Emergency Contraception
Review
You’re Posed a Question!
What we need to know and how to help
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Presentation Objectives:
• Review female reproductive/menstrual cycle
• Discuss available methods of birth control and the concept of emergency contraception
• Discuss background and history of emergency contraception
• Examine Utah Laws and Regulations governing availability and sale of emergency contraception
• Discuss pharmacist evaluation of indication for use.
• Describe the mechanism of action, timing, and safety of available products in the United States.
• Learn opportunities how pharmacists can identify opportunities to reduce barriers and improve access to product.

National Contraception Issues and Feelings!
• Health care law’s contraceptive mandate officially kicks in 8/1/12
• Most businesses will have to make sure their insurance plans cover birth control
  • Including those run by owners who personally believe birth control is immoral.
NY Times, 8/1/12
Why is Birth Control Such a Controversial Issue?

- Concern with the high cost of living and healthcare. Additionally, there are also issues of sexually transmitted diseases.
- People nowadays are requested to be careful with their sex partners and the fact that unmarried couples are liable to have sex which makes the use of contraception even more widespread.
- Married couples wishing to prevent themselves from having more children, unmarried couples do not want to run the risk of having children as well as preventing themselves from sexually transmitted diseases.
- Feminist view in that they believe that it is basically the woman’s choice to use or not to use contraception.
- Though there are several people who oppose contraception, on the whole there are indeed many more who support it as understand the practical side of the issue.

AlwaysHealth.com, accessed 4/2/12.

Female Reproductive Cycle

- Menstrual cycle begins with the first day of menses
- Marks beginning of “follicular phase”
  - Gonadotropin-releasing hormone (GnRH) directs the anterior pituitary gland to secrete:
    - FSH (follicle stimulating hormone)
    - LH (luteinizing hormone)
  - It is these hormones that direct events that result in production of a fertile ovum
Menstrual Cycle

- Three distinct phases:
  - Follicular phase
  - Ovulation phase
  - Luteal phase
- Begins with first day of menses, marking the beginning of the follicular phase
  - Median range of cycle length is 28 days but can range from 21-40 days
  - Menstrual bleeding can last anywhere from 3-7 days, normally averaging 5 days.

Follicular Phase

- Bleeding occurs as estrogen and progesterone levels from previous cycle decline
  - Top layers of thickened uterine lining break down and be shed
  - FSH levels begin to rise (w/in first 4 days of cycle)
    - Stimulate a small group of follicles each containing an egg to develop
    - Between days 5-7, one will become dominate as we see FSH levels decline
    - Follicle begins to produce estrogen
  - On average, lasts 13-14 days

Ovulation Phase

- As estrogen levels rise and remain elevated for a period of time, a surge in LH from the pituitary gland occurs
  - LH stimulate the final stages of follicular development and maturation (rupture and release of oocyte)
  - Ovulation occurs 10-16 hours after peak LH surge
  - After ovulation, the oocyte is released and travels the fallopian tube where fertilization and continued transport to the uterus for implantation occurs.
Luteal Phase

• Lasts approximately 14 days after ovulation (unless fertilization occurs)
• After release of egg, ruptured follicle closes, and forms a corpus luteum (along with other follicles) and produce estrogen and progesterone.
• Results in thickened uterus, thickened mucus in cervix, and raise in body temperature.
• IF the egg is not fertilized, the corpus luteum:
  ➢ degenerates and ceases hormone production
  ➢ progesterone levels decline
  ➢ endometrial lining shedding and menstruation
  ➢ NEW cycle begins

Probability of Pregnancy

• Evaluation of unprotected intercourse or timing/rhythm method

<table>
<thead>
<tr>
<th>Evaluation of Time Frame</th>
<th>Percent of Probability of Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 days prior to ovulation</td>
<td>15 percent</td>
</tr>
<tr>
<td>1 or 2 days prior to ovulation</td>
<td>30 percent</td>
</tr>
<tr>
<td>Day of ovulation</td>
<td>12 percent</td>
</tr>
<tr>
<td>1 or 2 days after ovulation</td>
<td>Nearly Zero</td>
</tr>
</tbody>
</table>

