An Update on Emergency Contraception for the Pandemic and Beyond

David Turok, MD, MPH
Objectives & Outline

1. Copper IUD is most effective
2. Ulipristal acetate (Ella) most effective oral
3. Access & weight matter (for oral methods)
4. Evidence - EC & quick start intersection
Reproductive Justice
Biological Facts & EC

- People mostly have sex for fun
- Biology is imperfect
- Contraception is imperfect
- Rape & intimate partner violence happen
- Sperm-Egg union does not discriminate
What is EC?

- Prevents pregnancy after intercourse
- EC doesn't interrupt an existing pregnancy
- Must be initiated in a specific time frame
  - Copper IUD within 5-7 d of UPI
  - Ulipristal acetate 30 mg (UPA, Ella) within 5 d
  - Levonorgestrel 1.5 mg (LNG, Plan B) within 3 d
  - Mifepristone
The Fertile Window:

-5 to +1 days from ovulation

Day 3 - 4

EC Targets
- Follicular maturation
- Follicular rupture
- Ovum transport
- Sperm function
- Fertilization
- Endometrial receptivity
Sperm Attrition

Number of sperm (millions)

Ejaculation
Cervical mucus
Fallopian tube

Time (minutes)

Fritz and Speroff, Clinical Gyn, 2015, p.246.
WHEN IS EMERGENCY CONTRACEPTION MOST LIKELY TO BE EFFECTIVE?

https://helloclue.com/articles/sex/emergency-contraception-when-its-most-effective
How Does it Work?

- Disrupts ovulation
  - **LNG** blocks LH surge
  - **UPA** blocks ovulation prior to the LH peak
- ? Disrupts fertilization +? But not pregnancy
  - Copper IUD

Gemzell-Danielsson et al Contraception 2013;87:300.
When To Use It

• When giving a new contraception RX
• After unprotected intercourse
• New contraceptive start
• After sexual assault
### How Well Does it Work? EC Efficacy

<table>
<thead>
<tr>
<th>EC Method</th>
<th>Cycle Pregnancy Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper IUD</td>
<td>0.1%</td>
</tr>
<tr>
<td>UPA</td>
<td>1.2 – 1.8%</td>
</tr>
<tr>
<td>LNG</td>
<td>1.5 – 2.6%</td>
</tr>
</tbody>
</table>

Shen, Cochrane Database Syst Rev 2019; 1:CD001324
Glasier Lancet 2010; 375:555
IUD EC Efficacy: A Systematic Review of 35 Years of Experience

- 42 of 274 studies identified in English or Chinese
- 8 types of IUD
- 7034 women
- Pregnancy rate = 0.09%

Percent of EC Pregnancies Among Ulipristal Acetate & LNG EC Users by BMI

- BMI <25 kg/m²
- BMI 25-29.9 kg/m²
- BMI ≥30 kg/m²

- ± 143-175 Lbs
- ≥176 Lbs

Graph showing the percent of EC pregnancies among Ulipristal Acetate (UPA) and LNG EC users by BMI categories.
Results – Total LNG AUC$_{0-24}$

LNG AUC 0-24 in women with normal and obese BMI

Mean [LNG (ng/mL)]

Time (h)

Normal BMI
Obese BMI

Results – Total UPA AUC$_{0-24}$

UPA AUC 0-24 in women with normal and obese BMI

Normal n=12
Obese n=8

Doubling Oral LNG for Obese Women

BMI >30, LNG 3.0 mg

BMI >30, LNG 1.5 mg

Study Comparing Emergency Contraception Effectiveness in Women Who Weight ≥ 80 kg

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

Sponsor:
Health Decisions

Collaborator:
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Information provided by (Responsible Party):
Health Decisions

ClinicalTrials.gov Identifier: NCT03537768

Recruitment Status: Recruiting
First Posted: May 25, 2018
Last Update Posted: October 8, 2019

See Contacts and Locations
Percent of Pregnancies Among UPA & LNG EC Users

Sex outside fertile window | sex inside fertile window | No further intercourse | Yes further intercourse

The Copper (& LNG) IUD for EC Works Exceptionally for All Women

- Elevated BMI = 0-0.1%
- Intercourse in the fertile window = 0-0.1%
- Further intercourse in the cycle = 0-0.1%
Can you use Levonorgestrel EC as Regular Contraception?

