Contraception for Obese Women

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ACOG DISTRICT II UPSTATE MEETING
APRIL 29, 2016
I am a Nexplanon ® trainer for Merck.
Objectives

- Understand how obesity may affect pharmacokinetics of contraception,
- Understand safety and efficacy of methods available in the United States.
- Discuss contraceptive counseling for our patients.
6.7 million pregnancies

% Preganacies

Intended

Unintended

51

21

23

Fetal Demise
Abortion
Births
Pregnancies

Finer LB. Contraception, 2011
Emergency Contraception

- Copper IUD
  - 5 days

- Levonorgestrel (LNG)
  - 150 mg oral
  - 72 hrs

- Ulipristal acetate (UPA)
  - 30 mg oral
  - 120 hrs
EC
Copper IUD

- 7,034 postcoital insertions
  - 10 pregnancies
  - 0.14% failure
- Egypt
  - RCT
  - 300 women
  - 2% failure IUD
  - 22% no treatment
## LNG vs. UPA

<table>
<thead>
<tr>
<th>Confounding factors</th>
<th>Subgroups</th>
<th>Pregnancy, n/N (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>UPA</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Normal or underweight (&lt; 25 kg/m²)</td>
<td>27/2232 (1.2) [0.8–1.8]</td>
</tr>
<tr>
<td></td>
<td>Overweight (25–29.9 kg/m²)</td>
<td>13/744 (1.7) [1.0–3.0]</td>
</tr>
<tr>
<td></td>
<td>Obese (≥30 kg/m²)</td>
<td>20/469 (4.3) [2.8–6.5]</td>
</tr>
<tr>
<td>Conception probability*</td>
<td>Outside fertile window (0)</td>
<td>25/2227 (1.1) [0.8–1.7]</td>
</tr>
<tr>
<td></td>
<td>Inside fertile window (&gt;0)</td>
<td>35/1218 (2.9) [2.1–4.0]</td>
</tr>
<tr>
<td>Further intercourse</td>
<td>No</td>
<td>49/3274 (1.5) [1.1–2.0]</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11/171 (6.4) [3.6–11.1]</td>
</tr>
</tbody>
</table>

*Conception probability includes the number of days past ovulation.
Tiers of efficacy

Most effective

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- Prevents pregnancy >99% of the time
- Male/Female Sterilization
- IUD/IUS
- Implants

Very effective

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- Prevents pregnancy ~91-99% of the time
- Pills
- Injectable
- Patch
- Ring

Moderately effective

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- Prevents pregnancy ~81-90% of the time
- Male/Female Condom
- Sponge
- Diaphragm

Effective

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- Prevents pregnancy up to 80% of the time
- Fertility awareness
- Cervical cap
- Spermicide
BOX. Categories for Classifying Hormonal Contraceptives and Intrauterine Devices

1 = A condition for which there is no restriction for the use of the contraceptive method.

2 = A condition for which the advantages of using the method generally outweigh the theoretical or proven risks.

3 = A condition for which the theoretical or proven risks usually outweigh the advantages of using the method.

4 = A condition that represents an unacceptable health risk if the contraceptive method is used.
**US Medical Eligibility Criteria**

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**TABLE. (Continued) Summary of classifications for hormonal contraceptive methods and intrauterine devices**

<table>
<thead>
<tr>
<th>Condition</th>
<th>COC/P/R</th>
<th>POP</th>
<th>DMPA</th>
<th>Implants</th>
<th>LNG-1UD</th>
<th>Cu-1UD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Obesity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. ≥30 kg/m² BMI</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>b. Menarche to &lt;18 yrs and ≥30 kg/m² BMI</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>History of bariatric surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Restrictive procedures: decrease storage capacity of the stomach (vertical banded gastroplasty, laparoscopic adjustable gastric band, laparoscopic sleeve gastrectomy)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>b. Malabsorptive procedures: decrease absorption of nutrients and calories by shortening the functional length of the small intestine (Roux-en-Y gastric bypass, bilipancreatic diversion)</td>
<td>COCs: 3</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>
Sterilization