Contraception

• Implies the prevention of pregnancy following sexual intercourse
  ➢ Inhibits sperm from coming in contact with a mature ovum (barrier method)
  ➢ Prevent ovulation from occurring
  ➢ Prevent a fertilized ovum from successful implantation into the endometrium (creation of an unfavorable uterine environment)
• Commonly employed agents and methods:
  ➢ Oral and Transdermal contraceptives
  ➢ Long-acting injectable estrogens and progestins
  ➢ Condoms
  ➢ Spermicides
  ➢ Withdrawal method
  ➢ Diaphragm and other barrier devices
  ➢ Periodic abstinence
  ➢ IUDs
### Examples of Contraception Effectiveness

#### Episodic Methods:

<table>
<thead>
<tr>
<th>Product</th>
<th>Percent of Women with Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lowest Expected</td>
</tr>
<tr>
<td>Spermicide’s</td>
<td>3</td>
</tr>
<tr>
<td>Condoms, male use</td>
<td>2</td>
</tr>
<tr>
<td>Diaphragm w/ spermicide</td>
<td>6</td>
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</tbody>
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#### Hormonal Methods:

<table>
<thead>
<tr>
<th>Product</th>
<th>Percent of Women with Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lowest Expected</td>
</tr>
<tr>
<td>Oral Contraceptives</td>
<td>0.1</td>
</tr>
<tr>
<td>Progestin-only Oral Contraceptives</td>
<td>0.5</td>
</tr>
<tr>
<td>Transdermal Contraceptives</td>
<td>1</td>
</tr>
<tr>
<td>Contraceptive Rings (Nuvaring)</td>
<td>1</td>
</tr>
<tr>
<td>Progestin Implants</td>
<td>0.3</td>
</tr>
<tr>
<td>Depo-Provera shot</td>
<td>0.3</td>
</tr>
<tr>
<td>Lunaelle</td>
<td>0.1</td>
</tr>
</tbody>
</table>

#### IUD (hormonal and non-hormonal)

<table>
<thead>
<tr>
<th>Product</th>
<th>Percent of Women with Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lowest Expected</td>
</tr>
<tr>
<td>Copper T 380A (Paragard)</td>
<td>0.8</td>
</tr>
<tr>
<td>Progesterone T (Progestasert)</td>
<td>1.5</td>
</tr>
<tr>
<td>Levonorgestrel IUD (Arena)</td>
<td>0.1</td>
</tr>
</tbody>
</table>
How does hormonal contraception work?

• Estrogen:
  - Prevention of estrogen surge, which prevents LH surge
  - Prevents ovulation
  - Suppression of gonadotropin secretion during follicular phase
    - preventing follicular maturation
    - preventing ovarian hormone production

• Progesterone:
  - Creates thick cervical mucus to hinder sperm penetration
  - Impairs normal tubal motility and peristalsis

Concept of Emergency Contraception

• In the US each year, nearly 50% of all pregnancies are unintended.
• AKA “postcoital contraception” and the “morning after pill”
• Emergency measure to prevent pregnancy due to:
  - Unprotected intercourse (including sexual assault)
  - Failure of another method of contraception
• Allow access w/o hindrance
• Intended for use as an “occasional back-up method”, NOT primary method
Background and History of Emergency Contraception in the United States

• Initial study involving estrogen and progesterone in combination to prevent pregnancy after unprotected sex was done at Yale University in 1963.
• 1974, Canadian researcher Albert Yuzpe published a paper on the use of existing oral contraceptive pills as a post-coital contraceptive method.

More....Background and History

• Yuzpe Regimen (1974):
  ➢ Combining specific doses of oral contraceptive pills that have been used safely for past 30 years.
  ➢ Initial use was for victims of sexual assault.
• Princeton University: 1993
  ➢ Established a website for provider contact information.
  ➢ 1996, established in conjunction with RHTP, a EC hotline and now website:
    ➢ 1-888-NOT-2-LATE
    ➢ www.not-2-late.com

Last Slide on Background and History.. I Promise!

