2 years ago
- Now on metformin for type 2 diabetes; considering switch to insulin due to poor control
- Would like to use a hormonal method of contraception, if possible

Diabetes and Contraception

- Progestins may increase insulin resistance, but not to the point of clinically significant ▲ blood glucose
- Estrogen increases risk of thrombosis in vessels damaged by diabetic vascular disease
- CHC may be used in diabetics in the *absence* of clinically-manifest vascular disease, including
  - Retinopathy, nephropathy
  - Peripheral vascular disease, heart disease

US MEC 2010: Diabetes

	OC/P/R	POP	DMPA	Impl	LNG-IUD	Cu-IUD
History of gestational diabetes	1	1	1	1	1	1
Nonvascular disease						
i. Noninsulin-dependent	2	2	2	2	2	1
ii. Insulin-dependent	2	2	2	2	2	1
Nephropathy/retinopathy/ neuropathy	3/4	2	3	2	2	1
Other vascular disease or diabetes of >20 yrs' duration	3/4	2	3	2	2	1

Diabetes and Contraception: Management

- Adjust insulin or oral hypoglycemic as necessary
- Combined hormonal contraceptives
  - Evaluate CV risk profile
  - Use low E (thrombosis) + low P (glucose control)
  - If possible, co-manage with primary care provider
- Progestin only methods
  - May cause insulin resistance and ▲blood glucose, but usually clinically insignificant
  - Do not increase risk of arterial thrombosis
- IUCs are safe and effective choice
- *Discuss preconception care with all diabetic women*

Case Study: Liver Disease

- 24 year old G_2 P_0 TAB_2 woman would like to use "the Pill" or OrthoEVRA patch
- Previous history of IV drug use, but now clean
- Has 4 or 5 sexual partners per year
- Tested positive for hepatitis B virus (HBsAg+) 2 years ago; liver enzymes are mildly elevated
- Tested negative for hepatits C and HIV
- Occasional drinker; no longer smokes

US MEC 2010: Liver Disease

		OC/ P/R	POP	DMPA	Imp-plant	LNG-IUS	Cu-IUC
Cirrhosis	Mild, compensated	1	1	1	1	1	1
	Severe, decomp-ensated	4	3	3	3	3	1
Viral hepatitis	Acute or flare	I:3/4 C:2	1	1	1	1	1
	Carrier/ Chronic	1	1	1	1	1	1

Liver Disease and Contraception: Management

- Few studies of CHC and liver disease
- Combined hormonal contraceptives
  - Determine the specific diagnosis
  - Order/review liver function tests
  - If no/ minimal ▲: OK to start; repeat LFTs in 2-3 mo
- Progestin only methods have no effect on liver disease
- IUCs are safe and effective choice

Case Study: Obese Adolescent

- 19 year old G_0 woman is seen for a periodic health screening visit (aka, a "Well Woman" visit)
- In monogamous relationship for the past year
- Feeling well; no complaint of vaginal discharge, abnormal bleeding, dyspareunia
- Weight: 210 lbs; BMI: 32 kg/m^2
- Using contraceptive patch; asks about use of DMPA
- Questions…
  - Which methods are best relative to her BMI and age?

Body Weight and Contraception

- Four issues about body weight relate to each method
  - Will the method cause excess weight gain?
  - Is the failure rate higher in obese women?
  - Are there medical risks attributable to the method in obese women (compared average weight)?
  - What is the WHO-MEC category and why?
- Pregnancy and childbirth among obese women are far more dangerous than are contraception or sterilization

Body Weight and Contraception

	OC	Patch	DMPA	Implant	IUC	Tubal
Weight gain	No	No	Yes*	No	No	No
↑ failure rate in obese	No Δ	Yes #	No Δ	No Δ	No Δ	No Δ
Medical risk in obese women	↑DVT risk	No studies	None	None	Difficult insertion	Surgical complications
US-MEC	2	2	1/2 **	1	1	Not rated

* Mainly in obese adolescents and those who experience a >5% body weight increase within 6 months of DMPA initiation

