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Emergency Contraception

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Case 1: A 20-year-old college student presents to the emergency department (ED) with her boyfriend at 3 a.m. She states that after having intercourse, they noticed that the condom had broken and her partner had ejaculated. She heard about the "morning-after pill" and is there to get it.

Case 2: A 32-year-old female presents to the ED approximately 1 hour after being attacked in the park and being raped. She believes the assailant did not use a condom and that he did ejaculate in her vagina. Her last menstrual period was two weeks ago. After providing medical treatment and forensic evidence collection, she asks you, "Doctor, can I get pregnant from this? What can I do?"

Introduction

There are approximately 3 million unintended pregnancies in the United States each year.[1] Most of these result from the nonuse of contraception or from a noticeable contraception failure such as a broken condom. Unintended pregnancies could be prevented with the use of emergency contraception (EC). In 2000, an estimated 51,000 pregnancies were prevented by EC, accounting for 43% of the decline in the abortion rate since 1994.[2]

For the emergency physician, sexual assault represents the most common presenting complaint associated with the potential for an unintended pregnancy. Annually, approximately 40,000 people in the United States visit EDs after sexual assault.[3] Pregnancy is estimated to occur in approximately 5% of sexual assaults.[3] Thus, pregnancy prevention is an important part of the care for these patients. For the emergency physician, EC represents the most viable treatment option. However, while highly effective when used properly, it is associated with a number of issues that make it much less commonly used.

EC is defined as a drug or device used after unprotected inter-

course to prevent an unwanted pregnancy.[4] While sometimes called the morning-after pill or postcoital contraception, EC is the preferred term as it avoids giving the mistaken impression that treatment must be taken the morning after sexual intercourse, and it emphasizes that the treatment is not intended to be used as an ongoing method of contraception. Reasons for using EC center on sexual assault, contraceptive failure, or unplanned sexual intercourse.[5,6] (*See Table 1.*) Currently available options for EC include emergency contraceptive pills, both with and without estrogens, and copper-bearing intrauterine devices.

This review will discuss the background, pharmacology, ED use, and controversies surrounding the use of EC in the ED.

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Reproductive Physiology

Once semen is ejaculated into the vagina, it undergoes a sequence of biochemical changes enabling it to fertilize an ovum; this process is called capacitation. Within one hour after ejaculation, sperm are maximally motile and semen is completely liquified. Motile sperm migrate at a rate of 2-3 mm/minute. The sperm's flagella, vaginal and uterine contractions, and the negative vaginal pressure following orgasm help to propel the sperm through the female reproductive tract. The first sperm reach the fallopian tube within five minutes after ejaculation, with maximal numbers present 4-6 hours later. Sperm must reach the ampulla of the fallopian tube for fertilization to occur. Motile sperm remain present in the female genital tract for up to 48-60 hours after intercourse. Capacitated sperm lose their ability to fertilize an ovum about 24 hours after ejaculation.

The female menstrual cycle is typically 28 days and consists of three phases: menses, proliferative phase, and secretory phase. In general, around day 14 (mid-cycle) a luteinizing hormone surge occurs. This surge triggers ovulation, whereby an ovum is released into the fallopian tube. Mature ova are fertile for only 15-18 hours after ovulation and degenerate if not fertilized. In general, one mature ovum is released per ovulation. Once a sperm and ovum encounter each other, complex reactions occur that cause fertilization of the ovum, and mitosis begins. A preembryo is formed within 24 hours. The embryo descends down the fallopian tube and continues to undergo rapid cell division and growth. At approximately day 7 after fertilization, the embryo implants into the uterine wall following another series of complex reactions.

A woman has the greatest chance of getting pregnant during the interval from 5 days before to 1 day after ovulation. Overall, a woman of childbearing age has an 8% chance of pregnancy with a single act of unprotected intercourse two days before ovulation.[7,8] There is a 25% chance of pregnancy with repeated sexual intercourse within in a single menstrual cycle. In women 19-26 years of age, the chance of pregnancy may be as high as 50% when unprotected intercourse occurs during this same period.[9]

Emergency Contraception

The use of EC reduces the risk of pregnancy by about 75%. If 100 women had unprotected intercourse once during the second or third week of their cycles, about 8 would become pregnant; after treatment with EC, only 2 would become pregnant, thus resulting in a 75% reduction.[10] In general, use of EC will reduce a woman's risk of pregnancy to 1-2%.[1] The effectiveness depends on the regimen used and on the time between unprotected intercourse and treatment.

