# LONG ACTING REVERSIBLE CONTRACEPTIVES (LARC) FOR ADOLESCENTS

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### LARC FOR ADOLESCENTS

#### \* OBJECTIVES

- To review the advantages of LARC's for adolescents, specifically the single implant rod and intra-uterine device.
- \* To describe the pros and cons of both methods to improve candidate selection for LARC in adolescents.
- \* To increase Pediatric Providers comfort with these highly effective methods of adolescent contraception.



Finer, Zolna. Contraception. 2011.

### High Rate of Contraceptive Misuse

#### 1 million pregnancies/year due to misuse or discontinuation of OCs

0





#### Month 3 and 3 Pills Missed

Rosenberg MJ, et al. J Reprod Med. 1995. Potter L, et al. Fam Plann Perspect. 1996. Mosher WD, et al. Advance Data. 2004.



Rosenberg MJ. Am J Obstet Gynecol. 1998.

# Typical Vs. Perfect Use

% of Women w/ Unintended Pregnancy within 1<sup>st</sup> Year of Use



Hatcher R, et al. Contraceptive Technology. 2004.

# Satisfaction with Contraceptive Methods



Revisiting Your Regular Women's Health Care Visit. 2004.

### Nexplanon Implanon

Single Implantable rod placed under local anesthesia in medial upper arm.

Progestin only (estrogen free) efficacy for 3 years and rapidly reversible (one week) after removal.

New inserter decreases non placement of rod and depth of insertion. Rod now has a radioopaque strip.



### Features of Contraceptive Implants

- Highly effective
- Not motivation dependent
- Can be used during lactation
- Discreet, virtually invisible
- Rapidly reversible



more...

Reinprayoon D, et al. *Contraception*. 2000. Diaz S. *Contraception*. 2000.

#### Features of Contraceptive Implants (continued)

- Stable hormone levels
- Extended protection
- Contain no estrogen
- Safe



Reinprayoon D, et al. *Contraception*. 2000. Diaz S. *Contraception*. 2000.

# Limitations of Contraceptive Implants

- \* Can cause irregular bleeding
- Requires clinician visits for insertion and removal
- \* Does not protect from STDs



# Long-acting Protection

- Indicated for the prevention of pregnancy
- Long-acting; up to 3 years
- New implant can continue beyond 3 years
- Reversible at any time

# Pharmacology

Class	Progestin-only
Route	Subdermal
Formulation	Implantable rod; 68 mg etonogestrel
Bioavailability	~100%
Metabolism	Hepatic via CYP3A4
Half-life	~ 25 h
Excretion	Primary urine; some fecal

ANON. Obstet Gynecol. 2007

### **Mechanism of Action**

- Suppresses ovulation
- \* Increases cervical mucus viscosity
- \* Alters endometrium

IMPLANON<sup>™</sup> Physician insert, 2006

## **Clinical Expectations**

- No anemia
- No reduction in bone mineral density
- No increased risk of DVT
- Little pain at insertion site
- Changes in bleeding pattern
- Drug-drug interactions

more...

### Clinical Expectations (continued)

- Associated non-contraceptive benefits
  - \* Acne may decrease
  - \* Dysmenorrhea may improve
- Minor weight change
- Mild side effects:
  - \* Breast pain
  - \* Headache

# Changes in Bleeding Pattern

"Irregularly irregular" cycles, including:

- Frequent irregular bleeding
- Heavy menstrual flow
- Prolonged bleeding
- Amenorrhea
- Spotting
- Unpredictability of bleeding pattern over time

Affandi B. *Contraception*. 1998. Zheng SR, et al. *Contraception*. 1999.

### **Bleeding Patterns are Unpredictable**



Funk S, et al. Contraception. 2005.

