Contraceptive Update

Patty Cason MS, FNP-BC
UCLA School of Nursing
Envisionsrh.com
Disclosures

• Advisory Board/Consultant
  Teva, Cooper Surgical, Medicines 360, Merck, ContraMed, Evofem

• Trainer/Trainer
  Teva, Merck, ContraMed, Medicines 360
Objectives

• Describe two innovations in IUDs
• Discuss extended use of implants and IUDs
• Demonstrate use of patient-centered questions to assist patients with contraceptive decision making
Reproductive Intentions/Goals
PATH Questions

1. Do you think you would like to have (more) children some day?

2. When do you think that might be?

3. How important is it to you to prevent pregnancy (until then)?

(Callegari, Aiken et al. 2017)
Reproductive Intention/Goals

Clarifies motivation and degree of acceptability regarding pregnancy...so we can offer appropriate interventions

+/- Contraception

+/- Preconception Care

Infertility Services or Adoption
Best Question

“Do you have a sense of what is important to you in your birth control method?”
Particular characteristics of Contraceptive Methods

• Do you have a sense of what is important to you about your method?

• Do you have a sense of what you are looking for in a contraceptive method?
Particular characteristics of Contraceptive Methods

“It sounds like one of the things that is important to you is that your birth control is very good at preventing pregnancy. Do you have a sense of what else is important to you?”
Attitude about

- Need to conceal contraception;
  - no supplies?
  - normal bleeding pattern?
- Return to fertility
- Non-contraceptive benefits
- Side effects

- Effectiveness
- Hormones
- Menstrual cycle and bleeding profile
- Length of use
- Control over removal
- Object in her body
Nexplanon

UPDATES
Formal (Merck) training for insertion/removal required
Migration of Implant

N=38 cases of migration:

- lung/pulmonary artery (n=9)
- chest wall (n=1)
- vasculature at locations other than the lung/pulmonary artery (n=14)
- extravascular migrations (n=14) to other body sites (e.g., the axilla and clavicle/neck line/shoulder)

(Kang, Niak et al. 2017)
1.3 Migrations per Million Placements

- 7 cases reported pain, discomfort, dyspnea
- 3 cases describe pulmonary fibrosis and skin reactions from migration to the vasculature, chest wall and other distant body sites
- 16 cases reported surgical removal in an operating room setting

(Kang, Niak et al. 2017)
Clinicians are now advised to avoid placement in the biceps groove, no matter how superficial that placement might be.

Place over the triceps

(Rowland, Mansour et al. 2017)
Mirena
Liletta
Nexplanon
EXTENDED USE
Etonogestrel implant

• The EPIC Study-- part of Contraceptive Choice project, 291 women provided 444 user-years of extended use. No pregnancies

• 7-country study, 390 used implant beyond 3 years more than 200 of them used for at least 5 years. No pregnancies

Threshold For Ovulation Suppression

>90 pg/mL

Serum ENG median levels remained above 90 pg/mL for women of all BMIs

(McNicholas, Swor et al. 2017)
>90 pg/mL

• The absolute threshold of contraceptive effectiveness remains poorly defined

• May be <90 pg/mL as secondary mechanisms such as cervical mucus changes may prevent pregnancy should ovulation occur

(McNicholas, Swor et al. 2017; Xu, Wafe et al. 2012)
Mirena Levonorgestrel-releasing Intrauterine System 52 Mg
7 Year Data

- Mirena FDA approved for up to 5 years
- Data show that it is highly effective for at least 2 additional years of use
- 6th year failure rate 0.25
- 7th year failure rate 0.43 (n=496)
- Another trial showed 7-year pregnancy cumulative failure rate 0.5 (n=398)

(McNicholas 2017; Rowe, Farley et al. 2016)
52-mg LNG-IUD Data Suggest

- Efficacy as long as 15 years
- Healthcare professionals, policy makers and stakeholders could take advantage of the present information to decide to maintain the same device at least up to seven years
- Furthermore, amenorrhea could be a good indicator of contraceptive effect

(Bahamondes, Fernandes et al. 2017)
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<tr>
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</thead>
<tbody>
<tr>
<td>No bleeding</td>
<td>55.1</td>
<td>62.5</td>
<td>61.3</td>
<td>70.6</td>
<td>75.0</td>
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<tr>
<td>Spotting</td>
<td>26.7</td>
<td>20.8</td>
<td>25.8</td>
<td>18.6</td>
<td>1.7</td>
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<tr>
<td>Irregular</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heavier</td>
<td>2.3</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Regular</td>
<td>8.8</td>
<td>5.2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td># Starting period</td>
<td>776</td>
<td>107</td>
<td>58</td>
<td>30</td>
<td>23</td>
</tr>
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</table>

(Bahamondes, Fernandes et al. 2017)
# Reason for Discontinuation

<table>
<thead>
<tr>
<th>Months (years) after IUS placement</th>
<th>61–84 (5-7)</th>
<th>85–108 (7-9)</th>
<th>109–132 (9-11)</th>
<th>133–156 (11-13)</th>
<th>157–180 (13-15)</th>
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<tbody>
<tr>
<td>Pregnancy</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Expulsion</td>
<td>0.3%</td>
<td>0.6%</td>
<td>0</td>
<td>1.1%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Planning pregnancy</td>
<td>1.3%</td>
<td>2.0%</td>
<td>0</td>
<td>0</td>
<td>7.1%</td>
</tr>
<tr>
<td>Bleeding pain</td>
<td>0.2%</td>
<td>2.3%</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

(Bahamondes, Fernandes et al. 2017)
Liletta* Levonorgestrel-releasing Intrauterine System 52 Mg

