

Contraceptive Technology Update

*Eva Lathrop, MD
Fellow, Family Planning Division
Department of Gynecology and Obstetrics
Emory University School of Medicine*

CONTRACEPTIVE TECHNOLOGY UPDATE

The Objective!

- *Review the latest contraceptive evidence for:*
 - *Extended use of combined pills*
 - *Quick Start initiation*
 - *The new progestin*
 - *The ring and the patch*
 - *Depo-provera and bone health*
 - *New guidelines for IUD use*
 - *The progestin-only implant*
 - *The importance of counseling*

What is the big picture?

- *Global Perspective:*
 - *Nearly 200 million women worldwide want to prevent pregnancy but are not using contraception*
 - *Without access to contraception, millions will become unintentionally pregnant each year*

Big Picture continued...

- **Domestic Perspective:**
 - *Half of all pregnancies in the US are unintended*
 - *Results in 1.4 million unplanned births and 1.3 million induced abortions yearly*
 - *Only 7% unmet need for contraception among women of reproductive age*
 - *Only half are fully protected from pregnancy*
 - *The average American woman spends 3 decades trying not to get pregnant...*

Let's talk about family planning...

New Combined Oral Contraceptives

- **Shorter withdrawal bleeds**
 - Loestrin 24 Fe™
 - Yaz™
- **Fewer withdrawal bleeds**
 - Seasonique™
 - Seasonale™
- **No withdrawal bleed**
 - Lybrel™



Cochrane Review

- *Bleeding*
 - *No difference or less bleeding/spotting with continuous dosing*
- *Menstrual associated symptoms*
 - *Headache, tiredness, bloating, cramping improved*
- *Compliance*
 - *No difference found*

Edelman 2005

Cochrane Review

- *Patient Satisfaction*
 - *Not well studied*
 - *Most women satisfied equally with either treatment*
- *Adverse events*
 - *No difference*
- *Safety*
 - *RCTs have little capacity for studying long-term outcomes*

Edelman 2005

Contraceptive Initiation

- *PWOP**
 - *Pills (patch, ring, depo) without a pelvic*
 - *Avoiding barriers*



*Planned Parenthood terminology
Stewart F, JAMA. 2001

Contraceptive Initiation

- Organizations that support without an exam
 - 1994 FDA
 - 1994 WHO
 - 1996 PPFA
 - 1996 ACOG
 - 2000 RCOG



Stewart F. JAMA, 2001

Initiation Timing

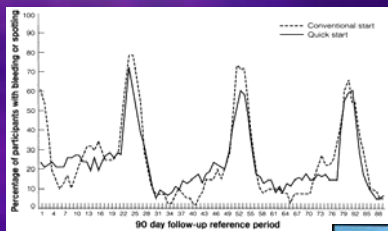
- Sunday start*
- Anytime during menses*
- Immediately (Quick start)*
- Immediately after abortion or miscarriage
- Immediately after EC*
- 3 weeks postpartum



*Backup method for 7 days is a good idea!

Westoff 2002, 2003; Lara-Torre 2002

Quick Start



Westoff 2002, 2003; Lara-Torre 2002

Hormonal Components

- **Progestin component**
 - 1st norethindrone
 - 2nd levonorgestrel
 - 3rd desogestrel
 - 4th antimineralocorticoid activity (drospirenone)
- **Estrogen component**
 - Ethinyl Estradiol
 - High (≥ 50 mcg)
 - Low (≤ 35 mcg)

The Newest Progestin



- **Drospirenone, in Yasmin™ and Yaz™ combined oral contraceptives**
- **Minimal diuretic and no androgenic effects**
- **Decreased PMS and PMDD-associated symptoms more than placebo**

Pearlstein 2005

Risk of Hormonal Components

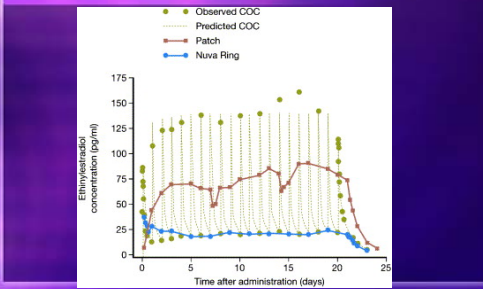
- **Thrombosis risk**
 - 4-5/100,000 reproductive-aged women
 - 12-20/100,000 low-dose OC users
 - Estrogen level
 - Progestin type?
 - Patch vs. ring. vs. pill
 - 48-60/100,000 pregnant women

Farmer R, J Obstet Gynaecol 1995; Abdollahi M, Thromb Haemost 2003; Lidegaard O, Contraception 2002; Jick, Contraception 2006