Trials of EC first were described in the 1930s using high-dose stilbestrel. Over the next several decades, other regimens were tried that used high-dose estrogens alone or in combination with high-dose progestins. Many of these regimens were limited by their side effects. The use of oral EC became popular in 1974 when a Canadian physician, Albert Yuzpe, introduced a regimen consisting of 0.1 mg ethinyl estradiol and 0.5 mg levonorgestrel given within 72 hours of intercourse and repeated 12 hours later.

Table 1. Indications for Use of Emergency Contraception

- Sexual assault
- Lack of contraceptive use during coitus
- Mechanical failure of male condom (breakage, slippage, or leakage)
- Dislodgment, breakage, or incorrect use of diaphragm, cervical cap, or female condom
- Failure of spermicide tablet or film to melt before intercourse
- Error in practicing withdrawal (coitus interruptus)
- Missed combined oral contraceptives (any two consecutive pills)
- Missed progestin-only oral contraceptives (one or more)
- Expulsion or partial expulsion of an intrauterine device
- Exposure to potential teratogen while not using effective contraception
- Late injection of injectable contraceptive (> 2 weeks late for progestin-only formulation or > 3 days late for a combined estrogen plus progestin formulation)

Around the same time, a group of Latin American physicians proposed the use of progestin-only pills. Despite this early work, it was not until 1995 when several prominent non-governmental agencies, including Planned Parenthood, convened and developed a consensus statement calling for the need to make access to EC a practical reality.[11] Two EC specific products first became available in the United States in 1998.

Both the American College of Emergency Physicians (ACEP)[12] and the American College of Obstetrics and Gynecology (ACOG)[13] recommend EC for sexual assault survivors. In addition, the ACOG advocates this treatment be available over-the-counter for all women who wish to use it.[14] Further support for its use comes from the National Sexual Violence Resource Center (NSVRC), which advocates for legislation mandating all hospitals to offer EC for sexual assault victims, litigation for victims denied EC, and state regulations and monitoring of hospitals for compliance in providing EC to sexual assault survivors.[15]

Oral Emergency Contraception

EC comes in two orally administered forms—combined pills and progestin-only pills. Combined EC pills (ECPs) are ordinary birth control pills containing the hormones estrogen and progestin. The hormones that have been studied exclusively in clinical trials of ECPs are the estrogen ethinyl estradiol and the progestin levonorgestrel or norgestrel.

The Yuzpe regimen has since been the most commonly used method.[1,5] Until recently, this method was available by prescription as a specific EC product (Preven) and consisted of four pills, each containing 0.25 mg of levonorgestrel and 0.25 mg of ethinyl estradiol; a urine pregnancy test; and a patient information booklet.[16] Preven is no longer available from the manufacturer. A similar approach with the same efficacy is to use pills from a package of combination birth control pills that contain both the ethinyl estradiol and norgestrel or levonorgestrel in the dosages mentioned above. This combination is found in 18 brands of combined oral contraceptives in the United States. Many more products are available in other countries. Table 2 lists the oral contraceptives that can be used for EC in the United States.[5,10]

A more effective regimen for EC is the use of progestin-only contraceptive pills. Currently there is one FDA-approved product in the United States (Plan B). It consists of two 0.75-mg tablets of levonorgestrel taken 12 hours apart within 72 hours of unprotected intercourse.[17] Clinical trials comparing the progestin-only regimen to the combined regimen indicate that the progestin-only approach is more effective, reducing the risk of pregnancy to 1%.[18] Recent data have shown that the levonorgestrel regimen can be given once in a single dose, rather than in a divided dose, with the same efficacy.[19]

Mechanism of Action

EC prevents a pregnancy from starting. It is generally accepted that it does not interrupt an early established pregnancy. This difference is addressed in many educational resources available to clinicians and their patients.[5,10,20] (*See Table 3.*)

The mechanism of action of ECPs is not well understood and a single mechanism has not been identified. Like other hormonal contraceptives, ECPs probably work through multiple mechanisms that vary based on the timing of administration within the menstrual cycle.[21]

Proposed mechanisms of action include effects on sperm, the ovulation process, and/or the endometrium. The fertile days of the menstrual cycle are the days in which an act of sexual intercourse can give rise to pregnancy. These days are the interval from 5 days before to one day after ovulation.[7] Thus, sperm have to wait 1-5 days in the female genital tract before coming into contact with the ovum. This interval provides an opportunity to interfere with the migration and function of sperm and/or the process of ovulation. ECPs may prevent the contact of sperm and egg. The chance fertilization will take place even under ideal circumstances (intercourse during the most fertile days) does not exceed 50%. Minor alterations in the process greatly will decrease this probability.[22]

