

Contraceptive Update

Montana Family Planning Annual Training
Missoula, MT
March 24, 2010

Learning Objectives

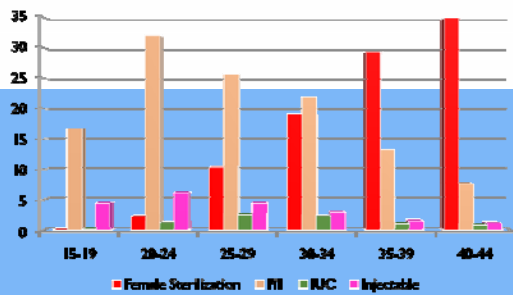
- 1 • Describe highly effective contraceptive methods available to American women
- 2 • Describe prescribing regimens that optimize contraceptive effectiveness and quality of life
- 3 • Identify contraceptive methods both newly available and in clinical trials

Who needs contraceptives?

- 62 million U.S. women
 - Are in their childbearing years (15-44)
- 7 in 10 women
 - Are sexually active and do not want to become pregnant
- A woman wanting 2 children
 - Spends roughly 30 years trying to prevent pregnancy

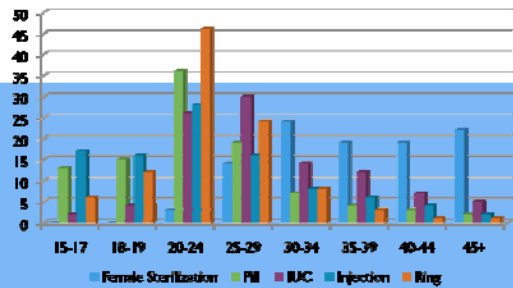
1. Mosher, WD et al. Use of Contraception and Use of Family Planning Services in the US: 1982-2002. Advance Data from Vital Health Statistics, No 350, 2004
2. The Alan Guttmacher Institute (AGI) Fulfilling the Promise: Public Policy and US Family Planning clinics. New York: AGI, 2000

Contraception Choice by Age



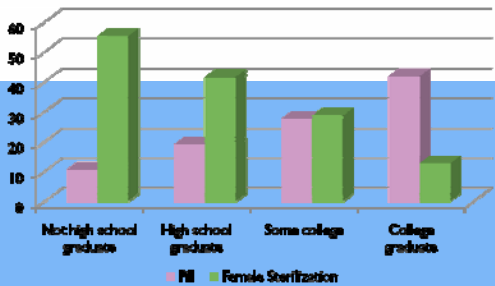
Mosher WD, et al. Advance data from vital statistics. No 350. 2004.

Contraceptive Choice by Age in Montana



Contraceptive Ending Method by Age Ahlers & Associates 2009

Contraception Choice by Education



Sterilization Regret

- Cumulative risk of regret – 12.7%
 - Women sterilized under age 30 probability 20.3%
 - Women sterilized older than 30 probability 5.9%
 - Women sterilized within 1 year of delivery probability 20.7 to 23.7%

What's been added to the Market since 2002

- New prescribing regimens
 - Shorter hormone free (pill-free) period
 - Extended use Combined Oral Contraceptive
 - Continuous Use Combined Contraceptive
- New Devices
 - Patch (Ortho Evra®)
 - CCVR (NuvaRing®)
 - Single rod implant (Implanon®)
 - LNG-IUS (Mirena®)

New Starts

- Options for COC pill initiation: On label
 - First Day – take first pill on first day of menses
 - ~~Sunday Start – take first pill on first Sunday of menses~~
 - Use a back-up method if pill initiated days 5-7 of cycle; or use back-up for 7 days regardless of cycle
 - Avoids menses on weekend
- Up to 25% of young women failed to initiate pills as instructed with these options
 - Forgot instructions, didn't fill prescription, developed worries about pill taking, conceived

Improve Compliance with Quick Start

- If reasonably sure she is not pregnant start COC pills immediately
 - If more than 5 days since onset of menses, use a back up method for seven days
- Directly observed therapy
- Increase adherence w/o increase BTB
 - 19% started day 1-7
 - 26% started day 7-15
 - 55% started day 15+