- 22 trials, 12,400 participants
- 5.0 preg/100 woman-yrs (95% CI 4.4 to 5.6)
- Safe to use oral LNG EC multiple times/cycle

Repeated use of pre- and postcoital hormonal contraception for prevention of pregnancy
Cochrane Systematic Review 2014
EC and Ongoing Contraception ASEC

THE AMERICAN SOCIETY FOR EMERGENCY CONTRACEPTION

The American Society for Emergency Contraception (ASEC) works to improve access to and knowledge about EC throughout the United States. Read more about our mission statement here.

**ASEC is working to provide EC to college students who need help during the COVID-19 crisis. Click [here](http://americansocietyforec.org/uploads/3/4/5/6/34568220/asec_fact_sheet-_hormonal_contraception_after_ec.pdf) to donate and support**
The Interaction Between UPA & Progestogens

1. Does UPA alter the onset of ovarian quiescence when COCs are started after EC - **NO**

2. Do Progestogens when started with UPA affect preventing/delaying ovulation – **YES**

3. Should you delay restarting COCs if you miss pills and take UPA– **NO**
RCT of UPA vs Placebo at Mid-Cycle Then all started CHC (30mcg EE/150mcg LNG) N=76

47 (62%) ovarian quiescence

25 (33%) ovulated

OR 0.97 (95% CI: 0.39–2.46)

Figure 2 Cumulative proportions of subjects having reached quiescence in the 21 days of COC.

Figure 3 Cumulative proportions of subjects having ovulated in the 21 days of COC.
Do Progestogens Mess with UPA? Implications for Ongoing Contraception After UPA

- 3 arm RCT of 71 people
- Primary outcome: ovulation < 6 days
  - UPA & desogestrel – 13/29 (45%)
  - UPA & placebo – 1/29 (3%)
  - Placebo & desogestrel 11/29 (38%)
  - \( P = 0.0054 \)
Missing 3 Pills and Taking UPA

- CHC users in cycle 2 missed pilled on D5,6,&7
- Day 8 took UPA 30 mg
- RCT of **immediate vs. delayed start (5 days)** of CHCs
- Hoogland score to assess ovulation
- No one ovulated within 5 days of UPA
- In **immediate restart 0/26 ovulated** in the cycle
- In **delayed start 4/23 (17%) ovulated** in the cycle
- \( p=0.04 \)
Ongoing Contraception

EC Method

Copper IUD

Oral LNG

LNG

Ongoing Contraception

Easy, ready to go

Start, Abstain or backup x 1 week

Hold hormones for 5 days

Approach to selection of emergency contraception after unprotected intercourse

EC Method

Emergency contraception (EC) is a method of contraception that may be used to prevent pregnancy after sexual intercourse. EC is most effective if taken within 72 hours of intercourse and is estimated to be 89% effective if taken within 24 hours. EC works by preventing ovulation, thickening the cervical mucus, or interfering with sperm activity. EC is available in a variety of forms, including pills, rings, implants, and injections. EC is considered a backup method to be used in conjunction with other forms of contraception.
Desires IUD?

Insert IUD

Assess risk of pregnancy

High Risk:
- multiple &/or mid-cycle UPI

Offer UPA*
- Use back up. Delay hormonal contraception for 5 days

Low Risk:
- UPI outside fertile window, contraception failure
Prefers more effective EC or ongoing contraception?

More effective EC

Offer UPA*
Delay hormonal contraception for 5 days, continue abstain/backup x 1 week (12 days total)

Ongoing hormonal contraception

Offer LNG
Start hormonal contraception today, continue abstain/backup x 1 week
Stuff We’ve Learned About IUDs and EC

- Fewer pregnancies with CuT380 than oral LNG x 1 year

- CuT380 IUD anytime with a negative pregnancy test

- AND what about the LNG IUD for EC???????
U.S. Medical Eligibility Criteria for Contraceptive Use, 2016

*Except for pill, patch, ring, injectable, and implant users.