It has been shown that administration of levonorgestrel 3-10 hours after intercourse affects sperm migration between 3 and 9 hours after treatment.[4,22] It reduced the number of sperm recovered from the uterine cavity; increased uterine fluid pH, which immobilized sperm; and increased cervical mucous viscosity, which impeded further passage of sperm into the uterine cavity. This study used only 57% of the currently recommended dose of levonorgestrel but is highly relevant to its actions used as an EC. Effects on sperm function in vitro are dose-dependent and results from studies differ. In general, the data indicate that levonorgestrel in doses used for EC have no direct effect on sperm function.[4] There are no similar studies on the Yuzpe regimen.

During the ovulatory process, a normal gonadotropin surge occurs, triggering a series of local responses that lead to the release of a fertilizable oocyte and the formation of a corpus luteum. This complicated process requires a normal gonadotropin surge and proper evolution of the signaling cas-

Table 2. Oral Emergency Contraception Options Available in the United States

BRAND	DISTRIBUTOR	PILLS PER DOSE+	ETHINYL ESTRADIOL PER DOSE (MCG)	LEVONORGESTREL PER DOSE (MG)†
Plan-B	Duramed	1 white	NA	0.75
Preven	Gynetics	2 blue	100	0.50
Alesse	Wyeth	5 pink	100	0.50
Aviane	Barr	5 orange	100	0.50
Cryselle	Barr	4 white	120	0.60
Enpresse	Barr	4 orange	120	0.50
Lessina	Barr	5 pink	100	0.50
Levlen	Berlex	4 light orange	120	0.60
Levlite	Berlex	5 pink	120	0.50
Levora	Watson	4 white	120	0.60
Lo/Ovral	Wyeth	4 white	120	0.60
Low-Ogestrel	Watson	4 white	120	0.60
Nordette	Wyeth	4 light orange	120	0.60
Ogestrel	Watson	2 white	100	0.50
Ovral	Wyeth	2 white	100	0.50
Ovrette	Wyeth	20 yellow	0	0.75
Portia	Barr	4 pink	120	0.60
Seasonale	Barr	4 pink	120	0.60
Tri-Levlen	Berlex	4 yellow	120	0.50
Triphasil	Wyeth	4 yellow	120	0.50
Trivora	Watson	4 pink	120	0.50

*Plan-B and Preven are the only dedicated products specifically marketed for EC. The remaining have been declared safe and effective.[10]

+Treatment schedule is 1 dose within 120 hours after unprotected intercourse and another dose 12 hours later. See text for updated dosing information.

† The progestin in Ovral, Lo/Ovral, Low-Ogestrel, Cryselle, and Ovrette is norgestrel, which contain 2 isomers, only 1 of which (levonorgestrel) is bioactive; the amount of norgestrel in each tablet is twice the amount of levonorgestrel.

cades inside the follicle. Failure of this process can result in ovulatory dysfunction and compromised fertilization. Several studies have explored the possibility that ECPs alter the ovulatory process in women. The results of the studies seem to depend on the timing of ECP administration relative to the ovarian cycle.[21] Levonorgestrel given within 2-3 days prior to ovulation was able to completely suppress the luteinizing hormone (LH) peak.[4] The closer to ovulation that EC is given, the lesser the LH peak and shorter the cycle.[4] Both drug regimens tend to exert their greatest effect in the follicular phase. In general, depending on when EC is administered relative to the LH peak and ovulation (during the follicular phase), it has the capacity to interfere with the ovulatory process by inhibiting, suppressing, or delaying the LH surge or follicle rupture or by interfering with the formation or function of the corpus luteum.[4,22]

The only post-fertilization mechanism that has been investigated is an alteration in endometrial receptivity that could interfere with implantation.[22] Some studies found alterations in endometrial morphology or in the expression of progesterone-dependent molecules. Other studies showed negligible or no effect on the endometrium. With regard to levonorgestrel, several published reports do not support the hypothesis that it has a post-fertilization mechanism.[4,22]

From the results of these studies, it appears that the most plausible mechanism of action of EC is its effect on the blockade or delay of ovulation. This is especially true for levonorgestrel, which does not seem to prevent or affect fertilization or implantation.[4,22] Medical experts agree that EC is not medical abortion.[5] Six to seven days lapse between a sexual act and the establishment of a pregnancy (implantation). EC acts in this window to prevent pregnancy. Once a pregnancy is established, both the combination and progestin-only regimens cannot interrupt it.[5]