• 1997, US FDA approved 6 brands of oral contraceptives for off label prescription use as emergency contraception.
• 1998, Preven® was the first dedicated product approved for emergency contraception.
• 1999, Plan B®(levonorgestrel 0.75mg) the first progestin only form of EC was approved.
• After failed attempts, the FDA eventually widened EC to OTC status for sale to consumers in 2006.
• Plan B® One-Step was approved in 2009 as a single dose of 1.5mg levonorgestrel.
Emergency Contraception State Laws

- 21 states have statutes related to EC
- 16 states enacted legislation requiring hospitals or other facilities to:
  - Provide information and/or initiate EC to victims of sexual assault
- 9 states allow pharmacists to initiate EC if they are working in collaboration with a physician and/or completed a training program
- Access: in 2009 the FDA made progestin only pills available to individuals (men and women) age 17 and older

Utah Law and Regulations Governing Availability and Use (2009)

- Defined emergency contraception as the use of a substance approved by the Food and Drug Administration, to prevent pregnancy after sexual intercourse.
  - Requires specified health care facilities and practitioners to provide victims of sexual assault with unbiased, accurate, scientifically valid written and oral medical information regarding EC
    - Orally inform the victim they may obtain EC at the facility
    - Offer a complete regimen of EC
    - Provide this regimen to the victim at their request
    - Authorized person is present at the facility, on-call to dispense or prescribe EC

Available Products for Emergency Contraception

- Levonorgestrel
  - Plan B® One Step
  - Next Choice™ One Dose
  - Next Choice™
- Progesterone Receptor Antagonists
  - Ulipristal
    - Ella®
  - Mifepristone/RU-486 (indication/use not authorized in the US)
- Yuzpe Regimen
  - Estrogen and Progesterin Combinations
    - Ethinyl Estradiol and levonorgestrel or norgestrel
  - Vaginally inserted copper intrauterine device (copper T380A)
Indications for Use of Emergency Contraception

- Unprotected intercourse
  - To include forgetting to use a condom or diaphragm
- Condom breakage, tearing or incorrect use during intercourse
- Being 2-3 days late in resuming a hormonal contraceptive regimen
- Dislodging, breakage/tearing, or early removal of diaphragm
- Taking medications that can reduce effectiveness of hormonal contraception
- Exposure to a teratogen
- After a sexual assault

Additional “Pearls” of Information for Emergency Contraception

- Use an alternate method if 2 or more days of OCP’s are missed
- Progestin only OCP’s should be taken daily at the same time each day
- If a patient is taking an antibiotic regimen it is recommended to use an alternate/backup method
- If patient is taking anticonvulsant medications it is recommended to use an alternate/backup method
- Ill patient (vomiting and/or diarrhea) who is taking OCP’s should use alternate/back method

Levonorgestrel (Plan B® One Step)

- Extensively studied worldwide as an emergency contraceptive since 1970’s.
- In the US each year, nearly half of pregnancies are unintended
  - Nearly half of unintended pregnancies occurring each year are terminated by elective abortion
- When taken within 72 hours of unprotected sex, condom or diaphragm failure:
  - A single 1.5mg dose, levonorgestrel reduces risk of pregnancy by as much as 89%
  - Original Plan B® and Next Choice®, two dose regimen each containing 0.75mg of levonorgestrel
MOA and Timing of Levonorgestrel

- May act by one or more of the following actions:
  - Inhibition/delay of ovulation
  - Interference with fertilization or tubal transport
  - Altering of endometrial receptivity to prevent implantation
  - Causes regression of the corpus luteum

Levonorgestrel Efficacy, Safety and Side Effects

- When taken w/n 72 hours of unprotected intercourse
  - Reduced risk of pregnancy between 60 and 94%
  - Most effective when taken w/n 72 hours, but has shown effectiveness up to 120 hours
    - Efficacy is greatest when taken as early as possible
- Common Side Effects:
  - Nausea & vomiting
  - Abdominal Pain
  - Fatigue
  - Headache
  - Heavier than normal menstrual bleeding
- Will not affect or terminate an existing pregnancy