Hormonal Components

- *Patch and Ring*
 - *Both are estrogen and progestin containing contraceptive methods*
 - *Any patient with a contraindication to estrogen has a contraindication to the patch and the ring (and the pill)*

Patch vs. Ring vs. Pill



Wilhemius Van Den Heuvel, Contraception 2005

Thrombosis & the Ring

- *Delivers 15 mcg EE and 120 mcg etonogestrel per day*
- *No difference in the effects on coagulation and fibrinolysis vs. the pill*
- *No long-term data on risk of venous thromboembolism vs. the pill*

Magnusdottir EM et al., Contraception, 2004.

Thrombosis & the Patch

- Designed to deliver 20mcg EE and 0.15 mg norelgestromin daily
- In actuality:
 - Steady state blood levels have been shown to be up to 60% higher than for 35mcg EE pill
 - Peak hormone levels are lower than a 35mcg EE pill

What does this mean?

- Company and FDA issued a warning
- 2007 Cole et al.
 - 49,048 women-years of exposure
 - RR 2.2 (95% CI 1.3-3.8)
- 2006 Jick et al.
 - 58,752 women-years of exposure
 - RR 1.1 (95% CI 0.7-1.8)
- 2007 Jick et al.
 - Additional 17 months of data
 - OR 1.1 (95% CI 0.6-2.1)
- 2008 Boston Collaborative Drug Surveillance
 - RR 2.0 (95% CI 0.9-4.1)

DMPA and Bone Mineral Density

- Suppression of hypothalamic-pituitary axis (LH) leads to low serum estrogen levels
 - Progestin can also reduce ovarian estradiol production
 - Estrogen decreases to perimenopausal levels
- Low serum estrogen decreases bone mineral density (BMD)
 - Inhibits osteoblasts (form bone)
 - Increases osteoclasts (resorb bone)

DMPA and BMD: Early Observations

- *Contraceptive doses of DMPA-IM 150 mg cause suppression of estradiol*
 - *Estrogen deficiency associated with BMD loss*
- *Estrogen deficiency induced by DMPA-IM 150 associated with decline in BMD*
 - *Resumption of ovarian estrogen production upon discontinuation of DMPA-IM 150 associated with recovery of BMD*

DMPA-IM 150 = depot medroxyprogesterone intramuscular injection, 150 mg/mL
BMD = bone mineral density

DMPA-IM 150: BMD in Current Adult Users

- *In meta-analysis of older data, BMD decreased in current users compared with nonusers, but was within 1 SD of the mean in nonusers*
- *Recent data show BMD decreases in current users*

Recovery of BMD After DMPA Discontinuation

- *Compare BMD in adult (age 25-35) women using*
 - *DMPA-IM 150 every 12 weeks, or*
 - *Nonhormonal contraception*
- *Study mandated by FDA at time of DMPA approval for contraception (1992)*

Study Design

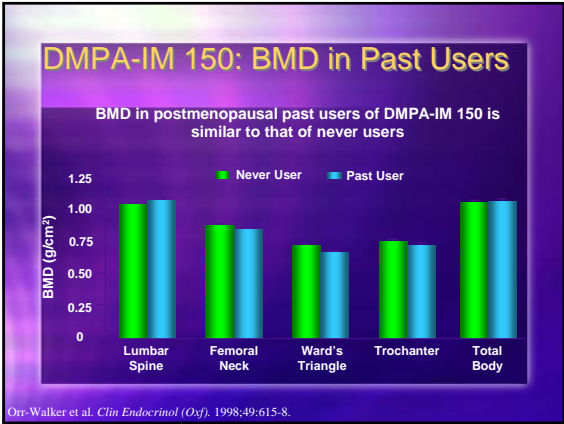
- *Open-label, prospective, matched-cohort study*
- *Treatment: up to 240 weeks (4.6 years)*
- *Post-treatment follow-up: up to 96 weeks (1.8 years)*

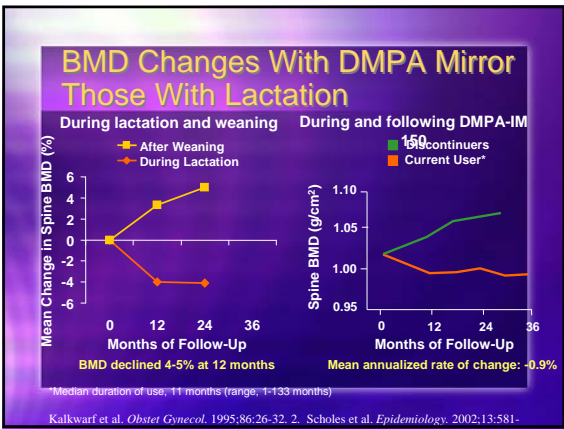
Summary of Findings

- *BMD of lumbar spine and total hip in DMPA-IM 150 users:*
 - *Declines during use*
 - *Substantial recovery following discontinuation*
- *Largest and longest term study of BMD with DMPA use*