Male

► Efficacy
  ► Short-term failure = sperm present at 24 wks
    ► Dependent on technique
      ► <1% with cautery and/or fascial interposition
      ► ~15% with ligation alone
  ► Long-term failure - less data available
    ► 1 year: 0.7%
    ► 5 year: 1.1%

► Requires contraception for 3-mo after procedure - until efficacy confirmed
  ► ~42% do not comply
LARC
Long Acting Reversible Contraception

- LNG IUS
  - Mirena®
  - Liletta®
  - Skyla®
- Copper IUD
  - Paragard®
- Etonogestrel subdermal contraceptive implant
  - Nexplanon®
  - Implanon®
Mirena®

- 52 mg LNG
  - 20 mcg LNG/day
- 5 yrs
- Menorrhagia indication
  - Amenorrhea ~20% at 1 yr

Mirena Prescribing Information 2014
### Skyla®

#### Skyla prescribing information 2013

<table>
<thead>
<tr>
<th>Condition</th>
<th>First 90 days</th>
<th>Second 90 days</th>
<th>End of year 1</th>
<th>End of year 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amenorrhea¹</td>
<td>&lt;1%</td>
<td>3%</td>
<td>6%</td>
<td>12%</td>
</tr>
<tr>
<td>Infrequent bleeding²</td>
<td>8%</td>
<td>19%</td>
<td>20%</td>
<td>22%</td>
</tr>
<tr>
<td>Frequent bleeding³</td>
<td>31%</td>
<td>12%</td>
<td>8%</td>
<td>4%</td>
</tr>
<tr>
<td>Prolonged bleeding⁴</td>
<td>59%</td>
<td>17%</td>
<td>9%</td>
<td>3%</td>
</tr>
<tr>
<td>Irregular bleeding⁵</td>
<td>42%</td>
<td>28%</td>
<td>23%</td>
<td></td>
</tr>
</tbody>
</table>

#### 28-day Cycle Equivalent

<table>
<thead>
<tr>
<th>Cycle 1 N=1,588</th>
<th>Cycle 4 N=1,535</th>
<th>Cycle 7 N=1,468</th>
<th>Cycle 13 N=1,345</th>
<th>Cycle 39 N=781</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days on treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of bleeding days</td>
<td>7.3</td>
<td>5.6</td>
<td>3.5</td>
<td>3.4</td>
</tr>
<tr>
<td>Number of spotting days</td>
<td>9.2</td>
<td>6.1</td>
<td>4.8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

- **13.5 mg LNG**
- **14 mcg/day**
Liletta®

- **52 mg LNG**
  - 18 mcg/day
- **3 yrs**
- **Amenorrhea**
  - 19% first year
  - 26% second year
  - 38% third year

<table>
<thead>
<tr>
<th>28-day Cycle Equivalent</th>
<th>Cycle 1 N=1,691</th>
<th>Cycle 4 N=1,525</th>
<th>Cycle 7 N=1,223</th>
<th>Cycle 13 N=791</th>
<th>Cycle 26 N=438</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days on treatment</td>
<td>Mean 1-28</td>
<td>Mean 85-112</td>
<td>Mean 169-196</td>
<td>Mean 337-364</td>
<td>Mean 674-728</td>
</tr>
<tr>
<td></td>
<td>SD 5.2</td>
<td>SD 3.3</td>
<td>SD 2.6</td>
<td>SD 2.3</td>
<td>SD 1.7</td>
</tr>
<tr>
<td>Number of bleeding days</td>
<td>Mean 5.8</td>
<td>Mean 2.3</td>
<td>Mean 1.5</td>
<td>Mean 1.2</td>
<td>Mean 0.8</td>
</tr>
<tr>
<td></td>
<td>SD 5.2</td>
<td>SD 3</td>
<td>SD 2.6</td>
<td>SD 2.3</td>
<td>SD 1.7</td>
</tr>
<tr>
<td>Number of spotting days</td>
<td>Mean 8.9</td>
<td>Mean 4.3</td>
<td>Mean 3.0</td>
<td>Mean 2.7</td>
<td>Mean 2.0</td>
</tr>
<tr>
<td></td>
<td>SD 6.0</td>
<td>SD 4.2</td>
<td>SD 3.6</td>
<td>SD 3.4</td>
<td>SD 2.7</td>
</tr>
</tbody>
</table>