Timing of Administration

It generally is accepted that the earlier EC is administered, the greater the risk reduction of pregnancy occurring. This reduction also is dependent on the time of the menstrual cycle in which the sexual act and treatment with EC occur. A meta-analysis of eight studies including 3000 women total concluded that, when used within 72 hours of sex, the combined regimen prevents about 74% of unplanned pregnancies.[19]

The largest study of the progestin-only regimen was a randomized trial conducted by the World Health Organization (WHO).[18] This multicenter, multicountry trial included 1001 women and showed that, when used within 72 hours, 85% of pregnancies were prevented. This WHO study compared the

Table 3. EC Resources for Physicians and Patients

- Consortium for Emergency Contraception: www.cecinfo.org
- Emergency Contraception Web Site: http://not-2-late.com
- Emergency Contraception Hotline: 1-888-NOT-2-LATE
- ARHP EC Train-the-Trainer PowerPoint slide set: http://www.arhp.org/ec/
- Emergency Contraceptive Pills: Common Legal Questions about Prescribing, Dispensing, Repackaging, and Advertising. New York: The Center for Reproductive Law and Policy; 1999. To order, call 212-514-5534.
- Emergency Contraception: Resources for Providers. Seattle (WA): Program for Appropriate Technology in Health, 1997. To order, call 1-800-669-0156
- Emergency Contraception: Client Materials for Diverse Audiences. Seattle (WA): Program for Appropriate Technology in Health, 1998. To order, call 1-206-285-3500 or e-mail info@path.org.
- Emergency Oral Contraception. ACOG Practice Bulletin. Number 25. Washington (DC): The College; 2001. To order, call 508-750-8400
- Emergency Contraception: Is the Secret Getting Out? Menlo Park (CA): The Henry J. Kaiser Family Foundation; 1997. To order, call 1-800-656-4533 (ask for no. 1352).
- Expanding Global Access to Emergency Contraception. Consortium for Emergency Contraception. 2000. To order, www.path.org/cec/.
- Emergency Contraception (AP114) [patient education pamphlet]: American College of Obstetrics and Gynecologists. To order, call 1-800-763-2264, ext 830.

Yuzpe method with the progestin-only method and showed that the latter was significantly more effective than the combined regimen. The relative risk for pregnancy in this study was 0.36 (95% CI, 0.18 to 0.70), indicating that the chance of pregnancy among women who received levonorgestrel was about one-third that of those who received the Yuzpe regimen.[5,18]

Further analysis of the WHO study shows that the prevented fraction was 77% if the Yuzpe regimen was taken on the first day after intercourse, but only 31% if used on the third day. The levonorgestrel regimen also showed decreased effectiveness with time. Other studies have not supported this observation.[18,23] In fact, several studies have indicated that ECPs retain substantial effectiveness when used more than 72 hours after intercourse.[5,23] These studies suggest that EC confers protection up to 120 hours after intercourse.

With regard to timing of administration, the 72-hour time limit should be a guideline—women should be advised to use the treatment as soon as possible after the need is recognized, but treatment should not be withheld from those who present later.[5]

Contraindications

With the exception of allergies or sensitivity to the drugs, there are no contraindications to EC. The WHO notes that the method is not indicated for women with a suspected or confirmed pregnancy because the treatment will not work if the patient is already pregnant.[24] Thus, most practitioners will check either a urine or serum pregnancy test prior to administering EC. However, it should be noted that no known harm would occur to the woman, the course of her pregnancy, or the fetus if EC were used accidentally.[1,5,13] Checking a pregnancy test is done, therefore, to determine a pre-existing condition.

No studies have compared the risk of complications after EC in women with medical conditions or other risk factors and in women without them. The FDA-approved package inserts of the two U.S.-dedicated EC products (Preven and Plan B) list several precautions that appear to be derived from the package inserts for the combined oral contraceptive pills and are unlikely to apply, since the duration of use for EC is so short.[16,17]

The WHO guidelines state that breastfeeding and history of ectopic pregnancy are not contraindications to the use of EC.[24] In addition, in women with history of severe cardiovascular complications, angina pectoris, migraine, or severe liver disease, the benefits of EC treatment generally outweigh the possible risks from the medication and the risk from becoming pregnant. Smoking and age are not listed as contraindications. Use of EC has been shown not to alter clotting factors.[5]

Although data are lacking, some clinicians may prefer to prescribe the progestin-only regimen for women with classic contraindications to estrogen therapy. It should be remembered that in these women, pregnancy also may increase the chance of adverse outcomes, and the contraceptive benefit of even estrogen-containing EC may outweigh the risk of foregoing treatment.