Declines in BMD Reversible After Discontinuation of DMPA

- *In 2 cross-sectional studies, (median duration of DMPA use ~3 years in both studies) BMD in past users not significantly different from that of never users at any site*
 - *Studies evaluated premenopausal and postmenopausal past users*
- *No increased incidence of fractures noted in >30 years of worldwide use*





DMPA Recommendations

- No restriction on the use of DMPA or on the duration of use, among women aged 18 to 45
- Among adolescents and women over 45, the advantages of using DMPA generally outweigh the theoretical safety concerns regarding fracture risk. Review risk/benefits with patient.

World Health Organization 2005

LARC Methods...

- *Long acting and reversible contraception*
- *IUDs*
 - *Copper T*
 - *Levonorgestrel Intrauterine system*
- *Implants*
 - *Implanon*

IUD Practice Changes

Medical Eligibility Criteria (MEC) Changes

- *IUD use in women younger than 20 years is safe (category 2)*
- *Actinomyces, bacterial vaginosis, trichomonas, or cervicitis do not require IUD removal*
- *If PID occurs in an IUD user, treatment is the same as in non-users and removal is not necessary*

World Health Organization 2004

New Paragard™ Package Insert



- *Can include nulliparous and nulligravid women*
- *Women not in a mutually monogamous relationship*
- *Women with a history of STI's or PID that do not have current risks*
- *Women with a history of ectopic pregnancy*

Mirena LNG-IUS - what's new?

- **FDA Label changes:**
 - Cavity depth 6-10 cm
 - Pregnancy is RARE - but pregnancy with device insitu is not associated with increased risk of birth defects
 - No evidence of an increased risk of breast cancer (observational studies)
 - No adverse effects on health, growth, development of breast feeding infants
 - Removed from contraindication list - hx of ectopic or risk factors for ectopic pregnancy

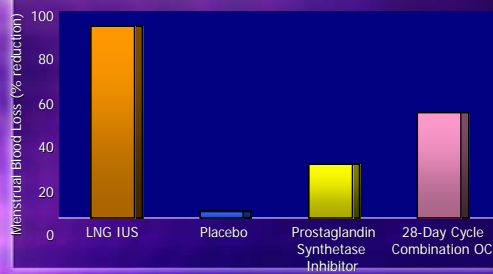
Mirena™ IUS for Menorrhagia



- Releases levonorgestrel to the endometrium over 5 years
- 77% improvement in menorrhagia at 3 months, 100% at 36 months
- Decreased uterine size and bleeding with fibroids

Kriplani 2007, Magelhaes 2007

Mirena: Reduction in menstrual blood loss



Milsom I. et al. *Am J Obstet Gynecol.* 1991

Implanon

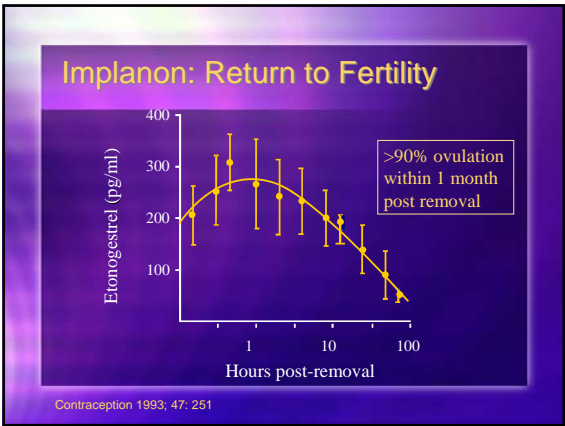
- Progestin-only single rod implant
- 40 mcg/day etonogestrel
- Effective for 3 years
- Efficacy: 99.9%