No difference in days bleeding

Westhoff C, et al. *Contraception* 2002; 66:141-145
Lara-Torre E, Schroeder B. *Contraception* 2002; 66(2): 81-85
Westhoff C, et al. *Obstet Gynecol* 2007; 09: 270-1276

Quick Start

- Increases number of women still using pills by third cycle over traditional start regimens
- Quick start is endorsed by WHO

Lara-Torre E, Schroeder B. *Contraception* 2002;66(2):81-85
WHO. *Selected practice recommendations for contraceptive use, 2nd ed. 2004*. Geneva

Quick Start in Real Life

- If she has had unprotected intercourse in the last 72-120 hours (5 days)
 - Emergency contraception immediately
 - Levonorgestrel 0.75 mg (Plan B, Next Choice) two tablets at once
 - Effective in preventing pregnancy 87-90% if taken within 72 hours and 72-87% if taken between 72-120 hours
 - Start pill pack the next day

WHO. *Selected practice recommendations for contraceptive use, 2nd ed. 2004*. Geneva
Rodrigues I, Grou R. *JOG*. 2001;184:4

Quick Start in Real Life

- If she is worried about an undetectable pregnancy
 - ▣ Start pills right away
 - ▣ Repeat urine pregnancy test in 2-3 weeks
 - The hormones of contraceptive pills will not harm a pregnancy
- If she is amenorrheic and reasonably sure she is not pregnant
 - ▣ Start pills at any time
 - ▣ Use back up contraception the first seven days

Quick Start - Patch

- Apply patch immediately and use back up contraception for 5 days
 - ▣ No difference in days bleeding between quick start and conventional start in 2nd and 3rd cycles



Murthy AS, Creinin MD, Harwood B, Schreiber CA. *Contraception* 2005;72(5):333-336

Extended Regimen - Patch

- Not Recommended
 - ▣ Lack of data
 - ▣ Higher serum estrogen levels

Van den Heuvel MW. *Contraception*. 2005;72(3):168-174

Quick Start - Transvaginal Ring

- Insert ring immediately, using back up contraception for 7 days
 - Less bleeding with ring users than quick start pill users (17 vs. 21.4 days)
 - No correlation in amount of bleeding with cycle day at initiation



NuvaRing package insert, Organon
Westhoff C, Osborne LM, Schafer JE, Morrioni C. *Obstet Gynecol*. 2005 Jul;106(1):89-96

Extended Regimen - Vaginal Ring

- Vaginal ring use suppressed ovulation (LH, progesterone, follicle diameter) over 5 weeks continuous use
- Most studies limited, looked only at postponement of withdrawal bleeding
- One study reports less pelvic pain
- Plausible to expect similar results in decreased bloating, fatigue, headache as in continuous COC use

Sulak PJ, Smith V, Coffee A. *Obstet Gynecol*. 2008 Sep;112(3):563-71

Managing BTB - Extended Ring Use

- Randomized continuous use with ring changed monthly or introduction of 4-day ring free interval if BTB/BTS for 5 days
 - Flow for both groups less on continuous use than on 21/7 regimen
 - Introduction of 4-day ring free interval has less BTB/BTS than continuous use

Sulak PJ, Smith V, Coffee A, et al. *Obstet Gynecol* 2008 Sep;112(3):563-71

Quick Start – Progesterone Injectable

- Initiate first injection within 7 days of menses
- Initiate at any time if reasonably sure she is not pregnant and use back up for 7 days
- Amenorrheic patients may initiate injection at any time if reasonably sure she is not pregnant and use back up for 7 days



WHO. Selected practice recommendations for contraceptive use, 2nd ed. 2004: Geneva

Depo Now vs. Bridge Method

- Women aged 14-26 y/o with negative urine HCG randomized to:
 - DMPA immediately
 - Bridge alternative contraception with return for injection at next menses
- Pregnancies 4 times higher in the bridge group