Liletta prescribing information 2015
Paragard®
Copper IUD

- Copper Ions
- Approved for 10 years
- Can be used as EC

Fortntey J. J Reprod Med 1999
Trussell J. Contraceptive Technology 2007
IUDs and Obesity

- Lower serum levels of LNG
- Mechanism of action local, not systemic
- No variance in failure rates
- Insertion difficulty
  - Ultrasound guidance
  - OR at time of D+C

<table>
<thead>
<tr>
<th>BMI</th>
<th>1 yr</th>
<th>2 yr</th>
<th>3 yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>25-29.9</td>
<td>0</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>30+</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Pocius K. *Curr Obstet Gynecol Rep* 2015
Xu H. *Obstet Gynecol* 2012
Subdermal Contraceptive Implant

- Brand name
  - Nexplanon®
  - Implanon®
  - Etonogestrel
- 3 years
Implant Effectiveness

No participants >130% IBW

- N=13
- Median BMI=41 (33-52)
- ENG plasma concentrations
  - 133 pg/ml
  - 102 pg/ml
  - 98 pg/ml

- Used implant >1 yr
  - 32% 1-2 yr
  - 36% 2-3 yr
  - 32% 3-4 yr
- 35=median obese BMI
- Median serum levels
  - 216 pg/ml- normal weight
  - 288 pg/ml- overweight
  - 225 pg/ml- obese
- Lowest recorded 117 pg/ml

Mornar S Am J Obstet Gynecol 2012
Morrell K. Contraception 2014
Implant Effectiveness

CHOICE

- 1,168 women
  - 37% normal weight
  - 28% overweight
  - 35% obese

- 1 unintended pregnancy
  - BMI = 30
  - Shortly after initiation

Xu H. Obstet Gynecol 2012
Health Effects

- Weight gain
  - Self perceived
  - 1.6 kg/3 yrs - 2.1/1yr
  - Similar to that of copper IUD

- Lipids
  - Slight increases
  - Regulatory agencies use MPA data
  - Little data concerning baseline hyperlipidemia

CDC MEC 1 and 2

Vickery Z Contraception 2013
Makarainen L Fertil Steril 1998
Simmons K Contraception for the medically challenging patient 2014
Injectable Contraceptive

- DMPA
  - Brand name Depo Provera®
- 150 mg/ml IM or 104 mg/0.65 ml SQ
- Q 13 weeks
- Efficacy not affected by weight
  - Clinical trials involved obese participants
  - No pregnancies

Jaina J Contraception 2004
Rodriguez M Rev Endo Met Disorders 2011
Injectable Contraceptive Weight gain

- Adult
  - 2 kg
  - Similar to non-hormonal IUD
  - Baseline weight had little effect

- Adolescents
  - Decreased lean body mass
  - Increased fat mass
  - Baseline weight relevant

Lopez L Cochrane Database of Systematic Reviews 2013
Injectable Contraceptive Metabolic Effects

- SC
  - HDL decline
  - Decreased β-cell compensation for insulin resistance
- IM
  - Lipids
    - Initial HDL decline
    - Recovered by 3 years
  - Little effect on glucose metabolism

CDC MEC 1 and 2
Progestin Only Oral Contraceptives

- Mini-pill
- Norethindrone and Norgestrel
- Efficacy not affected by weight
- No effect on weight
- No metabolic effects
- Reconsider for bariatric surgery

CDC MEC 1 and 2

Lopez L, Cochrane Database of Systematic Reviews 2013
Combined Hormonal Contraception

- Combined oral contraceptives
  - COC
- Contraceptive vaginal ring
  - CVR
  - Nuvaring®
- Contraceptive patch
  - CP
  - Ortho Evra®
COC Pharmacokinetics
COC Pharmacokinetics