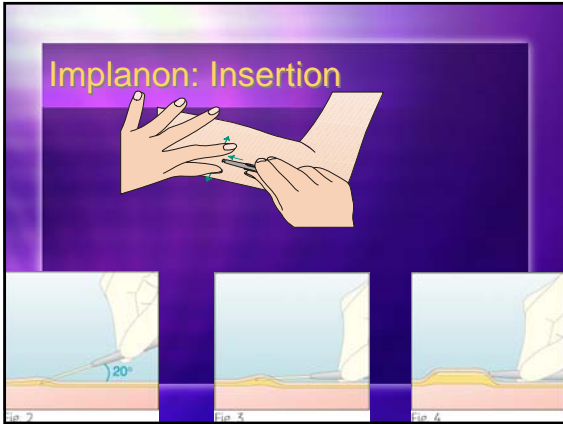



Implanon: Bleeding Patterns

Bleeding Pattern	Implanon	Norplant	Statistically Significant
Amenorrhea	22%	5%	Yes
Infrequent bleeding	27%	21%	Yes
Frequent bleeding	6%	3%	No
Prolonged bleeding	12%	9%	No

Data on file. Organon, Inc. 1999





Clinical Significance of Side Effects

- *Most symptoms reported by women on combined hormonal contraceptives are significantly worse during the placebo week – usually two times as much (Sulak, 2000)*
- *Breakthrough bleeding is the side effect most likely to lead to discontinuation of estrogen-containing methods*
- *Amenorrhea is the side effect most likely to lead to discontinuation of progestin-only methods*

So, what about side effects?

- *Common low risk side effects are the number one reason for discontinuation of chosen methods*
- *50% of pregnancies in the US are unintended*
- *150-200 million women worldwide desire fertility control, but are not using contraception - many reasons for this - one of them is fear of side effects/rumored side effects.*

Continuation Rates

% Continuation at One Year

Pills, patch, ring	68%
Condoms	60%
DMPA	56%
Copper T	78%
LNG-IUD	81%
Implanon	82%

Adapted from Espey ACOG 2008

Reasons for Discontinuation

- *Problems with access: 45%*
- *SIDE EFFECTS: 34%*
- *Other 21%*

Westhoff et al 2007

Why do women stop their chosen method?

- *Break-through-bleeding is one of the most common side effect leading to discontinuation of estrogen containing methods*
- *Amenorrhea is the side effect most likely to lead to discontinuation of progestin only methods*
- *Most women on a combined method report a two-fold increase in symptoms during the placebo week*

© Cornell 2008, Sulak 2000

What if.....

- *Decreased unintended pregnancies*
- *Decrease in teen pregnancies*
- *Decreased maternal mortality*
- *Decreased number of abortions*
- *Decreased infant mortality*
- *Strong and healthy families*
- *Women who are empowered to reach their reproductive goals*

What is our role as the Reproductive Health Care provider?

- *Help our clients navigate through the choices that are available to them*
- *Empower patients to make decisions that fit their needs.*

What about counseling?



The Importance of Counseling

- **Goal:**
 - assist women initiate and continue with the easiest and most effective method with the fewest side effects....
 - help her choose the best method for her....

New Counseling Tool

- **Contraceptive efficacy**
 - Easier for patients to understand
 - English/Spanish/French
 - Chart available at:
 - WHO: www.who.int/reproductive-health
 - FHI: <http://www.fhi.org/nr/shared/en/FHI/Resources/EffectivenessChart.pdf>

Comparing Typical Effectiveness of Contraceptive Methods



Top Tier Methods

- *Copper T IUD (Paragard)*
- *Levonorgestrel IUD (Mirena)*
- *Etonogestrel implant (Implanon)*
- *Tubal sterilization*
 - *Laparoscopic*
 - *Hysteroscopic (Essure)*

Comprehensive Counseling

- *Comprehensive counseling includes:*
 - *Efficacy*
 - *Clear directions for use*
 - *Expected side effects*
 - *Risks and benefits profile*
 - *Noncontraceptive benefits*
 - *Reminder: she is NOT locked in to staying on the initial method chosen*
 - *Encourage communication*
 - *Encourage contact BEFORE discontinuation*

Blumenfel 2008

In support of structured counseling....

- *Cochrane Review*
- *Structured counseling vs "standard" counseling*
- *One well done study showing a significant benefit to the intervention*
- *Less likely to discontinue chosen method at 12 months*
- *If they did discontinue - it was less likely to be due to menstrual disturbances or dissatisfaction*

Halpern, Grimes 2006

Follow up visits...

- *Importance of the follow up visit in terms of patient satisfaction and improved continuation rates.*
- *Components of the follow up visit:*
 - *Review instructions for use*
 - *Review actual use patterns*
 - *Ask about any side effects she is experiencing*
 - *Review strategies to manage side effects*
 - *Give her the option of switching methods*
 - *Encourage continued communication*
 - *Review her reproductive goals*

Thanks for listening!!

- *Questions?*
- *Comments?*
- *How will this change your practice?*