Rickert VI, Tiezzi L, Lipshutz J, et al. J Adolesc Health 2007 Jan;40(1):22-8

New WHO Guidelines Reinjection DMPA

- May be given up to four weeks late (up to 17 weeks from previous injection)
 - No need for testing to rule out pregnancy
 - Does not change reinjection schedule but does extend grace period from 2 weeks to 4 weeks
- DMPA dosages
 - 150 mg IM
 - 104 mg SQ

WHO. RHR. Selected practice recommendations for contraceptive use, revision of second edition. Available at www.who.int/reproductivehealth/publications/sprr/sprr_2008_update.pdf

Quick Start – Copper IUC

- If menstruating, insert within 12 days of onset or anytime if reasonably sure not pregnant
 - No back up contraception needed
- If amenorrheic, insert anytime *if it can be determined* there's no pregnancy
 - No back up contraception needed



WHO. Selected practice recommendations for contraceptive use, 2nd ed. 2004: Geneva

New Indication: IUC and Nulliparity

- Copper containing IUC approved for use in nulliparous women in 2005
 - Slightly higher incidences of pain upon insertion, continued abdominal pain, and spontaneous expulsion
 - No decreased return to fertility

Hubacker D. Contraception. 2007; 75(6 Suppl):S8-S11

Quick Start – LNG-IUS (Mirena®)

- Insert within 7 days of menses onset
 - No back up contraception needed
- If > 7 days since onset of menses, insert anytime if reasonably sure not pregnant
 - Use back up contraception for 7 days
- If amenorrheic, insert anytime *if it can be determined* not pregnant
 - Use back up contraception for 7 days



WHO. Selected practice recommendations for contraceptive use, 2nd ed. 2004: Geneva

New Indication Mirena® in Nulliparous Women

- Manufacturer of Mirena® has not sought FDA labeling
 - Studies demonstrate same differences between parous and nulliparous women as found in copper IUC
 - WHO does not distinguish between IUCs in the medical eligibility criteria
 - Insertion of Mirena® in nulliparous is off label but not experimental

Prager S, Darney PD. Contraception. 2007 Jun;75(6 Suppl):S12-5.

Switching from IUC to Hormonal Contraception

- Quick start the hormonal contraception (pill, vaginal ring, patch)
- Remove IUC at the next menses

WHO. Selected practice recommendations for contraceptive use, 2nd ed. 2004: Geneva

New Regimen: Shorter Pill-free Period

- Traditional monophasic: consistent dose 21 days of active pills followed by 7 days inert pills
- New monophasic: 24 consecutive days followed by 4 days inert pills
 - 20ug EE/3 mg drospirenone (Yaz®)
 - 20 ug EE/1 mg norethindrone (Lo-Estrin 24 Fe®)

Four Day Pill-Free Period

- ▣ Decreased hormone free interval
 - ▣ Today's lower steroid doses more rapidly cleared
 - ▣ 7 days of hormone free period allows follicular growth to begin
 - ▣ 4 day hormone free period expected to cause complete suppression of FSH, preventing follicular development

Willis SA, et al. Greater inhibition of the pituitary-ovarian axis in oral contraceptive regimens with a shortened hormone-free interval. Contraception 74(2006):100-103

Premenstrual Symptoms

- ▣ Emotional lability
- ▣ Bloating/swelling
- ▣ Breast tenderness
- ▣ Headache
- ▣ Pelvic pain
- ▣ Fatigue

New Regimen: Extended COC

- ▣ Only products with FDA approval are EE/Levonorgestrel marketed as Seasonale®, Seasonique® and LoSeasonique®
 - ▣ 91 day extended cycle pack containing 84 active pills followed by 7 inert tablets or 7 low dose EE
- ▣ Numerous studies COC use 84-168 days

PMS and Extended Regimen

- Six RCT's show significant improvement:
 - Bloating
 - Fatigue
 - Genital irritation
 - Headache

EdelmanA. Cochrane Database Syst Rev. 2005;(3)CD004695.