# Management of Bleeding

- Few data available
- Considerations
  - Ethinyl estradiol
  - NSAIDs
  - Combination OCs
  - Watchful waiting



Meirik O. *Hum Reproduct Update*. 2003 Weisberg E. *Hum Reprod*. 2006

### Bleeding Does Not Result in Anemia

Mean Hgb (g/dL)



Affandi B. *Contraception*. 1998. Zheng SR, et al. *Contraception*. 1999.

# **Drug-drug Interactions**

### Some CYP3A Inhibitors and Inducers

#### **Potent Inhibitors**

amiodarone (Cordarone) atazanavir (Reyatz) cisapride (Propulsid) clarithromycin (Biaxin) itraconazole (Sporanox) ketoconazole (Nizoral) nefazodone (Serzone) nelfinavir (Viracept) ritonavir (Norvir) telithromycin (Ketek) troleandomycin (TAO) voriconazole (Vfend)

#### **Moderate Inhibitors**

amprenavir (Agenerase) aprepitant (Emend) ciprofloxacin (Cipro) diltiazem (Cardizem) erythromycin fluconazole (Diflucan) fluvoxamine (Luvox) fosamprenavir (Lexiva) grapefruit juice norfloxacin (Noroxin) verapamil (Calan)

#### Inducers

carbamazepine (Tegretol) efavirenz (Sustiva) nevirapine (Viramune) phenytoin (Dilantin) phenobarbital rifabutin (Mycobutin) rifapentine (Priftin) rifampin (Rifadin) St. John's Wort topiramate (Topamax) > 100 mg/d

ANON.Obstet Gynecol. 2007 Schindlbeck C. Arch Gynecol Obstet. 2006.

### Minor Weight Change

#### Mean weight change less than 4 pounds

At year 1 = 2.8 lbs At year 2 = 3.7 lbs





### Insertion Site Symptoms

Condition	n	%
Pain	48	3.4
Redness	6	0.4
Swelling	5	0.4
Hematoma	4	0.3
Expulsion	0	0

N = 1,409

Organon data on file.

## Adverse Effects

All Studies	N=942
Bleeding irregularities <sup>1</sup>	11.0%
Emotional Lability <sup>2</sup>	2.3%
Weight Increase	2.3%
Headache	1.6%
Acne	1.3%
Depression <sup>3</sup>	1.0%

<sup>1</sup> Includes frequent heavy, prolonged spotting and other patterns of bleeding irregularity.

<sup>2</sup> Among US subjects, 6.1% experienced emotional lability that led to discontinuation.

<sup>3</sup> Among US subjects, 2.4% experienced depression that led to discontinuation.

Implanon Physician Insert, 2006



Lakha F. Contraception. 2006

# Discontinuation 'Real-Life'

Reasons given for Implanon removal before completion of the 3-year period (n=60)



Agrawal A. *J Fam Plann Reprod Health Care*. 2005 Implanon Physician Insert, 2006

# Patient Counseling Topics

- Description of implant
- Efficacy
- Return to fertility
- Bleeding patterns
- Managing potential side effects
- Overview of insertion and removal
- Follow-up

### Patient Follow-up

- \* Expect bleeding irregularities
- \* Plan on removal after 3 years, or at anytime
- \* Make sure the implant is palpable
- \* Report any adverse effects immediately

### Patient Follow-up (continued)

- \* Discuss use of interacting medications now and in future
- \* Encourage healthy lifestyle
  - \* Safe sex (does not prevent STIs/HIV)
  - \* No smoking

# Insertion Timing

- Standard or new start
  - Insertion within 5 days of initiation of menses
- \* Switching from combined OC
  - \* Insertion within 7 days of last active tablet



## Insertion Timing (continued)

- \* Switching from progestin-only method
  - \* Insertion any day with progestin only-pill
  - \* Same day as IUD or implant removal
  - \* On due date for next contraceptive injection

## Insertion Timing (continued)

#### \* After abortion

- \* Within 5 days of 1st trimester abortion
- \* Within 6 weeks of 2nd trimester abortion
- \* After childbirth
  - \* Within 6 weeks

more...