Medication interactions with EC are minimal. One case report described an increased international normalized ratio (INR) after use of the levonorgestrel regimen in a woman on warfarin.[5] No other data are specifically available about interactions between EC regimens and other drugs. Interactions between ECPs may be similar to standard oral contraceptive pills. Certain medications, including rifampin, some anticonvulsant drugs, and St. John's wort, may decrease the efficacy of oral contraceptive pills. Despite popular belief, no credible evidence suggests that commonly used antibiotics reduce the efficacy of oral contraceptive pills.[5]

EC is not intended for frequent use. The ECPs are less effective and have more side effects than other methods of ongoing contraception.[5,11] Despite these limitations, EC can be used more than once in the same menstrual cycle. Repeated need for EC is a sign that the patient's current contraceptive approach is not working well for her and that she should be counseled on ways to prevent emergencies in the future.

Side Effects

The most common side effects of EC are nausea and vomiting. The Yuzpe regimen is associated with a 42% incidence of nausea and 16% incidence of vomiting.[25] The WHO trial found that nausea and vomiting were significantly lower for the progestin-only regimen, 23% and 6% respectively.[18] Other studies also have shown levonorgestrel to have lower rates of gastrointestinal upset.[5] In addition, single dose levonorgestrel (both pills

simultaneously) did not seem to significantly increase the incidence of nausea and vomiting.[19]

The best way to minimize nausea and vomiting is to use the progestin-only regimen when possible. A randomized clinical trial showed that if the Yuzpe regimen is used, the anti-emetic drug meclizine (Antivert, Bonine) can significantly reduce the chance of these side effects.[25] From this study, it could be implied that other antiemetics also would be effective. The antiemetic should be administered 30-60 minutes prior to the dose of ECP and continued per dosing recommendation for the particular agent. Antiemetic strategies for patients taking EC are presented in Table 4.[10]

Optimal management of the patient who vomits after taking EC is unknown. Some feel that vomiting indicates that sufficient quantities of hormone have been absorbed. Others recommend repeating the dose, especially if the vomiting occurred within one hour of administration.[5] In cases of severe vomiting, the pills can be administered vaginally, thus being absorbed through the vaginal epithelium.[26]

Another important side effect is irregular vaginal bleeding. This bleeding should not be confused with menses, which is the much-anticipated evidence of success. Women should be informed that EC does not bring on menses immediately. Most women will have their period within 1 week of the expected time, but some may have early or delayed menses.[5]

Other reported adverse outcomes in women with both regimens include dizziness, fatigue, headache, breast tenderness, and lower abdominal pain.[5,23] These symptoms usually are minor, may be treated symptomatically, and usually spontaneously resolve in a few days.

Clinicians may have concern about the risk of venous thromboembolism (VTE) in women who use EC. There has been a long established risk of VTE in women taking estrogen-based contraceptives who were older than 35 years, overweight, and smokers. One strategy is to use the progestin-only regimen in women at risk for VTE. A population-based cohort study found that of 73,302 women who received prescriptions for EC from 1989 to 1996, only 19 had developed VTE. Of these 19, none were exposed to EC in the 45 days prior to the VTE event. Crude incidence rate estimates for VTE are 0/100,000 person-years for current EC users. The authors conclude that the risk of VTE attributable to EC is not substantially higher than the risk for users of traditional oral contraceptives.[27]

One side effect that warrants discussion is the risk of ectopic pregnancy. There is concern that the use of levonorgestrel can increase the risk of ectopic pregnancy. There is little data on the risk of ectopic pregnancy following its use. From 1982 to 2002, a MEDLINE search failed to reveal any reported case of ectopic pregnancy after using levonorgestrel as EC. In 2003, Sheffer-Mimouni et al[28] reported three cases of ectopic pregnancy following the use of levonorgestrel in women without apparent risk factors for ectopic pregnancy. In all three cases, the levonorgestrel was administered peri- or postovulation. Since then, the total reported cases of levonorgestrel-associated ectopic pregnancy are 19.[29]