\# If weight > 90 kg, increase of 2-4 failures/ 100 couples/year

** < 18 yrs of age and ≥30 kg/m^2 BMI

Obese Adolescent and Contraception: Management

- DMPA is not an ideal choice for her because of the potential for additional weight gain
  - If DMPA chosen, obtain a baseline weight and recheck in 6 months
- All methods work as well in obese women as with average weight women, except the contraceptive patch
- The efficacy of emergency contraceptive pills is poor in obese women
- IUCs and implants are an excellent choice for adolescents, obese women, and obese adolescents

Case Study: Breast Lump in OC User

- 41 year old G_2P_2 lawyer using OC's for 9 years
- Regular withdrawal bleeds; wants to continue
- Past history is unremarkable
- Breasts nodular; 3 x 3 cm "prominence" R-UOQ
  - No fixation; no nipple discharge
- At breast clinic, told that biopsy not needed
  - Plan to "observe" over the next 3 months
  - "Up to the GYN" to decide whether to continue on OC's

Breast Disease: US MEC 2010

	OC/ P/R	POP	DMPA	Imp-plant	LNG-IUS	Cu-IUC
Undiagnosed breast mass	2	2	2	2	2	1
Family history of breast cancer	1	1	1	1	1	1
Benign breast disease	1	1	1	1	1	1
Breast cancer; current	4	4	4	4	4	1
Past breast cancer (no evidence of current disease for 5 years)	3	3	3	3	3	1

Contraception in a Woman with a Breast Mass

- Women with (biopsy-proven) fibroadenoma may use hormonal contraceptive methods
- CHC users with abnormal breast findings
  - Guidelines recommend continuation of CHC until diagnosis is made; inform client of risks/ benefits
  - Non-suspicious findings: plan follow-up exam
  - Suspicious findings: specialist referral for diagnostic mammogram *and* FNAC

Contraception in a Woman with a Breast Mass

- Based on US-MEC criteria (category 2), *continue* OCs during observation period
- Given age & findings, order diagnostic mammogram
- Management plan explained to the patient…she was willing to follow this plan
- Reference algorithms for breast abnormalities
  - *http://qap.sdsu.edu/screening/breastcancer/bda/index.html*

Case Study: Seizure Disorder

- 26 year old woman is seen with a request for oral contraceptives
- She has had a seizure disorder since age 17; using carbamazepine (Tegretol) daily
- Seizures usually are well controlled, but she still experiences occasional episodes
- Last visit to neurologist was 4 yeears ago; carbamazepine prescriptions are provided by PCP
- Is she a good combined OC candidate?

Seizure Disorders

- Goals of contraceptive management of women with seizure disorders
  - Seizure control with anti-epileptic drugs (AEDs)
  - Highly effective contraception, as exposure to some AEDs is associated with congenital anomalies
  - Minimize drug interaction of AEDs and contraceptive
- *Enzyme inducing* AEDs reduce CHC efficacy by
  - ▲ "secondary metabolism" of both E + P by induction of CYP450 (3A4) enzymes
  - ▲ SHBG → ▼free progestin (less so with EE)

AEDs: *Non* Inducers of Hepatic Enzymes

Generic name	Brand name
Ethosuximide	Zarontin
Levetiracetam	Keppra
Tiagabine	Gabitril
Valproic acid	Depakene, Depakote
Vigabatrin	Sabril
Zonisamide	Zonegran
Clonazepam	Klonopin
Pregabalin	Lyrica

Enzyme Inducing Anti-Epileptic Drugs (AEDs)

Drug	Brand name	E reduction	P reduction
Carbamazepine	Tegretol ®	42%	58%
Felbamate	Felbatol ®	13%	42%
Oxcarbazine	Trileptal®	48%	32%
Phenobarbital	generic	64-72%	None
Phenytoin	Dilantin ®	49%	42%
Topiramate (>200 mg only)	Topamax ®	15-33%	None

Thorneycroft I, Epliepsy and Behavior 2006;9:31

Other Uses of EI-AEDs

Drug	Brand name	Common Other Uses
Carbamazepine	Tegretol ® Equetro ®	Trigeminal neuralgia, schizo-phrenia, bipolar disorder
Felbamate	Felbatol ®	Neuropathic pain, migraines
Lamotrigine	Lamictal ®	Bipolar, PTSD
Oxcarbazine	Trileptal®	Bipolar, neuropathic pain
Phenobarbital	generic	None
Phenytoin	Dilantin ®	None
Topiramate	Topamax ®	Migraines, bipolar, obesity