Implanon physician Insert Reinprayoon D, et al. *Contraception*. 2000. Diaz S. *Contraception*. 2002.

### Insertion Timing (continued)

- \* Considered safe with lactation after 6 weeks
- \* Clinical study: low concentrations present in milk; no associated adverse events

Implanon physician Insert Reinprayoon D, et al. *Contraception*. 2000. Diaz S. *Contraception*. 2002.

# 'Quick Start' Method

- Inserted at any time during menstrual cycle
- Use of back-up barrier contraception for 7 days
- If inserted when emergency contraception is used, do urine pregnancy test in 3 weeks





Condom

**Cervical Cap** 



# Advantages

- High contraceptive effectiveness
- No need for user compliance
- Long life-span
- Minimal requirement for medical follow-up
- Low, stable serum hormone levels minimizing metabolic effects
- Rapid reversibility
### Disadvantages

- High initial cost
  - Counsel properly to prevent early discontinuation
- Insertion/removal requires visit to trained clinician
  - All prescription contraceptives (OCs, Injections, Rings, Patches, IUDs) also need health care provider visit

#### Disadvantages (continued)

- Misperceptions surrounding implant history
  - Proven track record of single-rod implant has overcome past obstacles

Power J. Cochrane Database Syst Rev. 2007

# Characteristics of Intrauterine Contraception

- Highest patient satisfaction among methods
- \* Rapid return of fertility
- \* Safe
- \* Immediately effective
- \* Long-term protection
- Highly effective



Belhadj H, et al. *Contraception*. 1986.; Skjeldestad F, et al. *Advances in Contraception*. 1988.; Arumugam K, et al. *Med Sci Res*. 1991.; Tadesse E. *Easr Afr Med J*. 1996.

### IUCs Available in the United States





#### LNG IUC

- \* 20 mcg levonorgestrel/day
- \* Approved for 5 years' use
- \* Copper T 380A IUD
  - \* Copper ions
  - \* Approved for 10 years' use

# Dispelling Common Myths About IUCs

#### In fact, IUCs:

- \* Are not abortifacients
- \* *Do not* cause ectopic pregnancies
- \* *Do not* cause pelvic infection
- \* *Do not* decrease the likelihood of future pregnancies
- \* Are not large in size

more...

Hubacher D, et al. *N Engl J Med.* 2001.; Stanwood NL, et al. *Obstet Gynecol.* 2002.; Forrest JD. *Obstet Gynecol Surv.* 1996.; Lippes *J. Am J Obstet Gynecol.* 1999.

### Dispelling Common Myths About IUCs (continued)

#### In fact, IUCs:

- \* Can be used by nulliparous women
- Can be used by women who have had an ectopic pregnancy
- \* *Do not* need to be removed for PID treatment
- \* Do not have to be removed if actinomyces-like organisms (ALO) are noted on a Pap test

Duenas JL. *Contraception*. 1996.; Stanwood NL. *Obstet Gynecol.* 2002. Forrest JD. *Obstet Gynecol Surv*. 1996; Lippes J. *Am J Obstet Gynecol*. 1999. Otero-Flores JB. *Contraception*. 2003.; WHO. 2009.; Penney G. *J Fam Plann Reprod Health Care*. 2004.

#### Mechanism of Action: Copper T IUD

- Primary mechanism is prevention of fertilization
  - Reduce motility and viability of sperm
  - \* Inhibit development of ova
- Inhibition of implantation is a secondary mechanism

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Alvarez F, et al. *Fertil Steril*. 1988.; Segal SJ, et al. *Fertil Steril*. 1985; ACOG. *Statement on Contraceptive Methods*. 1998.

### Mechanism of Action: LNG IUC

- Primary mechanism is fertilization inhibition
  - \* Cause cervical mucus to thicken
  - \* Inhibit sperm motility and function
- Inhibition of implantation is a secondary mechanism



Jonsson B, et al. Contraception. 1991.; Silverberg SG, et al. Int J Gynecol Pathol. 1986.



