Objectives

After this session, participants will be able to:

- Recognize the obesity epidemic and its effect on our patients
- Describe Risks & Benefits of contraceptive options vs. risk of pregnancy in obese women
- Utilize 2010 CDC US Medical Eligibility Criteria for Contraception Use to advise obese patients on contraceptive options
- Understand contraceptive effectiveness in normal weight vs obese women

Disclosures and Credits

- Scientific Advisory panel: Medicine 360
- Speakers panel: none
- Stock: none
- Big Thank You to Carolyn Westoff MD for sharing her slides with me

Calculating Body Mass Index (BMI)

*Calculated* the same way for adults and teens

- **Kilograms and meters (or centimeters)**
  
  \[
  \text{Formula: } \frac{\text{weight (kg)}}{[\text{height (m)}]^2}
  \]

- **Pounds and inches**
  
  \[
  \text{Formula: } \frac{\text{weight (lb)}}{[\text{height (in)}]^2 \times 703}
  \]

Body Mass Index (BMI)

<table>
<thead>
<tr>
<th>Terminology</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5 to 24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25 to 29.9</td>
</tr>
<tr>
<td>Obesity</td>
<td>30 or greater</td>
</tr>
<tr>
<td>Class I</td>
<td>30 to 34.9</td>
</tr>
<tr>
<td>Class II</td>
<td>35 to 39.9</td>
</tr>
<tr>
<td>Class III</td>
<td>40 or greater</td>
</tr>
</tbody>
</table>

Obesity Trends Among US Adults

1985
- No Data
- <10%
- 10%–14%

1990
- No Data
- <10%
- 10%–14%

1995
- No Data
- <10%
- 10%–14%
- 15%–19%
- ≥20%

2000
- No Data
- <10%
- 10%–14%
- 15%–19%
- ≥20%

2004
- No Data
- <10%
- 10%–14%
- 15%–19%
- 20%–24%
- ≥25%
Obesity Trends Among US Adults 2005

No Data          <10%           10%–14% 15%–19%           20%–24%          25%–29% ≥ 30%

Obesity Trends Among US Adults 2006

No Data          <10%           10%–14% 15%–19%           20%–24%          25%–29% ≥ 30%

Obesity Trends Among U.S. Adults 2008

No Data          <10%           10%–14% 15%–19%           20%–24%          25%–29% ≥ 30%

2/3 of US reproductive-age women overweight or obese


Obesity – Non-Hispanic White only

Obesity Rates & Race Among US Adults 2006-2008

White non-Hispanic
Obesity Rates & Race Among US Adults 2006-2008

Disparities in Unintended Pregnancy

- US, 2001 unintended pregnancies
  - 51/1,000 women 15-44
  - 76/1,000 women < HS education
  - 78/1,000 Hispanic women
  - 98/1,000 Black women
  - 112/1,000 women < 100% FPL

Factors Associated with Obesity

- Increasing age
- Female gender
- Black race, Hispanic ethnicity
- Lower individual level SES (income, education, assets)
- Community SES disadvantage

Health Consequences of Obesity

- Cardiovascular disease
  - HTN, DM, DVT/PE
- Musculoskeletal/joint disease
- Endometrial cancer
- Fertility impairment
- Treatment complications

Pregnancy Complications in Obesity

- Gestational diabetes mellitus
- Preeclampsia
- Planned and emergency cesarean delivery
- Postpartum hemorrhage
- Macrosomia
- Low Apgar score
- Stillborn fetus
Impact of obesity on fertility

- Obesity may reduce frequency of ovulation, which results in irregular menstrual cycles (Murthy, 2010).
- High insulin levels, (insulin resistance w/ obesity) can cause ovulatory dysfunction & lower SHBG (Wuntakal & Hollingworth, 2009).
- Higher androgen levels in women with abdominal obesity vs peripheral obesity (Carmina, 2009).


Impact of obesity on fertility continued

- Adipose tissue converts elevated androgens to estrogens.
- Adipose tissue produces leptin proportionate to % of fat.
- Leptin inhibits ovarian follicular development.
- Obese women with regular menstrual cycles, (indicating ovulation) similar time to conception when not using contraception as do women with normal weight (Richman, 2008).

Obesity Increases VTE Risk

- Consistent evidence: systematic review & cohort and case–control studies.
- The risk appears to be at least double that for normal weight subjects.
- Risk increases with age.
- Plausible mechanisms:
  - Obesity may limit venous return.
  - Changes in coagulation system.