Management of Women Using EI-AEDs

- Ideal contraceptives
  - IUCs (Mirena, ParaGard)
  - DMPA: high efficacy; improves seizure control
    - No drug interactions with any AED
    - Unknown if DP-104 reduces seizure activity
- Oral contraceptives…non-evidence based
  - Use at least 35 mcg EE + high progestin product
  - Shorten hormone free interval to 4 days or less
- Avoid "low progestin" contraceptives
  - OrthoEvra patch; progestin only pills

Thorneycroft I, Epliepsy and Behavior 2006;9:31

Lamotrigine (Lamictal)

- Each drug increases the metabolism of the other
- In a lamotrigine (single drug) users started on OCs
  - Lamotrigine levels drop by 49% (41-64%)
  - Seizure activity increases
  - Side effects of lamotrigine ▲when OC stopped
- If using OCs, use higher start dose of lamotrigine
- If using lamotrigine and initiating OCs
  - Double lamotrigine dose *before* starting OCs
  - If side effects in HFI, reduce lamotrigine by 25% in HFI
  - Before stopping OCs, cut lamotrigine dose by half
- No effect of progestin only methods on lamotrigine

2010 US-MEC: Lamotrigine

- OC/P/R are considered US-MEC 3 because pharmacokinetic studies show levels of lamotrigine decrease significantly during COC use
- This recommendation applies *only* where lamotrigine monotherapy is taken with COCs
- Anticonvulsant treatment regimens that combine lamotrigine and non-enzyme inducing AEDs (such as sodium valproate) do not interact with COCs

2010 US Medical Eligibility Criteria

Drug	OC	P/R	POP	DMPA	Implant	Cu-IUC	LN-IUC
Rifampin (E-I)	3	3	3	1	2	1	1
E-I Anticonvulsants	3	3	3	1	2	1	1
Lamotrigine	3	1	1	1	1	1	1
Antifungal drugs	1	1	1	1	1	1	1
Other antibiotics	1	1	1	1	1	1	1

Case Study: A History of Depression

- 28 year old G_0 P_0 woman using 20 ug EE monophasic OC for 2 years; no problems
- Feeling sad over the past 3 months, so tried St John's Wort tablets with no effect
- Her family medicine clinician recommended that she try fluoxetine (Prozac)
- Is the Pill making her depression worse?
- Will anti-depressants reduce OC efficacy?

Do Hormonal Contraceptives Cause or Worsen Depression?

- Older studies suggested that progestins *could*
  - Make pre-existing depression worse
  - *Cause* depression in a small % of users
  - "More likely" with progestin-only methods
- Newer (and better) studies show that *none* of these assertions is correct
- 2010 US Medical Eligibility Criteria
  - *All* methods are categorized as "US-MEC-1"

St John's Wort and OC Use

- St John's Wort widely used for depression
- Many studies show induction of CYP450 (3A4)
  - "Comparable to rifampin and carbamazepine when given for ≥10 days" (Markowitz, NEJM 2003)
- Studies of SJW in OC users

Study	Hormone level	ovulation	Follicle growth
Hall 2003	P, E ▼	no	NA
Pfrunder 2003	P ▼42%	no	no
Murphy 2006	P ▼15%	probable 38%	yes

- "Caution patients that OC effectiveness may be reduced"

OCs and Treatment of Depression and Bipolar Disorder

- Depression
  - Possible effect: St John's Wort
  - No effect
    - SSRIs (fluoxetine), SNRIs (venlafaxine)
    - Tricyclics (imipramine, amitryptaline)
- Bipolar Disorder
  - Enzyme-inducing anti-epileptic drugs (WHO-3)
    - Carbamazepine, Oxcarbazine, Lamotrigine, Topiramate
  - No effect
    - Lithium, Aripiprazole (Abilify), Valproate

Depression and Contraception Management

- If started on OCs (or patch, ring) and St John's wort continued, counsel regarding possibility of reduced method effectiveness
- Acceptable methods: all
- Unacceptable risk: none

Inflammatory Bowel Disease USMEC 2010

CONDITION	COC/ P/R	POP	DMPA	Imp-lants	LNG-IUD	Cu-IUD
IBD (Ulcerative colitis, Crohn's disease)	2/3	2	2	1	1	1

For women with IBD with increased risk for VTE (active or extensive disease, surgery, immobilization, steroid use, vitamin deficiencies, fluid depletion), the risks for COC/P/R use generally outweigh the benefits

Case Study: Breastfeeding

- A 30 y.o. female is PPD#2, ready to be discharged from hospital and desires contraception. She plans to breastfeed.
- Which hormonal methods are safe for her to use?