Adapted from Trussell J. In Hatcher RA, et al. *Contraceptive Technology: 20<sup>h</sup> revised ed,* 2011.

### Safety: IUCs Do Not Cause PID

- PID incidence for IUC users is similar to that of the general population
- \* Risk is increased only during the first month after insertion
- Preexisting STI at time of insertion, not the IUC itself, increases risk

Svensson L, et al. *JAMA*. 1984.; Sivin I, et al. *Contraception*. 1991.; Farley T, et al. *Lancet*. 1992.

#### Safety: IUC Does Not Cause Infertility

\* IUC is not related to infertility

\* Chlamydia is related to infertility



Tubal infertility by previous copper T IUD use and presence of chlamydia antibodies, nulligravid women

### Safety: IUCs May Be Used by HIV-Positive Women

- No increased risk of complications compared with HIV-negative women
  - No increased cervical viral shedding
- \* WHO and CDC Category 2 rating



WHO. 2009.; CDC. MMWR. 2010.; Morrison CS, et al. Brit J Obstet Gynaecol. 2001.; Richardson B, et al. AIDS. 1999.

# Safety: IUCs May Be Used in Nulligravid Women

- No evidence of increased infertility in nulliparous users of IUCs
- \* Risk of PID and subsequent infertility is dependent on non-IUC factors



WHO. 2009.; Hubacher D, et al. *NEJM*. 2001.; Delbarge W, et al. *Eur J Contracept Reprod Health Care*. 2002.

### LNG IUC vs. OCs in Nulligravid Women Termination Rates, Reasons

Reason	LNG IUC termination rate per 100	OC termination rate per 100
Pain*	6.66	0
Hormonal	4.95	9.75
Bleeding	2.52	0
Spotting	0	1.25
Expulsion	1.20	NA
Other medical	2.13	1.09

#### \*Statistically significant difference

Suhonen S, et al. Contraception. 2004.

#### Potential Side Effects

During insertion	First few days	First few months	Туре
Variable pain and/or cramping	Light bleeding	Inter- menstrual bleeding	<i>Copper T:</i> Heavier or prolonged menses <i>LNG</i> :
Vaso-vagal reactions	Mild cramping	Cramping	Gradual decrease in menstrual flow

Sivin I, et al. Contraception. 1991.; Silverberg SG, et al. Int J Gynecol Pathol. 1986.

#### **IUC Non-contraceptive Benefits**

	Protection against endometrial cancer	Alternative to hysterectomy or endometrial ablation	Treatment of heavy bleeding/ dysmenorrhea
Copper T IUD	$\checkmark$		
LNG IUC	$\checkmark$	$\checkmark$	$\checkmark$

Hill DA, et al. *Int J Cancer.* 1997; Rosenblatt KA, et al. *Contraception.* 1996; Hurskainen R, et al. *Lancet.* 2001; Hurskainen R, et al. *JAMA.* 2004 Andersson JK, et al. *Br J Obstet Gynaecol.* 1990.

### **IUC Is Cost Effective**

- Higher one-time startup, but incurs substantially lower cost over time
- Both IUC manufacturers offer patient payment plan options
- Bulk discounts are available to clinicians





Darney P. *NEJM*. 2002.; Trussell J, et al. *Am J Public Health*. 1995.; Chiou CF, et al. Contraception. 2003.

#### I.U.C. – Skyla



#### **Costs for Patients**

- Patient costs are a factor in choosing contraceptive method
- \* Up-front costs concern some women
- Costs of side effects associated with some contraceptives are high compared with those for an IUC
- Public clinics and pharmaceutical company patient assistance programs can be explored for low-income or uninsured patients

Screening: Poor Candidates for Intrauterine Contraception

- \* Known or suspected pregnancy
- \* Puerperal sepsis
- Immediate post septic abortion
- Unexplained vaginal bleeding
- \* Cervical or endometrial cancer

more...

WHO. 2009.