Table 4. Strategies to Reduce the Risk of Nausea Following EC

OTC

- 2 meclizine hydrochloride (Antivert, Bonine) 25-mg tablets 1 hour before first ECP dose
- 1-2 diphenhydramine hydrochloride (Benadryl) 25-mg tablets 1 hour before each ECP does; repeated as needed every 4-6 hours
- 1-2 dimenhydrinate (Dramamine) 50-mg tablets or 4-8 teaspoons 30-60 minutes before each ECP dose; repeat as needed every 4-6 hours

PRESCRIPTION

- 2 meclizine hydrochloride 25-mg tablets 1 hour before the first ECP dose
- 1 trimethobenzamide hydrochloride (Tigan) 250-mg tablet or 200-mg suppository 1 hour before each ECP dose; repeat as needed every 6-8 hours
- 1 promethazine hydrochloride (Phenergan) 25-mg tablet or suppository 30-60 minutes before each ECP dose, repeat as needed every 8-12 hours

Previous reports have documented five cases of ectopic pregnancy after use of the Yuzpe regimen. Yet, until the 2003 report, there were none reported for levonorgestrel. In fact, in the WHO ECP study, a total of 42 pregnancies occurred (11 for levonorgestrel vs 31 for Yuzpe regimen). None of these pregnancies were ectopic.[18] One criticism is that the number of pregnant patients in the study may have been insufficient to display an increase in ectopic rate from the baseline rate of 2% of pregnancies in the general population. If the results from the WHO study and two other large, double-blind, randomized trials are combined, a total of 4098 women received levonorgestrel EC. In this group, 67 (1.6%) developed unintended pregnancies. None of the pregnancies were ectopic, but the 95% confidence level is wide.[18,30-32] These studies were underpowered to detect an increased risk of ectopic pregnancy.

It is thought that peri- or postovulatory administered levonorgestrel can affect tubal function. The high progesterone levels may cause ciliary dysfunction, thus leading to ectopic pregnancy.[33] Interestingly, continuously administered progestin-only pills lower the absolute rate of ectopic pregnancy; however, if pregnancy does occur, the chance it will be ectopic is threefold higher than for pregnancies while using no method.[34]

In June 2003, Britain's chief medical officer warned physicians in the United Kingdom to be extra vigilant regarding the post-coital use of levonorgestrel.[35] Twelve (6%) of 201 reported unintended pregnancies that developed after drug failure were ectopic. This apparently high rate was considered worrisome because it triples the baseline of 2%. Since its introduction in the United Kingdom, 3 million have been sold. If used correctly, an expected 1.6% failure rate would generate 16,000 unintended pregnancies. Using the 2% baseline rate, one might expect to see 320 cases of ectopic pregnancy. Both the number of actual unintended pregnancies and resultant ectopic pregnancies are lower.[30]

These figures are derived from voluntary spontaneous reports from health care providers; underreporting is well recognized. Therefore, the true number of clinical failure and ectopic pregnancy cases is unknown. It appears that the risk, if any, is very small. Even so, the chief medical officer still advised that women who do not have a normal period after progestin-only EC should be followed up and "the possibility of an ectopic pregnancy should be considered, particularly in women with a previous ectopic pregnancy, fallopian tube surgery, or pelvic inflammatory disease."[35]

The manufacturers of the drug specify in the package insert, "health providers should be alert to the possibility of an ectopic pregnancy in women who become pregnant or complain of lower abdominal pain after taking the drug."[30]

ED Management

As with any patient encounter, the ED physician needs to start with a history and physical exam. Figure 1 outlines a strategy for EC use in the ED. It is important to discern whether the woman is seeking EC because of a contraception failure or because of a sexual assault. In the latter, the physician's role also should include medical treatment and stabilization, evidence protection, and sexually transmitted infection prophylaxis. Treatment of the sexual assault survivor is beyond the scope of this article and should be done in accordance with hospital or regional policies.

The history should include a discussion of the patient's menstrual history and estimation of where she is in her current cycle. While some clinicians may want to check a urine or serum pregnancy test prior to administering EC, this is not necessary as EC has no effect on established pregnancy.[1,5,13] Pelvic examination is unnecessary unless the patient has vaginal complaints or is presenting following sexual assault. Ideally, the medication will be provided in the ED as a recent study has shown that women can have difficulty in obtaining EC at some pharmacies.[2] Routine follow-up is not necessary. Women should be advised to return or seek follow-up if any medical problems arise. If menses has not returned within one week after the expected time or within four weeks after administration of EC, a pregnancy test should be considered. Victims of sexual assault should be referred for follow-up according to established guidelines and policies. Women who wish to start contraception should be referred to their family physicians or gynecologists.