Headache and Extended Regimens

- Reduction in headache first detected day 25-28 of 168 day extended regimen of drospirenone 3mg/EE 30 mcg
 - Women with the highest severity headache showed significant improvement ($p < .0001$)

Migraine Headaches

- Migraine is a risk factor for ischemic stroke
- Risk effect is additive with hormonal contraception
- WHO Medical Eligibility
 - Migraine with aura-discontinue CHC
 - Obtain neurology evaluation for new onset
 - Migraine without aura and $< 35y/o$, or tension headache occurring during placebo period--extended cycles

WHO. Medical Eligibility Criteria for Contraceptive Use, 4th Ed. Geneva, Switzerland; 2004

Menstrual Issues with Extended Regimen

- Significantly less menstrual related symptoms over 1 year extended regimen
 - Less bleeding (daily flow scores)
 - Less pelvic pain
 - Less mood swings

New Guidelines: Forgotten Pills

- Adherence issues common among all age groups
 - 47% of women miss ≥ 1 pill per cycle
 - 22% miss ≥ 2 pills per cycle
 - Women are unaware of missed pills
 - Over 50% reported no missed pills when electronic data recorded only 19 to 33% of women had no missed doses

Rosenburg MJ, Vaughn MS, Burrhill MS. Fam Plann Perspect. 1998 Mar-Apr; 30(2):89-92. 104
Potter L, et al. Fam Plann Perspect. 1996 Jul-Aug;28(4):154-8

Making Up Missed Pills

- Missed or late pills
 - Take pill as soon as remember it or double pills if a day late
 - If 2 to 4 pills missed, take 2 pills ASAP
 - If in week 3, start new pack
 - If missed pills in first week, add emergency contraception and use 7 day back up
 - If missed pill in fourth week, skip placebo pills

■ COMPLICATED???

Alternate Plan for Missed Pills

- Use back up contraception for 7 days
 - If intercourse in the last 5 days
 - Use emergency contraception today
 - Restart daily OC's the next day
 - If no intercourse in the last 5 days
 - Take 2 active pills ASAP
 - Finish pill pack
- May skip placebo week if more than 4 missed pills

Hatcher RA, Nelson A. Contraceptive Technology 2007; 253

Managing BTB – Extended Regimen

- ▣ Women with heavier daily flow on a 21/7 regimen:
 - ▣ Are more likely to have BTB/BTS
 - ▣ BTB/BTS occurs earlier on extended regimens
- ▣ BTB/BTS generally decreased in second half of year of extended regimen
- ▣ IF BTB/BTS occurs for 7 days, a 3 day hormone free interval significantly more effective in managing bleeding than continuing hormones

Sutark PJ, Kuehl TJ, Coffee A, Willis S. Am J Obstet Gynecol 2006 Oct;195(4):935-41. Epub 2006 May 2

What's in the Pipeline?

- ▣ Low Dose Levonorgestrel IUS
- ▣ 12-month Continuous Cycle Vaginal Ring (CCVR)
- ▣ Spray-on Progestin only

Ultra Low Dose Levonorgestrel IUS

- Nulliparous and parous women age 18-40 y/o
- 3 years duration, randomized, 3 doses
- Phase II Clinical Trial Outcome measures
 - Pregnancy Rate
 - Bleeding Pattern
 - Expulsion
 - Side Effects

12-month CCVR

- Phase III clinical trials
- Releases a combination of 150 mcg of Nestorone and 15 mcg of ethinyl estradiol per day
- Users insert ring for three weeks, one week ring free and then re-insert the same ring for another three weeks
 - It will be effective for over 12 months

Spray On Progestin Only

- Nesterone gel in metered dose spray in phase I trial in Australia
 - Apply daily, dries in 60 seconds
 - Suppresses ovulation in 83% of participants
 - Thickens cervical mucus
 - Highly effective with breastfeeding



Male Contraceptives - Where are We?

- ## Experimental Male Contraception
- Wet heat & suspensories
 - Vas occlusion methods
 - Injectable silicone plugs – China
 - Pre-formed silicone plug called the IVD – Canada/US
 - Injectable compound called RISUG – India
 - In Phase III clinical trials
 - Hormonal methods