# Screening: Poor Candidates for Intrauterine Contraception (Continued)

- \* Uterine fibroids that interfere with placement
- \* Uterine distortion (congenital or acquired)
- \* Current PID
- \* Current purulent cervicitis, chlamydia, or gonorrhea
- \* Known pelvic tuberculosis

WHO. 2009.

#### IUC for Postpartum Use

- \* May be safely inserted in postpartum women
- \* LNG-IUD and CuT can safely be placed within 10 minutes of placental delivery.
- Both IUDs can be used between 10 minutes and 4 weeks.
- \* Some evidence to suggest higher expulsion should not deter insertion in the post-partum period.

#### **IUC Use During Lactation**

- \* Effectiveness not decreased
- Uterine perforation risk unchanged
- Expulsion rates unchanged
- Decreased insertional pain
- \* Reduced rate of removal for bleeding and pain
- \* LNG comparable to copper T in breastfeeding parameters

Chi I-C, et al. Contraception. 1989.; Shaamash AH, et al. Contraception. 2005.

#### IUC Use for Adolescents

- Appropriate for properly selected and counseled adolescents
- Follow-up and side-effect monitoring important
- Encourage use of condoms with new partners



#### Case Presentation: Nulligravid Adolescent "Anna," 17-year-old high-school senior

- \* Has been sexually active with boyfriend for 3 months
- \* Has been using condoms for birth control
- \* Does not want to use hormonal method of contraception

#### Consider: Copper T IUD or LNG IUS\*

\* After first few months, very little LNG enters the circulation.



### Nulligravid Adolescent Case: Clinical Considerations

- Insertion difficulty (smaller os and uterus than in parous woman)
- Insertion pain
- Possible increased risk of STIs (chlamydia) and PID (because of age <25 years)</li>

more...

Deans El, Grimes DA. Contraception. 2009.; Grimes DA. Lancet. 2000.



#### **Insertion Pain Management**

- \* A variety of ways of reducing pain during IUC insertion have been investigated.
- Evidence on pain relief during the IUC insertion procedure is mixed.

Grimes DA, et al. Cochrane Database of Systematic Review. 2006.; Hubacher, D, et al. Am J Obstet Gynecol. 2006.; Allen RH, et al. Cochrane Database of Systematic Review. 2009.; Rabin JM, et al. *Obstet Gynecol* 1989.

# Nulligravid Adolescent Case: Practice Tips

To reduce insertion pain:

\* Misoprostol:



200–800 µg a few hours before insertion

Clinical Pearl

- Can be given orally, buccally, or vaginally
- Consider stocking in clinician's office
- Medication may be dispensed early in the day and patient asked to return for insertion

# Nulligravid Adolescent Case: Practice

TIPS (continued)

To reduce insertion pain (continued):

- \* NSAID block before procedure
- \* Lidocaine instillation into endometrial cavity:
  - Follow 1-2-3 rule:
    - \* 1 mL of lidocaine
    - \* 2% solution
    - \* 3-minute wait before starting procedure



Clinical Pearl

# Nulligravid Adolescent Case: Practice Tips (continued)

- Same-day chlamydia testing (with normal clinical exam):
  - No need to wait for test results before insertion
  - Positive tests should prompt treatment without need to remove device



Clinical Pearl

### Nulligravid Adolescent Case: Practice Tips (continued)

- \* Os finder
- \* Uterine dilators
- \* Timing of insertion



#### Nulligravid Adolescent Case: Points

- Follow-up and side-effect monitoring important
- \* Counsel regarding signs of expulsi
- Encourage use of condoms with n partners



Hubacher D. Contraception. 2007.; Tomas A et al. J Pediatr Adolesc Gynecol. 2006.

