POST-FERTILIZATION EFFECTS OF EMERGENCY CONTRACEPTIVES
Post-fertilization Effects of Emergency Contraceptives

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CONSCIENTIOUS OBJEcTION

- **Illinois**: pharmacists were disciplined for refusing to fill prescriptions for emergency contraceptives (ECs); sue employer for religious discrimination
- **Texas**: pharmacists fired for refusing to fill EC prescription for a rape victim (moral grounds)
- **Wisconsin**: pharmacist was tried in court (similar to Texas situation) in violation of state regulations/standards of care
WHAT ARE SOME OF THE ISSUES?

→ Is contraception OK?
→ Who decides what constitutes an “emergency”?
→ When is someone considered “pregnant”?
→ When does life begin?
→ What is your perspective on the sanctity of human life?
→ Is there a right of conscience for healthcare providers?
→ How do ECs work?
   → Post-fertilization/post-conception effects of ECs?
      ie, Do ECs possess an abortifacient potential?
Emergency*:  
- 1. a sudden, urgent, usually unexpected occurrence or occasion requiring immediate action  
- 2. a state, esp. of need for help or relief, created by some unexpected event  

Contraceptive*  
- 1. tending or serving to prevent conception or impregnation.

These definitions seem simple enough...don’t they?

* [www.dictionary.reference.com](http://www.dictionary.reference.com)
Post-coital contraception
The morning-after pill
The 72-hour pill
Used up to 3-5 days after sexual intercourse to prevent pregnancy
Last chance...
No contraceptive, contraceptive failure/misuse, condom breakage/slippage, missing/forgotten hormonal pills, IUD misplacement, failed coitus interruptus
METHODS

- **High-dose combined oral estrogen/progestin**
  - Oldest method: Yuzpe (Yuzpe and Lance, 1977)
    - 2 doses of 100 mcg ethinylestradiol/0.5mg levonorgestrel; 12 hours apart (Ovran 50)
    - Side effects: N/V (high dose estrogen), bleeding

- **Progesterone-only**
  - 1.5mg levonorgestrel x 1 within 72 hours
    - Plan B® One Step*; Levonelle (Eur)
    - Previously Plan B® was a 2-dose (0.75mg/dose) regimen administered 12 hours apart

- **Antiprogestin (low dose)**
  - 10mg mifepristone x 1
    - 200mg tablet (Mifeprex; RU-486; medication abortion up to 49 days gestation)
  - 30mg ulipristal acetate x 1 within 120 hours
    - Ella®**

- **Intrauterine contraception**
  - Copper-T IUD

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*Plan B® is a registered trademark of Women's Capital Corporation, a subsidiary of Duramed Pharmaceuticals, Inc. Duramed is a subsidiary of Barr Pharmaceuticals, LLC

**ella® is a registered trademark of Laboratoire HRA Pharma; distributed by Watson Pharma Inc.
PlanB One-Step
(levonorgestrel) tablet, 1.5 mg
Emergency Contraceptive

NEW! Now only ONE dose

Rx only for women younger than age 17

Take as soon as possible within 72 hours (3 days) after unprotected sex. The sooner you take it, the better Plan B® One-Step will work.

Reduces the chance of pregnancy after unprotected sex (i.e., if a regular birth control method fails or after sex without birth control) Not for regular birth control.

NDC 51285-088-88

1 Tablet
Levonorgestrel 1.5mg
HOW DOES IT ALL WORK?

And Physiology, too
HOW DOES IT ALL WORK?
HOW DOES IT ALL WORK?