- Higher dose (HD)
  - 30 mcg EE/150 mcg LNG
  - 21/7 regimen
- Continuous dose (CD)
  - 20 mcg EE/100 mcg LNG
  - No placebo pills
- BMI 30+
- Initial 2 mos low dose COC with 21/7 regimen
- Increased time to steady state
- Follicular development

Edelman A Contraception 2014
COC Pharmacokinetics

- 30 mcg EE/150 mcg LNG
- Peak EE and LNG concentrations lower in obese group
- Trough concentrations same
- No difference in follicular development
- 2 ovulations

Edelman A Contraception 2014
COC Efficacy

- Cochrane Review
  - No difference when compliant
  - CHOICE- 1523 participants

<table>
<thead>
<tr>
<th>BMI</th>
<th>Unintended pregnancy rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;25</td>
<td>8.44%</td>
</tr>
<tr>
<td>25-30</td>
<td>11.03%</td>
</tr>
<tr>
<td>30-40</td>
<td>8.61%</td>
</tr>
<tr>
<td>&gt;40</td>
<td>10.84%</td>
</tr>
</tbody>
</table>

- Reconsider after bariatric surgery

Lopez L Cochrane Database of Systemic Reviews 2013
McNicholas C Obstet Gynecol 2013
COC
Metabolic Effects

- No weight changes
- Lipids
  - Decrease LDL obese pts compared with normal weight
- Glucose
  - No change fasting glucose and insulin
  - Marginally significant increase glucose with 30 mcg EE pill

CDC MEC 1, 2, 3

Gallo M Cochrane Database of Systematic Reviews 2014
Beasley A Contraception 2012
CVR

- EE 2.7 mg/ENG 11.7 mg
  - EE 0.015mg/day
  - ENG 0.12 mg/day
- 3-4 weeks
- Efficacy not affected by weight
- Neutral effect on lipids

Higginbotham S Contraception 2009
Simmons K Contraception for the medically challenging patient 2014
EE 35mcg/day
Norelgestromin 150 mcg/day
21 days
Transdermal
Limited data finds no effect on weight
Little data concerning effect on glucose and lipids
### CP Efficacy

Distribution of pregnancies by baseline body weight deciles.

<table>
<thead>
<tr>
<th>Decile</th>
<th>Body weight range (kg)</th>
<th>No. of pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;52</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>52 to &lt;55</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>55 to &lt;58</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>58 to &lt;60</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>60 to &lt;63</td>
<td>2</td>
</tr>
<tr>
<td>6</td>
<td>63 to &lt;66</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>66 to &lt;69</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>69 to &lt;74</td>
<td>0</td>
</tr>
<tr>
<td>9</td>
<td>74 to &lt;80</td>
<td>2</td>
</tr>
<tr>
<td>10</td>
<td>≥80</td>
<td>7</td>
</tr>
<tr>
<td>Sub 10a</td>
<td>80 to 85</td>
<td>1</td>
</tr>
<tr>
<td>Sub 10b</td>
<td>85 to 90</td>
<td>1</td>
</tr>
<tr>
<td>Sub 10c</td>
<td>≥90</td>
<td>5</td>
</tr>
</tbody>
</table>

Barrier Methods

- **Condoms**
  - Decrease STI transmission
  - Inexpensive
  - No prescription
  - No effect on weight or metabolic factors

- **Diaphragm**
  - Requires fitting
  - No affect on weight or metabolic factors
  - Requires re-fitting with weight changes

- **Sponge**
  - No prescription
  - No effect on weight or metabolic factors
  - May be difficult to insert and remove
Effective

- Fertility awareness
  - Compliance
  - Regular cycles
  - No effect of weight or metabolic factors, when successful

- Cap
  - Femcap
  - No custom fitting
  - Inexpensive
  - Requires spermacide

- Spermacide
  - Several different forms
  - No prescription
  - Inexpensive
  - Can affect vaginal mucosa
Take Home

- Obesity complicates pregnancy
- There are several options of contraception not affected by obesity
- There are several options of contraception that will not affect obesity or other co-morbidities
- Consider your patient’s risk of pregnancy when counseling contraception