BOX 1. How To Be Reasonably Certain that a Woman is Not Pregnant

A health-care provider can be reasonably certain that a woman is not pregnant if she has no symptoms or signs of pregnancy and meets any one of the following criteria:

- is ≤7 days after the start of normal menses
- has not had sexual intercourse since the start of last normal menses
- has been correctly and consistently using a reliable method of contraception
- is ≤7 days after spontaneous or induced abortion
- is within 4 weeks postpartum
- is fully or nearly fully breastfeeding (exclusively breastfeeding or the vast majority [≥85%] of feeds are breastfeeds),* amenorrheic, and <6 months postpartum

Are There Limits on When a Copper IUD Can be Placed for EC?

The copper IUD can be placed for EC:

- **IF...** within 5 days of UPI
- **BUT...** if the day of ovulation can be estimated
- **THEN...** it can be inserted after 5 days after UPI
- **IF...** it’s not more than 5 days after ovulation
COULD THIS BE SIMPLER?
1,963 Copper T380 IUD EC Users

- No pregnancies
- 1840 participants (93.7%) had usual cycle lengths of 25-35 days
- 850 (46.2%) UPI in the fertile window
- 84 (4.6%) had IUD insertion > 5 days after ovulation
- 52 (2.7%) had insertion > 5 days after UPI
Risk of Pregnancy with **Copper T380 IUD Placement 6-14 days after UPI**

134 People

0 Pregnancies

(97.5% CI 0–2.7%)

+52 (WU) + 64 (Goldstuck)

= 250 (0%, 97.5% CI 0 – 1.5%)

Thompson, Contraception 2019; 100(3):219-221

Risk of Pregnancy with LNG 52 MG IUD Placement 6-14 days after UPI

187 People
1 Pregnancy
(95% CI 0.01 – 2.9%)
Next Up: **RAPID EC**

- **RCT Assessing Pregnancy with IuDs (RAPID) for EC**
- Women interested in an IUD for EC
- Randomly assigned to copper or LNG IUD
- Primary outcome: non-inferiority pregnancy at 4 weeks
- Secondary outcome: IUD continuation continuation
- Recruitment goal = 706
Making EC More Available Today

• Offer EC every time you address contraception
• Give samples of UPA or LNG EC (FPE covers!)
• Don’t withhold copper or LNG IUD if recent UPI
• Remind people oral LNG EC is OTC
• Provide UPA Rx ahead of time
**Conclusion**

1. Copper IUD is most effective

2. Ulipristal acetate (Ella) most effective oral

3. Access & weight matter (for oral methods)

4. Evidence - EC & quick start intersection
Methods: Original Inclusion Criteria

- Secondary analysis of a prospective trial of copper T380 IUD EC users in China (n=1,963)
- Age 18-44
- Regular cycles between 24-42 days
- Known last menstrual period (LMP)
- Within 5 days (120 hours) of UPI
- All participants had a negative urine pregnancy test (hcg 25 IU/L)
IUD EC Insertion by Days Since LMP

Distribution of Days Since Last Menstrual Period to Insertion

Days Since Last Menstrual Period to Insertion

Percent
Day of UPI Relative to Ovulation

Turok et al. Human Reproduction 2103
# How Do I Share With My Patients?

## OOPS! Emergency Contraception: Birth Control That Works After Sex

<table>
<thead>
<tr>
<th>Types of emergency contraception</th>
<th>How well does it work?</th>
<th>How soon do I have to use it?</th>
<th>How do I use it?</th>
<th>Where can I get it?</th>
</tr>
</thead>
<tbody>
<tr>
<td>ParaGard IUD</td>
<td><strong>Almost 100% effective</strong></td>
<td><strong>Within 5 days</strong></td>
<td>It’s placed in the uterus by a doctor or nurse</td>
<td>From a doctor, nurse, or at a clinic</td>
</tr>
<tr>
<td>Ella</td>
<td><strong>2nd</strong></td>
<td></td>
<td>Keep working as super effective birth control.</td>
<td>Say it’s for EC so you are scheduled quickly.</td>
</tr>
<tr>
<td>PlanB One-Step or a generic</td>
<td><strong>3rd</strong></td>
<td></td>
<td>Take the pill as soon as you get it</td>
<td>From a doctor, nurse, or at a clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Remember to use it every time you have unprotected sex.</td>
<td>Get an extra pack for future emergencies.</td>
</tr>
</tbody>
</table>