Hormonal Contraceptive & Obesity

CDC MEC: COC, Patch, Ring

BMI > 30 = Category 2

Rationale:
- VTE more common, but absolute risk small.
- Equal rates of MI, weight gain.
- Decreased efficacy for patch >90kg (by weight not BMI).

CHCs and Weight Gain

- 3 placebo-controlled, RCTs did not find evidence supporting causal association between COCs or patch and weight gain.
- Most comparisons of different CHCs showed no substantial difference in weight.
- Available evidence insufficient to determine the effect of CHCs on weight, but no large effect evident.

**POP and Weight Gain**

- Little evidence of weight gain using POPs.
- Mean gain <2 kg for most studies up to 12 months.
- Similar wt gain for comparison group using another contraceptive.
- No significant ↑ in the risk of stroke, myocardial infarction, or VTE among users of POPs compared with non-users.


**Weight Gain and other HCs**

- Patch not associated with a significant increase in body weight.
- No evidence regarding weight change with the current vaginal ring.
- No evidence regarding weight change with ENG implants.


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**LNG IUS and Weight Gain**

- No studies of LNG IUS that met Cochrane inclusion criteria.


**DMPA**

- Equal efficacy for obese women
  - 150-mg intramuscular or 106-mg subcutaneous formulations of DMPA.
  - Increasing obesity correlating with decreasing serum levels of MPA.
    - still consistently above minimum needed for ovulation inhibition.


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**DMPA and Efficacy**

- Large inter-subject variability in serum DMPA levels.
- Fluctuating E2 levels reflective of follicular development occurred more in obese women.
- DMPA levels lower among obese vs. normal wt and lowest among extremely obese subjects.
- Median MPA levels remained above the level (200 pg/mL) needed to prevent ovulation.


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**DMPA and Weight Gain**

- About ¼ of DMPA users had early weight gain.
- Early weight gainers had greater intensity—much steeper slope of wt gain than regular wt gainers.
- Risk factors for early wt gain were
  - BMI < 30
  - Parity ≥1
  - Self-reported increased appetite after 6 months.
- Most DMPA users who gain excessive weight gain ≥5% within 6 months.
- We can use these data to predict who is at risk of excessive gain and counsel them appropriately.

**DMPA and Weight Gain**

- Teens on DMPA gain more weight than teens on COCs
- Teens who gained >5% of baseline weight at 3 months were at high risk at gaining even more weight at 12 months
- Overweight teens may be more likely to have significant weight gain on DMPA


**Contraceptive Ring And Efficacy**

NuvaRing is not associated with an increased failure rate for women in the highest weight decile (>166 lbs) versus the rest of the study population.


**Nuvaring Pharmacokinetics**

Serum concentration of EE and ENG in 18 normal weight and 19 obese study participants.


**COCs and Efficacy**

Four studies found statistically significant ↑ risk of contraceptive failure with ↑BMI


**Continuous COCs and Efficacy March 2012**

- Crude pregnancy rates were similar across weight and BMI deciles
- No discernable differences observed between deciles using either BMI or weight classification criterion

Westhoff CL, Hait HI, Reape KZ. Body weight does not impact pregnancy rates during use of a low-dose extended-regimen 91-day oral contraceptive Contraception 2012; 85(3):235-239.
Studies (2001-2008): OCs and Weight

<table>
<thead>
<tr>
<th>Year</th>
<th>Study Type</th>
<th>Weight</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vessey &amp; Painter-2001</td>
<td>Prospective cohort</td>
<td>Measured</td>
<td>No</td>
</tr>
<tr>
<td>Holt et al-2002</td>
<td>Ratio cohort</td>
<td>Self-reported</td>
<td>Yes</td>
</tr>
<tr>
<td>Holt et al-2005</td>
<td>Case-control</td>
<td>Self-reported</td>
<td>Yes</td>
</tr>
<tr>
<td>Brunner &amp; Hogue-2005</td>
<td>Ratio cohort</td>
<td>Self-reported</td>
<td>No</td>
</tr>
<tr>
<td>Brunner et al-2006</td>
<td>Case cohort</td>
<td>Self-reported</td>
<td>No</td>
</tr>
<tr>
<td>Zhang* 2006</td>
<td>Clinical Trial</td>
<td>Measured</td>
<td>No</td>
</tr>
<tr>
<td>Westhoff* 2008</td>
<td>Clinical Trial</td>
<td>Measured</td>
<td>No</td>
</tr>
</tbody>
</table>

*Abstract
Trussell J. Contraception 2009; 33:4-8.