GnRH  Follicle/Sac
FSH   Ovum/Egg
LH    Corpus Luteum
      (ruptured follicle)

Estrogen
Progesterone

hCG
CONCEPTION/IMPLANTATION LOGISTICS

- Availability of egg to be fertilized lasts about 24 hrs after ovulation
- Spermatazoa can survive for 5-6 days after being deposited in uterus
  - SCHEMATIC from Baird...
## TIMECOURSE OF CONCEPTION

<table>
<thead>
<tr>
<th>Day of intercourse relative to ovulation day</th>
<th>% Conception*</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5</td>
<td>8</td>
</tr>
<tr>
<td>-4</td>
<td>17</td>
</tr>
<tr>
<td>-3</td>
<td>8</td>
</tr>
<tr>
<td>-2</td>
<td>36</td>
</tr>
<tr>
<td>-1</td>
<td>34</td>
</tr>
<tr>
<td>0 (ovulation)</td>
<td>36</td>
</tr>
</tbody>
</table>

*Detection of hCG w/ or w/out clinical pregnancy

Adapted from Baird DT, Reproductive Biomedicine Online, March, 2009
CONCEPTION/IMPLANTATION LOGISTICS

- Availability of egg to be fertilized lasts about 24 hrs after ovulation
- Spermatazoa can survive for 5-6 days after being deposited in uterus
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- Implantation begins about day 7 (after ovulation; day 6 after fertilization) and is complete by about day 12: this is the “window of implantation”
OVULATION → IMPLANTATION

1. Fertilization (occurs within uterine tube 12–24 hours after ovulation)

2. Cleavage (first cleavage completed about 30 hours after fertilization)

3. Morula (3–4 days after fertilization)

4. Blastocyst (4 1/2–5 days after fertilization)

5. Implantation (occurs about 6 days after fertilization)

Frontal section through uterus, uterine tube, and ovary

Figure 29-5 Principles of Anatomy and Physiology, 11/e
© 2006 John Wiley & Sons
1. Prevent ovulation
2. Inhibit fertilization
3. Thwart implantation
1. Prevent ovulation
2. Inhibit fertilization
3. Thwart implantation

What about “emergency contraceptives”
HOW DOES PLAN B® WORK?

Usually administered within 72 hours of sexual intimacy; Plan B One-Step is a 1.5mg single dose of levonorgestrel.

"[EC] are not effective if a woman is already pregnant. Plan B One-Step is believed to act as an [EC] principally by preventing ovulation or fertilization...In addition, it may inhibit implantation (by altering the endometrium). It is not effective once the process of implantation has begun."

(FDA-approved labeling)
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Contraceptive properties are well established

- Ovulation (clearly)
- Fertilization (transit; mucous)
But, what’s the data on implantation (post-fertilization)?
POST-FERTILIZATION EFFECTS OF LEVONORGESTREL

- Animal data supports a lack of post-ovulation effects of ECs
- Theoretical/Statistical models raise concerns (earlier papers)
- More definitive study models fail to find any concerns
- NOTE: progesterone from the corpus luteum, post-ovulation, promotes implantation...how could levonorgestrel, a progesterone agonist, not do the same?

- So...post-fertilization effects of levonorgestrel?

The evidence does not support this proposed mechanism.

NOTE: The statement of this potential still exists in the approved FDA labeling of the product.
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HOW DOES ELLA® WORK?

Usually administered within 120 hours of sexual intimacy; ella is a 30mg single dose of ulipristal (an analog of mifepristone/RU486)

“When taken immediately before ovulation is to occur, ella postpones follicular rupture. The likely primary mechanism of action of ulipristal acetate for emergency contraception is therefore inhibition or delay of ovulation; however, alterations to the endometrium that may affect implantation may also contribute to efficacy.”

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Post-fertilization effects of ulipristal?

Chemically similar to mifepristone (RU486) – known, when given in sufficient doses, to be an abortifacient (the reason for such administration).

No evidence refuting or confirming this possibility; however, such seems quite plausible.

Approved by FDA....expected to be on market later in 2010
COUNSELING PATIENTS RE: EC

- This medication does not protect against STDs
- It should be taken < 72-120 hours (depending on the product) following unprotected intercourse
- Plan B® will not end an established pregnancy; however, the data on ella® does not support such counsel (do not take if already pregnant)
- It is not intended for regular use to prevent pregnancy
- ADRs
  - Headache, nausea/vomiting, potential for heavy bleeding
- This is a single-dose product
HAVE A GREAT DAY!