Post-partum Contraception: General Considerations

- Goals in choice of postpartum (pp) contraception
  - Efficacy: limit family size, adequate birth spacing
  - Support successful breastfeeding
  - In GDMs, avoid conversion to frank diabetes
- Most women begin intercourse within 1-2 months
  - 60-70% are sexually active by 6 weeks pp
  - 4% abstinent by the end of the 12th pp week

Post-partum Ovulation Patterns

- Resumption of ovulation in non-lactating women
  - Ovulate in 6-7 wks (median= 45 days)
  - None before 25 days from the delivery
- Resumption of ovulation in lactating women
  - Intensity, frequency, duration of suckling
  - Time elapsed since delivery
  - Maternal nutritional state
  - Rate of weaning: rapid > gradual weaning
  - Introduction of supplementary feeding (ovulation usually begins 6 weeks later)

Post-partum OC's: Effect on Lactation

- Quality (composition) of breast milk
  - No change, including iron and copper levels
- Quantity of breast milk
  - If started *before* establishment of lactation, high dose estrogen decreases quantity
  - If started *after* lactation is established, low dose OCs have minimal effect on quantity
- POPs have no effect on quantity or content milk
- Duration of BF: 3.7 mo OCs vs. 4.6 mo controls

Post-partum OC's: Newborn Risk

- 1% of ingested drug secreted in milk
- Ethinyl estradiol dose reaching newborn is comparable to daily ovarian estradiol production
- Effect of OCs on development of infants
  - No short term metabolic differences vs. controls
  - A long term (5 year) study shows no effect on neurological development
- Newborn growth rates not affected by OC use
  - Any loss of milk volume compensated by increased suckling or food supplements

Post-partum OC's: Maternal Risk

- Changes in maternal clotting factors persist for 4-6 weeks after term delivery
  - Increased VTE risk up to 4-6 week post-partum
- Concern that coagulation effects from each of pregnancy *and* OC's may increase risk of VTE
  - However, VTE rates have not been studied in postpartum low-dose OC users vs. controls
- Greater VTE risks not expected with progestin only methods, since no change in clotting factors

Post-partum Long-acting Progestins

- DMPA
  - Mildly lactogenic; no change in milk content
- Implant (Implanon, Norplant studies)
  - No effect on milk volume, content, or growth
- Administration before hospital discharge
  - Advantage
    - Protected if post-partum visit is missed
  - Disadvantages
    - Unnecessary for first 4 weeks
    - Anatomic bleeding vs. drug side effect

Postpartum Combined Hormonal Contraceptives (CHC)

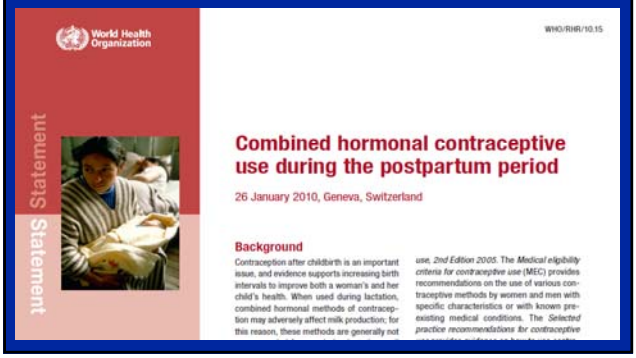
Non-breastfeeding Women

Post-partum interval	COCs/P/R
< 21 days	3
≥ 21 days	1

WHO Medical Eligibility Criteria for Contraceptive Use, 2009

US Medical Eligibility Criteria for Contraceptive Use, 2010

Guidance from WHO: September 2010



World Health Organization

WHO/RHR/10.15

Statement

Statement

Combined hormonal contraceptive use during the postpartum period

26 January 2010, Geneva, Switzerland

Background

Contraception after childbirth is an important issue, and evidence supports increasing birth intervals to improve both a woman's and her child's health. When used during lactation, combined hormonal methods of contraception may adversely affect milk production; for this reason, these methods are generally not