*The 340B price for Liletta is $50
LILETTA August 3rd 2017

- FDA approved extended use up to 4 years
- Submitted to FDA for 5 year indication
- The clinical trial is ongoing to 8 years
- LNG content at 5 year supports continued efficacy \textit{at least} until 5 years and likely 7

(Creinin, Jansen et al. 2016; Teal, Turok et al. 2018)
LEVONORGESTREL INTRAUTERINE DEVICE IN DEVELOPMENT
LevoCept Phase 2 clinical study

- Prospective, multi-center, single-arm, open-label
- 250 participants ages 18-40
- Start Date: 11/16
- Estimated Primary Completion Date: 7/18
- Estimated Study Completion Date: 7/20
- Primary outcome measure is effectiveness

(https://www.clinicaltrials.gov/ct2/show/NCT02882191)
Other Outcome Measures Include

• Study Device Placement
  – Ease of placement
  – Placement success
• Safety
• Tolerability
  – Bleeding and spotting patterns
  – Discontinuation rate and reasons

(https://www.clinicaltrials.gov/ct2/show/NCT02882191)
COPPER INTRAUTERINE DEVICES IN DEVELOPMENT

IUB
VeraCept
Mona Lisa® NT Cu380 Mini
IUB™

• Spherical intrauterine platform
• Nitinol frame; a biocompatible nickel-titanium alloy (used in vascular stents and Essure)
  – The IUB™ adapts to the uterine cavity
• 3 sizes ranging from 12 mm to 18 mm in diameter
• Out of 49 placements 9 expulsions
VeraCept
Intrauterine Copper Contraceptive

Copper Sleeves
Nitinol Frame
Retrieval Strings

32 mm
30 mm

Reeves, M., (2017)
VeraCept
Intrauterine Copper Contraceptive

- 175 mm$^2$ of copper
  - Near cervix and cornua
- Nitinol frame
  - Shape memory allows pre-loading
  - Less mass; smaller diameter inserter (3.7mm)
  - Compliant arms
  - Fundus seeking
- Pre-cut strings
<table>
<thead>
<tr>
<th><strong>Results Phase 2</strong></th>
<th><strong>12 months</strong></th>
<th><strong>18 months</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>286 women 2475 cycles 60% nullips</td>
<td>77.4%</td>
<td>81.6%*</td>
</tr>
<tr>
<td>Continuation</td>
<td>283 (98.9%)</td>
<td>283 (98.9%)</td>
</tr>
<tr>
<td>Successful placement</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pregnancies</td>
<td>63.6%</td>
<td>63.6%</td>
</tr>
<tr>
<td>No pain or some pain</td>
<td>2 (0.7%)</td>
<td>2 (0.7%)</td>
</tr>
<tr>
<td>Expulsions</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Adverse Events (all)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AE related to IUD</td>
<td>0</td>
<td>0</td>
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*extended beyond 1 year
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<thead>
<tr>
<th></th>
<th>VeraCept</th>
<th>Copper T380S</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 month continuation</td>
<td>167 (84%)</td>
<td>68 (68%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Discontinuations</td>
<td>31 (16%)</td>
<td>32 (32%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Expulsion</td>
<td>10 (5%)</td>
<td>12 (12%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Tolerability</td>
<td>7 (4%)</td>
<td>17 (17%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>14 (7%)</td>
<td>3 (3%)</td>
<td>0.19</td>
</tr>
<tr>
<td>Pregnancy (ectopic)</td>
<td>1 (0.6%)</td>
<td>0 (0.0%)</td>
<td>ns</td>
</tr>
<tr>
<td>Mean Pain Score (0 to 5 Likert scale)</td>
<td>1.4</td>
<td>2.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Pain score of 0 or 1</td>
<td>64%</td>
<td>12%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

(Reeves, Katz et al. 2017)
Head to Head
Comparison with PARAGARD

• Mona Lisa® NT Cu380 Mini
  – Copper surface of 380 mm²
  – 24 mm wide X 30 mm long
• Based on the Nova T 380
• Polyethylene frame with barium sulphate
Caya Diaphragm
Diaphragm

- Silicone
- Used with spermicide
- Can be inserted several hours prior to coitus but if > 1 hour must add additional spermicide
- Remove > 6 hours after coitus
Female Condom FC2
Insertive (Female) Condom

- Comes with silicone-based lubricant on the inside
- Additional lubrication can be used
- Does not have to be water soluble
- Does not contain spermicide
- STI protection that doesn’t rely on a partner maintaining an erection
FC2 also called: Insertive, Universal

- Helps to prevent pregnancy, STIs & HIV
- Can be used during anal sex (remove the inner ring)
- Now available with a prescription for no cost
HeyDoctor App

- Patients fill out a questionnaire, take a picture of themselves, license, and insurance card (optional)
- Pick up FC2 from a pharmacy
- AK, AZ, CA, CT, FL, GA, IL, IN, KY, MO, MT, NE, NY, NC, OH, OR, PA, RI, SC, TN, TX, VT, VA, WA, WI and WY (More states coming soon)

Promo Code **TryIt** for free visit
Uninsured or Underinsured

• Patient Assistance Program
  – 12-Pack for $28.95
  – 24-Pack for $47.95
• 340B Prime Vendor Program (PVP)
  – 12-Packs of FC2
Spermicide

• All available creams, gels, film, foam, and suppositories contain nonoxynol-9
• Whether used alone or with a barrier method

(Roddy, Zekeng et al. 1998; Trussel 2007)
Amphora®

- Spermicidal contraceptive
- Does not contain nonoxynol 9
- Phase 3 study underway
- Data expected Q1 2019
- Already licensed as a lubricant
- Potential additional indications: prevention of chlamydia, gonorrhea and recurrent bacterial vaginosis
References

REFERENCES