COC: and ovarian suppression

- **RCT 150 women**
- **No meaningful differences** between the normal-weight and obese participants,
- No difference between randomized 20mcg EE/100mcg LNG or 30mcg EE/150mcg LNG
- 21/7 formulation
- BMI 30 vs 30-39.9


Etonogestrel Implant and Obesity

No difference in efficacy seen in obese women, but not included in original trials

Chart review of >300 women found obese women significantly less likely to have implant removed for bleeding


Etonogestrel Implant and PK

In a 6-month study of 13 obese women had lower serum ENG than four normal weight women. HOWEVER, all serum levels were greater than therapeutic threshold. NO pregnancies reported in obese implant users.

Etonogestrel Implant and PK

Not studied in obese women
- No negative effect on the endothelial parameter NO or on the cardiovascular risk parameters
  - CRP
  - Cholesterol/HDL ratio
- ↓SHBG was seen & might be an advantage for the risk of DVT.

Mornar and Gilliam AJOG 2012

Emerging issues with EC
Pregnancies /1000 Women after Unprotected Intercourse

ParaGard, ella, Plan B/Next Choice, Yuzpe, Nothing

Efficacy Levonorgestrel and Ulipristal Emergency Contraception

- The variable with the most highly significant impact on the risk of pregnancy was BMI.
- The risk of pregnancy was 1.5 X if BMI > 25 and >3 X if BMI > 30 compared to BMI < 25.


LNG VS. UPA EC
Reduced Efficacy in Obese Women

- For obese women LNG >4X greater pregnancy risk vs. normal-weight or underweight women.
- For obese women UPA >2X greater risk of pregnancy vs. normal-weight or underweight women.
- Rapid risk of ↓ efficacy with LNG with increasing BMI.


EC and Pregnancy Risk

<table>
<thead>
<tr>
<th>Variable</th>
<th>Groups</th>
<th>Pregnancy, n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Overall</td>
<td>UPA</td>
</tr>
<tr>
<td>BMI</td>
<td>Normal</td>
<td>27/2232 (1.2)</td>
</tr>
<tr>
<td></td>
<td>Overweight</td>
<td>13/444 (1.7)</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>20/469 (4.3)</td>
</tr>
<tr>
<td>Conception Probabilitya</td>
<td>Low</td>
<td>25/2227 (1.1)</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>35/1218 (2.9)</td>
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<tr>
<td>Further Intercourse</td>
<td>No</td>
<td>49/3274 (1.5)</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11/469 (2.3)</td>
</tr>
</tbody>
</table>

*a High conception probability = day of ovulation minus 5 to plus 1.


Contraceptive Effectiveness & Obesity – Summary

- COCs, extensive data, little concern
- Ring, good data, no concern
- Implant, more data coming, no concern
- Depo, few data, minimal concern
- Patch, increasing data, decreasing concern
- LNG EC, one good study, substantial confusion

Does The Dosage Of Mifepristone Or Misoprostol Need To Be Increased For Obese Women?

No. Success rates no different for obese women than for non-obese women using the standard regimens.

Bariatric Surgery

- **Restrictive:**
  - Decreases stomach "storage capacity" & delays emptying
  - No effect on intestinal absorption
  - **Examples:** Vertical banded gastroplasty, laparoscopic adjustable gastric band, laparoscopic sleeve gastrectomy
- **Malabsorptive:**
  - Involves removal of much of stomach & bypasses foregut
  - Interferes with/ decreases intestinal absorption of calories and nutrients
  - **Example:** Biliopancreatic diversion (not common)
- **Restrictive-malabsorptive**
  - A combination of the above 2 mechanisms
  - **Roux-en-Y gastric bypass**
    - One of the most common operations in the US

Gastric (laparoscopic) banding

- [Image from ebariatricsurgery.com](image)

Roux-en-Y gastric bypass procedure

- [Image from ebariatricsurgery.com](image)

Contraception after bariatric surgery: Why?

- With decreasing weight and accompanying metabolic changes, menstrual cycles may normalize and fertility improve
- **Guidelines:** delay pregnancy 1 to 2 years after surgery
  - Postoperative complications, metabolic changes
- **Many surgical patients are women of reproductive age**
MEC RESTRICTIVE
bariatric surgery

<table>
<thead>
<tr>
<th>Type</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined pill, patch, ring</td>
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</tr>
<tr>
<td>Progestin only pills</td>
<td>1</td>
</tr>
<tr>
<td>DMPA</td>
<td>1</td>
</tr>
<tr>
<td>Copper IUD</td>
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</tr>
<tr>
<td>LNG IUD</td>
<td>1</td>
</tr>
<tr>
<td>Progestin Implant</td>
<td>1</td>
</tr>
</tbody>
</table>

MEC MALABSORPTIVE
bariatric surgery:

<table>
<thead>
<tr>
<th>Type</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined or progestin-only pill</td>
<td>3</td>
</tr>
<tr>
<td>Combined patch or ring</td>
<td>1</td>
</tr>
<tr>
<td>DMPA</td>
<td>1</td>
</tr>
<tr>
<td>Copper IUD</td>
<td>1</td>
</tr>
<tr>
<td>LNG IUD</td>
<td>1</td>
</tr>
<tr>
<td>Progestin Implant</td>
<td>1</td>
</tr>
</tbody>
</table>

Obesity & VTE with Hormonal Contraception

Obesity & VTE during OC use

| <25 | No | 1           |
| 25<30 | No | 2.52, 1.38-4.57 |
| ≥30  | No | 3.04, 1.66-5.37 |
| <25  | Yes| 4.15, 2.85-6.03 |
| 25<30 | Yes| 11.63, 7.46-18.14 |
| ≥30  | Yes| 23.78, 13.35-42.34 |

Combined effect of body mass index (BMI) and oral contraceptive (OC) use on the risk of venous thrombosis in women aged 18-39 years. (n = 742)

Pomp, te Cessie, Rosendaal, Doggen, 2007

Obesity & VTE during OC use

- 196 VTE cases, 746 controls

Non Users | RR = 1.0
OC users BMI < 30 | RR = 3.34
OC users BMI > 30 | RR = 6.04

Obesity & VTE during OC use

CDC MEC: Deep Venous Thrombosis

CDC MEC: Deep Venous Thrombosis

VTE risk, Obesity and the Ring

VTE risk, obesity and the Patch

- Risk of VTE in new ring users probably similar to COCs.
- No data yet to evaluate risk in obese subgroup.

- Obesity associated with ↑risk of VTE in patch users
- VTE risk is not materially different than that of users of LNG COCs in women <40 years.
- Can’t rule out some ↑risk in women aged ≥40
Obesity & VTE

UK MEC - 2009

- No change in effectiveness up to BMI = 40
- LNG-EC effectiveness merits further study
- Weight gain limited to subset of DMPA users.
- VTE risks important (& age matters)

Obesity & Contraception

Additional Points

- Remember Hysteroscopic BTL
- Remember Mirena to control bleeding & prevent endometrial cancer
- IUD insertions more challenging
- Mifepristone – no need to increase dose
- CHCs OK after bariatric surgery

Current Guidelines & Recommendations

- “(T)he Society of Family Planning strongly encourages the use of both hormonal and non-hormonal methods of contraception in obese women desiring pregnancy prevention with very few restrictions.”

Bottom line

The use of contraception is generally safer than pregnancy in obese women, even in those with chronic medical conditions
Venous Thrombosis and CHC

- DVT rates with increasing dose of estrogen
- OC and OrthoEvra have similar DVT risk (Jick, 2006)
  - NGM OCs: 4.2/10,000 women/year
  - Patch: 5.3/10,000 women/year
  - Age-adj RR: 1.1 (95% CI: 0.7-1.8)

- DVT risk declines with increasing duration of use
- Progestin type, dose have no (or minimal) impact

CDC MEC: History of DVT/PE

Not on Anticoagulant Therapy

- Higher risk for recurrent DVT/PE
  - History of estrogen-associated DVT/PE
  - Pregnancy-associated DVT/PE
  - Idiopathic DVT/PE
  - Thrombophilia; antiphospholipid syndrome
  - Active cancer (metastatic, on therapy, or < 6 months after clinical remission)
  - History of recurrent DVT/PE

Prior Venous Thrombosis and CHC

Conventional wisdom

- If a woman has h/o idiopathic or postpartum DVT or VTE, may be predisposed to recurrence if given exogenous estrogen
  - Hence, avoid E-containing contraceptives

- If DVT related to another condition (e.g., immobilization, trauma), without a history of recurrence, E-containing contraceptives may be considered Category 3

CDC MEC: Hypertension

Hypertension: What if the meds are working?

- ACOG: Women <35yr well-controlled HTN can use combined methods if:
  - Otherwise healthy
  - No evidence of end-organ vascular damage
  - NO SMOKING

- Absolute risks of MI, stroke are low
  - Balance with risks of pregnancy & benefits

- Current studies with low EE pills show minimal RR of stroke or increase BP
CHC and CVD

- Use of estrogen-containing contraceptives increases risk of cardiovascular events in women with pre-existing elevated baseline risk.

- Absolute number of cardiovascular events with estrogen use is small.

- Progestin-only contraceptives and the Cu-IUD do not increase risk of cardiovascular events more than that of the underlying condition.