use, 2nd Edition 2005. The *Medical eligibility criteria for contraceptive use* (MEC) provides recommendations on the use of various contraceptive methods by women and men with specific characteristics or with known pre-existing medical conditions. The *Selected practice recommendations for contraceptive*

Revised WHO MEC 2010

Postpartum CHC; Non-breastfeeding

	WHO MEC
a) < 21 days postpartum	
i) without other risk factors for VTE	3
ii) with other risk factors for VTE	3/4
b) ≥ 21 days to 42 days postpartum	
i) without other risk factors for VTE	2
ii) with other risk factors for VTE	2/3
c) > 42 days postpartum	1

US MEC 2011 Revision
Postpartum CHC; Non-breastfeeding

	US MEC
a) < 21 days postpartum	4
b) ≥ 21 days to 42 days postpartum	
i) without other risk factors for VTE	2
ii) with other risk factors for VTE	2/3
c) > 42 days postpartum	1

US Medical Eligibility Criteria 2010
Post-partum Breastfeeding

CONDITION	OC/P/R	POP	DMPA	Implant
<1 month postpartum	3	2	2	2
1 month to 6 months	2	1	1	1
> 6 months postpartum	1	1	1	1

US Medical Eligibility Criteria 2010
Postpartum IUC Insertion

Postpartum (BF or non-BF women) including caesarean section	LNG-IUS	Cu-IUD
< 10 min after delivery of placenta	2	1
10 min after delivery of placenta to < 4 wks	2	2
≥ 4 wks post partum	1	1
Puerperal sepsis	4	4

History of Bariatric Surgery
USMEC 2010

	OC/P/R	POP	DM PA	Imp lant	Cu IUC	LN-IUC
Restrictive procedures: decrease stomach storage capacity	1	1	1	1	1	1
Malabsorptive procedures: shorten functional length of the SB	COCs: 3 P/R: 1	3	1	1	1	1

Bariatric procedures with a malabsorptive component have the potential to decrease OC effectiveness, further decreased by long-term diarrhea and/or vomiting

Peripartum Cardiomyopathy
USMEC 2010

	OC/P/R	POP	DM PA	Imp lant	Cu-IUC	LN-IUC
Normal or mildly impaired cardiac function						
<6 mo	4	1	1	1	2	2
>6 mo	3	1	1	1	2	2
Moderately or severely impaired cardiac function	4	2	2	2	2	2

Solid Organ Transplantation
USMEC 2010

	OC/P/R	POP	DM PA	Impl ant	Cu-IUC	LN-IUC
Complicated: graft failure, rejection, cardiac allograft, vasculopathy	4	2	2	2	I = 3 C =2	I = 3 C =2
Uncomplicated	2	2	2	2	2	2

Women with Budd-Chiari syndrome should not use COC/P/R because of the increased risk for thrombosis

10 (+1) Recommendations To Improve Contraceptive Care *Now*

1. **Pelvic exam? It isn't mandatory**
   - Do not require pelvic examination before you prescribe an oral contraceptive.
2. **Provide more, not less**
   - Prescribe (when possible, dispense) 6 to 12 months of an OC at office visits
3. **Make the case for long-acting reversibles**
   - Use intrauterine devices and subdermal implants as first-line contraception more often

OBG Management · 2011; 23 (8): 25-29

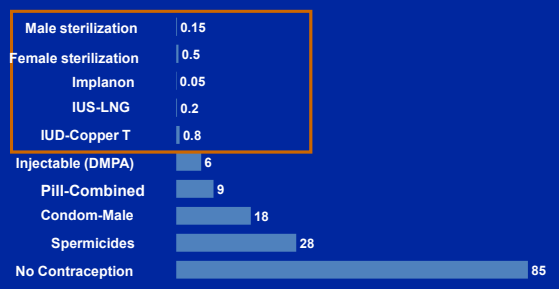
Why LARC* Methods?
*Long Acting Reversible Contraception