EC specific information and education should be provided to patients while in the ED. Women should be informed that EC does not convey protection form pregnancy should another unprotected intercourse occur in the same cycle. Women should be informed of all possible side effects and what to do if they vomit after taking the pills. They also should be told to expect their next menstruation earlier, as expected, or a few days late. Women should be advised to follow-up for pregnancy testing if their menses have not returned within 2-4 weeks from when it was expected. Finally, it is important to stress that EC does not protect against sexually transmitted infections and HIV and other measures always should be taken.

Factors Contributing to Lack of Use

Although EC substantially can reduce the burden of unintended pregnancy, its use in the United States has been neglected.[5] A 1994 survey from the Harry Kaiser Family Foundation of 1000 American women and 1002 men found that 55% had heard of ECPs but only 1% have ever used EC.[36] It has been shown that only 20% of rape victims received EC over a seven-year period in the 1990s.[15] A statewide survey of 205 hospitals, conducted by the New York State Coalition Against Sexual Assault & Family Planning Advocates of NYS, found that 14% of the 196 respondent hospitals did not have a standard policy for ECP administration. From these hospitals alone, as many as 1000 victims were being sent away from the ED without receiving EC on site.[37] Since that survey, New York state has enacted legislation mandating that hospitals counsel rape survivors about the use of EC to prevent pregnancy and offer the medication on site.[37]

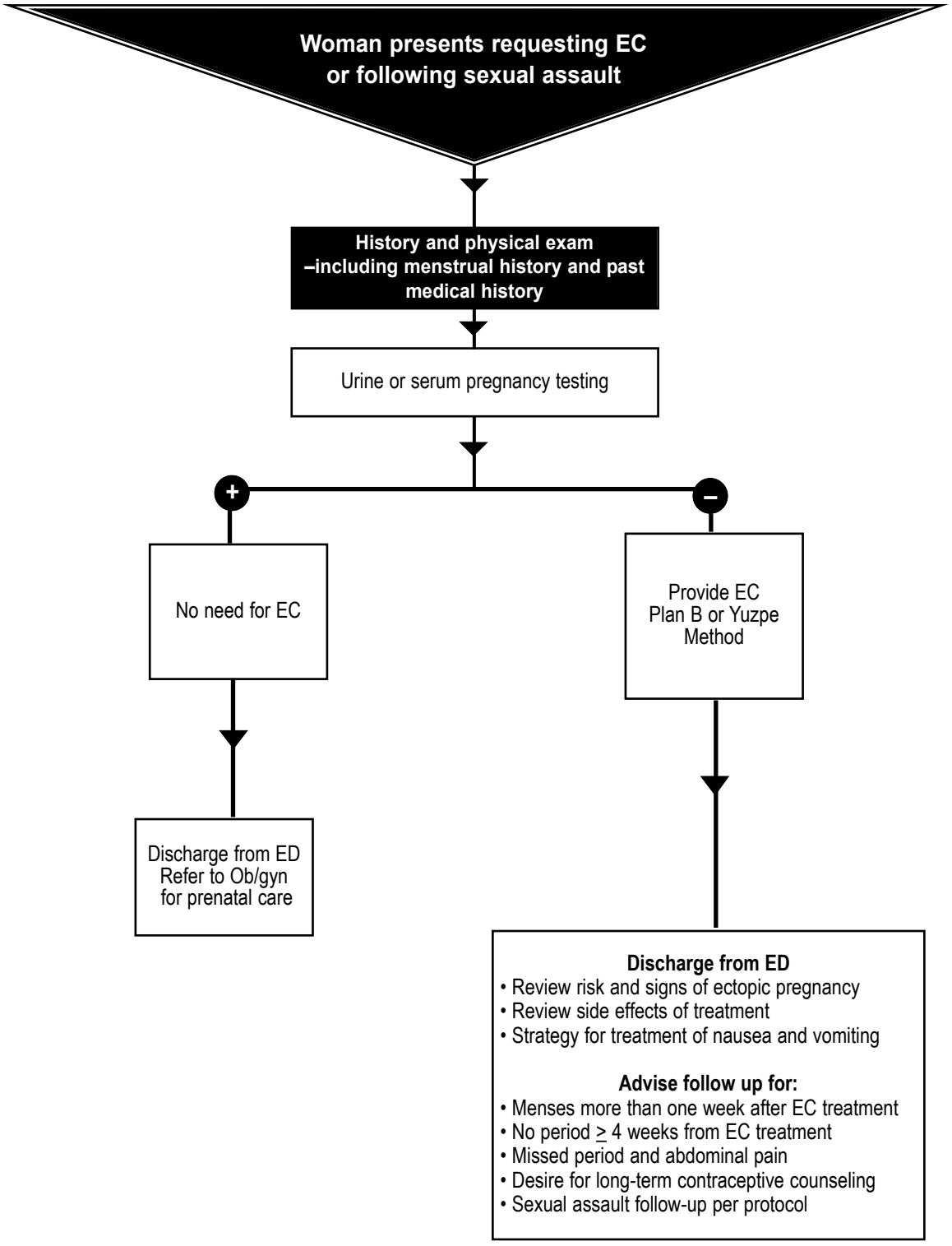
A number of factors contribute to the low use of EC. Most women and many health care providers are unfamiliar with this method and therefore do not consider using it or providing it when the need arises. Over the years, the Kaiser Family Foundation has commissioned several national studies of physicians and the public about EC. Their 2003 survey found that 80% of obstetrician-gynecologists and 36% of family practice physicians had prescribed EC in the last year; 25% of obstetricians-gynecologists and 14% of family physicians routinely discuss EC with their patients; 32% of women age 18-44 do not even know of its existence, and only 6% have ever used EC.[38] In addition to the lack of knowledge, physician attitudes toward the administration of EC likely play a significant role. Some clinicians have misperceptions about the clinical, logical, moral, and legal issues concerning EC or have a perceived lack of its need. A survey of emergency physicians found that 88% would offer EC to sexual assault survivors if the assailant was unknown, and only 73% would offer it after consensual sex.[3]