Ulipristal MOA, Efficacy, Safety and Side Effects

- Prescription only selective progesterone receptor modulator with mixed agonist and antagonist properties
  - Marketed under brand name Ella®
- MOA depends on timing of administration, but primary MOA appears to be delay of ovulation
  - Overall, results in approximately a 60% delay of ovulation by 5 days
- Use for EC within 120 hours after unprotected intercourse or contraceptive failure
- Common side effects see include headache, nausea, and abdominal pain
- Cycle length was increased by 2.8 days and duration of menses increased by nearly half a day
Yuzpe Regimen

- Combining specific doses of oral contraceptive pills that have been used safely for past 30 years.
  - Initial use was for victims of sexual assault
- Presently 21 brands of available OC's can be used for EC in the United States
- Some examples:
  - Cryselle®
  - Triphasil®
  - Alesse®
  - Lo/Ovral®

Patient Access, Pharmacy Opportunities

- Stocking EC has been a primary expectation of pharmacists and pharmacies
  - Limited awareness (consumer & provider) and created a low demand
  - Lack of focused attention and resources to inform the community
  - Absence of education and training to pharmacists and other providers

Barriers to Patient Access

- Encouragement of sexual risk taking behavior by increasing availability
  - Seen as promotion of no method at all
  - Increase risk for STDs and HIV?
- Demand for product has been low,
  - Pharmacies choose not to stock
- Pharmacies have cited moral objections to stocking EC
- Cost of product. Traditional OCPs are much more effective and more cost effective
Engaging the Pharmacy Community

- Pharmacies/pharmacists are seen as a vital health care provider
  - 63% of women said they would use pharmacy access for hormonal contraception for all forms including EC.
  - 41% not using any method said they would use a hormonal method if pharmacy access was available.
  - 55% said if EC were available at the pharmacy w/o advanced prescription, they would be more likely to use it.

Case Study #1

- A 18 year old female comes into your pharmacy upon hearing that you have Plan B One-Step in stock. As she approaches the counter, can you sell this to her?

Answer to Case #1

- Yes. By law we are able to provide this young woman with her request.
  - In 2009, the FDA made progestin only ECP available to those age 17 and older.
Case Study #2

• An 18 year old man comes into the pharmacy as asks to purchase Plan B One Step. What can you tell him?

Answer to Case Study #2

• There is no requirement that the purchaser has to be female, just as long as they are at least 17 years of age.

Case Study #3

• A 42 year old women comes into the pharmacy to purchase Plan B One Step. She is a current smoker and suffers from migraine headaches. Can she safely take the EC?
Answer to Case Study #3

- The only contraindication to the use of Plan B One Step is an established pregnancy, allergy to levonorgestrel or undiagnosed vaginal bleed. Migraine headaches and smoking are contraindicated with regular use of other hormonal contraceptives. Levonorgestrel has been shown to be safe and effective for women of all ages as EC.

Test Questions

1. (True___ False___) The menstrual cycle begins with the first day of menses.

2. The three distinct phases of the menstrual cycle (in order) are:
   a. Menstrual, Ovulation, Luteal
   b. Follicular, Luteal, Ovulation
   c. Menstrual, Ovulation, Luteal
   d. Follicular, Ovulation, Luteal

1. What percentage of yearly pregnancies in the US are unintended?
   a. 27%
   b. 35%
   c. 50%
   d. 67%

Test Questions

4. (Yes___ No___) A female patient with a (DOB 9/1/1995) comes into your pharmacy asking for Plan-B One Step. Can you sell this to them w/o a prescription by using today’s date as the date of sale?

5. (Yes___ No___) According to Utah Code (23-21b-101), individual pharmacies in Utah are required to carry Emergency Contraception.

6. Plan B One Step (levonorgestrel) should be taken within ___ hours of unprotected intercourse for greatest efficacy.
   a. 24 hours
   b. 36 hours
   c. 72 hours
   d. 120 hours
References


Emergency Contraception in Utah, section 26-21b-101 et seq and chapter 140 (HB340) amended section 26-21b-201, available online.


Martin KA, Barbieri R, Up To Date: Overview of the use of estrogen-progestin contraceptives. Available online (Accessed 4/18/12).