- IUCs and Implants are "forgettable"
  - Single motivational act for insertion
  - Do not require episodic, daily, weekly, monthly, or every 12 week user initiative
  - No need to take time to refill prescriptions or risk that prescriptions will not be refilled on time
  - Give continuous 24/7/365 contraceptive protection
  - Provide long term protection…3-10 years

Why LARC* Methods?
*Long Acting Reversible Contraception

- Are the most effective reversible methods available
- Are among the safest contraceptive methods…very few US-MEC category 3 or 4 grades
- Have superior continuation rates and highest patient satisfaction among methods
- Are an alternative to surgical sterilization
- Are the most cost effective and cost saving methods

Efficacy: 1st Year Failure Rates of Select Contraceptives (Typical Use)



Adapted from Trussell J. In Hatcher RA, et al. *Contraceptive Technology: 20th ed*, 2011.

The Contraceptive CHOICE Project

- Prospective cohort study enrolled 9256 women, 8/07-9/11
  - 14 to 45 years of age
  - No desire for pregnancy for at least the next 12 months
  - Spoke English or Spanish
  - Lived in the St. Louis region and recruited by providers, newspaper reports, study flyers, and word of mouth
- Not currently using a contraceptive method or were willing to switch to a new reversible contraceptive
- All participants chose a method and received it at no cost

Continuation and Satisfaction of Reversible Contraception

Peipert JF, et al. Obstet Gynecol 2011;117:1105–13

- Analyzed 12-month data from the first 5,087 participants enrolled in the CHOICE Project
- 4,167 participants who received a method within 3 months of enrollment and reached the 12-month telephone survey
- Findings
  - 68% LARC (45% LNG-IUS, 10% Cu-IUD, 13% implant)
  - 23% CHC (11% OCPs, 10% CVR, and 2% patch)
  - 8% DMPA

The Contraceptive CHOICE Project

	n	1 year continuation %	% Very satisfied	% Not satisfied
LNG-IUS	1,890	88	70	14
Cu- IUD	434	84	66	20
Implant	522	83	55	21
LARC	2,846	86	67	16
DMPA	313	56	42	46
OCPs	478	55	41	46
Patch	99	49	35	56
CVR	431	54	47	47
Non-LARC	1,321	55	43	47

Peipert JF, et al. Obstet Gynecol 2011;117:1105–13

Acceptance Of LARC Methods By Adolescent Participants In The Contraceptive CHOICE Project

Mestad R, et al, Contraception 2011; 84 493–498

- Of 5086 women, 70% of participants chose a LARC method
- Among adolescents aged 14–20 years
  - 69% of 14–17-year-olds chose LARC
  - 61% of 18–20-year-olds chose LARC (RR: 1.16, 1.03–1.30)
- Among adolescents choosing a LARC method
  - 63% of 14–17-year-olds chose the implant
  - 71% of 18–20-year-olds chose the IUD

Effectiveness of LARC

Winner B, Peipert JF, et. Al. N Engl J Med 2012;366:1998-2007

- Among 7486 women, there were 334 unintended pregnancies
- Contraceptive failure rates per 100 participant-years
  - OCs, patch, or ring (PPR) 4.55
  - LARCs 0.27
  - Hazard ratio 21.8; CI= 13.7-34.9
- Among users of PPR, women <21 years old had an unintended pregnancy rate almost twice as high as older women
- Rates of unintended pregnancy were similarly low among participants using DMPA, IUD, or implant, regardless of age

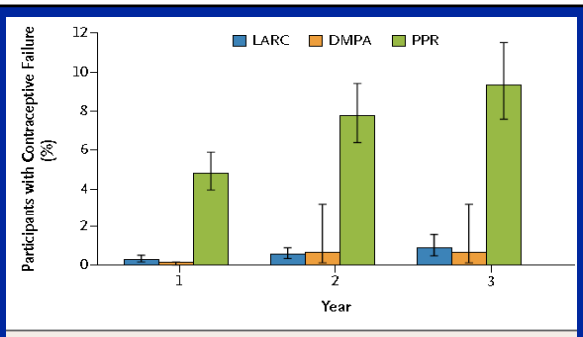
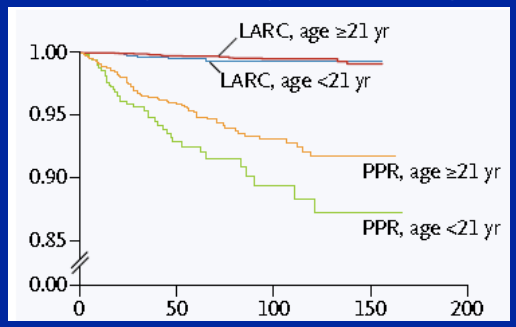