# Case Presentation: Heavy Menstrual Bleeding

- "Diane," 24-year-old nulligravida
- \* Medical history:
  - \* Heavy menstrual bleeding, dysmenorrhea
- \* Presents for relief of heavy bleeding and cramping
- \* Has tried OCs in the past, dislikes having to take a daily pill



#### **Consider: LNG IUS**

### Heavy Menstrual Bleeding Case: Clinical Considerations

- Evaluate for underlying cause of heavy bleeding
- \* Differential diagnoses:
  - \* Coagulopathy
  - \* Endometrial lesion, fibroid, or polyp
  - \* Anovulation

James AH et al. Am J Obstet Gynecol. 2009.; Kingman CEC et al. Br J Obstet Gynaecol. 2004.; Mansour D. Best Pract Res Clin Obstet Gynecol. 2007.

### Heavy Menstrual Bleeding Case: Practice Tips

#### \* Evaluate cause:

- \* Menstrual history
- History of other types of bleeding suggesting coagulopathy
- \* Endometrial biopsy
- \* Possible vaginal ultrasound
- \* Sonohysterogram



#### Clinical Pearl
## Heavy Menstrual Bleeding Case: Counseling Points

#### \* To be expected:

- \* Lower volume of menstrual bleeding
- \* Dysmenorrhea may improve
- Breakthrough spotting
- \* Unpredictable bleeding is common
- \* 3–6 months for LNG IUS to have full effect on endometrium

## IUC Counseling Topics (Continued)

- \* Side effects and possible complications
- Instructions on follow-up
- \* Non-contraceptive benefits
- \* Use of condoms with new partners

### IUC Side Effects & Complications

#### Side Effects

Menstrual effects

#### Complications

Infection Perforation Pregnancy Expulsion Missing threads

# Signs of Possible Complications

<b>Possible Explanation</b>
Perforation, infection
Dislocation or perforation
Infection

more...

Signs of Possible Complications (Continued)	
Symptom	Possible Explanation
Pain during intercourse	Infection, perforation, partial expulsion
Missed period, other signs of pregnancy, expulsion	Pregnancy (uterine or ectopic)
Shorter, longer, or missing threads	Partial or complete expulsion, perforation

## Management of Missing Threads

- \* Rule out pregnancy
- \* Probe for threads in cervical canal
- \* Prescribe back-up contraceptive method
- \* Obtain ultrasound or x-ray, as needed
- \* Remove a copper T IUD in abdomen promptly

# Management of STIs

#### If STI diagnosed:

- IUC removal not necessary if symptoms improve within 72 hours of treatment
- Treat infection
- \* Counsel patient about prevention of STI transmission

Penney G, et al. J Fam Plann Reprod Health Care. 2004.; WHO. Selected Practice Recommendations for Contraceptive Use. 2002.

# Management of PID

#### If PID diagnosed:

- \* IUC removal may not be necessary
- \* Treat infection
- Recommendations to remove IUC are not evidence-based

### LARC for Adolescents

- In Summary the implantable progestin-only rod Nexplanon and the nulliparous progestin IUD, Skyla offer adolescents long acting (three years), highly effective reversible contraception.
- They require no interventions by the young woman for the three year course.
- There can be irregular uterine bleeding with both methods, but this tends to improve in 3-6 months of use.

### LARC for Adolescents

- Surgical removal of the implant is required at the end of three years or sooner.
- Removal of the IUD by a health provider is preferred but some teens self remove their IUD's.
- The initial costs for both methods is more expensive than shorter acting contraceptives but comparable when averaged over 3 years. These methods have much higher effective contraceptive continuation rates, with proper counseling than shorter acting methods.
- Concurrent use of condoms is required for STI and HIV prevention.

## LARC for Adolescents RESOURCES

- \* <u>Contraceptive Technology</u>, Hatcher, R. et. al. 20<sup>th</sup> rev.edition 2011 <u>www.contraceptivetechnology.org</u>
- \* American College of Obstetricians and Gynecologists (ACOG) <u>www.acog.org</u>
- \* Association of Reproductive Health Professionals www.arhp.org
- \* Alan Guttmacher Institute <u>www.guttmacher.org</u>
- \* www.bedsider.org