Figure 1. Cumulative Percentage of Participants Who Had a Contraceptive Failure at 1, 2, or 3 Years, According to Contraceptive Method.

Winner B, Peipert JF, et. Al. N Engl J Med 2012;366:1998-2007.

Probability of Not Having an Unintended Pregnancy According to Contraceptive Method and Age



Winner B, Peipert JF, et. Al. N Engl J Med 2012;366:1998-2007.

The CHOICE Project: What's the "Secret Sauce"?

- Structured presentation of contraceptive options, starting with top tier methods
- Availability of LARC methods, on site…now!
- Removal of cost barriers

10 (+1) Recommendations To Improve Contraceptive Care *Now*

4. Take advantage of broader benefits
   - Use hormonal contraceptives for non-contraceptive indications
5. To encourage continuation, begin now
   - Get a "quick start" to improve adherence to oral contraceptives
6. Move away from every-day regimens
   - Consider a nondaily combined method, such as the patch or the vaginal ring, for current OC users

OBG Management · 2011; 23 (8): 25-29

10 (+1) Recommendations To Improve Contraceptive Care *Now*

7. Preemptive prescribing
   - Prescribe EC before your patient needs it
8. Pursue two urogenital pathogens
   - When you are not performing a speculum examination, screen for *N. gonorrhoeae* and *C. trachomatis* with a vaginal swab specimen or urine-based specimen
9. Get to know Ella
   - Become familiar with ulipristal acetate (Ella) for EC

OBG Management · 2011; 23 (8): 25-29

Emergency Contraceptive Products

- FDA age threshold for OTC dispensing
  - Available without prescription if 17 y.o. or older
  - Prescription only for women under 17 y.o.
  - Pharmacist may require proof of age
- Plan B® One-Step (now Teva; previously Duramed)
  - Single dose tablet ; 1.5 mg levonorgestrel
  - Labeled for 72 hours from last intercourse
  - Plan B (2 tablet product) is no longer available
- Next Choice® (generic/ Watson Pharma)
  - Same as the two tablet Plan B® product
  - Labeling: 1 tab Q12 hrs; off label: 2 tablets at once

Ulipristal Acetate (UPA): Ella®

- Selective progesterone receptor modulator
- Taken orally in single 30 mg dose
- Approved in Europe (2009) for up to 5 days
- Mechanism of action
  - Prevent ovulation, with follicles up to 18-20 mm
  - Inhibits implantation, but higher dose required
- Failure rate vs. LNG (meta-analysis 0-120 hours after last sex)
  - UPA 1.3% vs. LNG 2.2%
  - Odds Ratio = 0.55 (0.32-0.93)

Ulipristal Acetate (UPA): Ella®

Glasier AF, Lancet 2010;375:555

- Comparative trial of UPA 30 mg vs LNG 1.5 mg
  - 1,696 women used with 72 hours of intercourse
    - Failure rates: UPA 1.8% vs. LNG 2.6% (OR=0.68)
  - 203 women used with 72-120 hrs of intercourse
    - Failures: UPA- none vs. LNG- 3 pregnancies
  - Headache: UPA=19%, LNG=19%
- Conclusion
  - UPA is “not inferior” to LNG
  - UPA is effective for up to 5 days after exposure

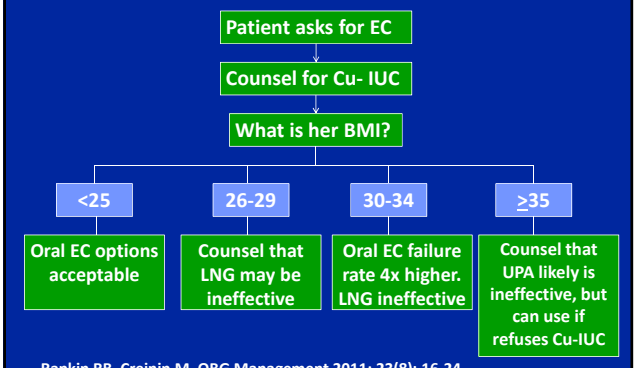
EC Failure and Body Weight

- Compared with women of normal weight (BMI <25)
  - Overweight women (BMI 25–30) had a risk of pregnancy 1.5 times greater
  - Obese women (BMI ≥30) had a risk of pregnancy more than three times greater

Why?

- Two recent have demonstrated that OC hormone absorption is slower in obese women than it is in women of normal weight

Rapkin RB, Creinin M, OBG Management 2011; 23(8): 16-24



Rapkin RB, Creinin M, OBG Management 2011; 23(8): 16-24

10 (+1) Recommendations To Improve Contraceptive Care *Now*

10. Now not later: An IUD, post-evacuation
    - Consider immediate, rather than delayed, IUD insertion after uterine evacuation for spontaneous or elective abortion in women who desire this form of contraception
11. Offer office-based hysteroscopic sterilization

OBG Management · 2011; 23 (8): 25-29

IUDs in Development

LNG20

Developer: Medicines 360

- 20mcg/day levonorgestrel compared to Mirena over 5 years
- Aim to improve use from 5 to 7 years and reduce cost
- Estimated study completion date: 12/2018

LNG-IUS12/16

Developer: Bayer/Schering

- Lower dose LNG 12 mcg and 16 mcg levonorgestrel compared to Mirena;
- Early studies show products provided effective contraception and were well tolerated
- NDA filed Dec 2011; awaiting FDA approval

Ring in Development

Nestorone/ Ethinyl Estradiol 1-Year Ring (CVR)

Developer: Population Council

- Releases 150 mcg Nestorone and 15 mcg ethinyl estradiol/day over 3-week period
- Used like NuvaRing
- Lasts for 13 cycles
- Awaiting FDA approval

NES / EE Core

8.4 mm (3/8") in cross section

58 mm (2 1/4") in diameter

Injectables in Development

Depo-SubQ Provera 104 *(DMPA-SC)* in Uniject

Developer: Pfizer

- Single, sterile, prefilled dose in a non-reusable package
- Easier to use and store (better access and continuation)
- Roll-out expected in 2013 (price issue)

Cyclofem

Developer: Concept Foundation

- Monthly injectable
- Concept Foundation seeking FDA approval which would allow reintroduction to the US market

http://www.path.org/projects/uniject-dmpa.php ;
http://www.conceptfoundation.org/hormonal-contraception.php

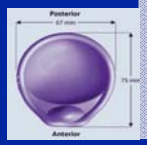
Female Condom in Development

Women's Condom

Developer: PATH

- Polyurethane condom pouch
- Foam dots that improve adherence to vaginal walls
- Soft outer ring
- Dissolving capsule

Diaphragm in Development



SILCS Diaphragm

Developers: PATH and SILCS, Inc.

- Cervical barrier device, one-size-fits most
- Developed with input from women and men in multiple countries
- Regulatory applications underway in Europe and US

OCs in Development

Quartette™ (Teva)

- OC continuous regimen of LNG 0.15mg /EE 20ug x42d
- 25ug x21d,
- 30ug x21d

Yaz Flex (Bayer)

- OC extended regimens of DRSP 3mg /EE 20ug

Nomac/E2 (Merck)

- Nomagestrel acetate 2.5mg
- 17-ß estradiol 1.5mg

Pill-Plus / ARC (BioSante & Pantarhei)

- OC containing estrogen, progestin, and androgen

Patches in Development

AG200-15 (Twirla™)

Developer: Agile Therapeutics

- NDA submitted for low-dose, once-weekly patch consisting of EE plus LNG
- Decision expected by first quarter 2013

BAY86-5016 (FC Patch low)

Developer: Bayer HealthCare Pharmaceuticals

- Ongoing Phase III trial of patch consisting of EE and gestodene