Access to EC often is limited. Some pharmacies may even refuse to carry these products. A study of Pennsylvania pharmacies conducted by the Clara Bell Duvall Law project found that only 35% of pharmacies were able to fill EC prescriptions that day. Of those unable to fill the prescription, 79% said the product was not in stock, 6% said it was against store policy to fill such prescriptions, and 7% said it conflicted with their personal beliefs.[2] Cost, too, may be a barrier. The estimated pharmacy price based on the average wholesale prices for ECPs are: Preven, $20; Plan B, $22; and combination OCPs, $35.[39] The price paid by the patient will be higher.[39] Many insurance companies do not cover any contraceptive products, including EC.

Special Considerations

Religious Affiliated Hospitals. There is always a debate about the moral and religious issues surrounding the use of EC. This is especially true among Catholic health care workers and health care organizations. EC should not be withheld, especially in cases of sexual assault, because of an individual's or institution's beliefs and religious affiliations. Interestingly, in the New York state survey on EC provision following sexual assault, 75%

Figure 1. ED Strategy for EC Administration



of the responding Catholic hospitals stated that it was their standard policy to provide EC to rape survivors.[37] The majority of guidelines for EC use by Catholic health care providers center on sexual assault. Directive 36 of the Ethical and Religious Directives for Catholic Health Care Services[40] states, "Compassionate and understanding care should be given to a person who is the victim of sexual assault. Health care providers should cooperate with law enforcement officials and offer the person psychological and spiritual support as well as accurate medical information. A female who has been raped should be able to defend herself against a potential conception from the sexual assault. If, after appropriate testing, there is no evidence that conception has

occurred already, she may be treated with medications that would prevent ovulation, sperm capacitation, or fertilization. It is not permissible, however, to initiate or to recommend treatments that have as their purpose or direct effect the removal, destruction, or interference with the implantation of a fertilized ovum." This directive clearly supports the use of EC in sexual assault cases as long as a pregnancy does not exist. As previously discussed, the effects of EC are pre-fertilization and have no effect on established pregnancies or fertilized ova.

Although the National Conference of Catholic Bishops developed these directives, individual dioceses can choose not to implement them or, as is the case in some states, the bishops can adopt their own guidelines. One such state is Pennsylvania. In 1998 the Board of Governors of the Pennsylvania Catholic Conference developed their "Guidelines for Catholic Hospitals Treating Victims of Sexual Assault."[41] In general, these guidelines allow appropriate medical interventions as long as there is no anticipated effect of an abortifacient. It further states that because the sperm is the result of unjust aggression, steps may be taken to prevent conception, including medications that prevent ovulation, sperm capacitation, or fertilization, and hygienic procedures like douching. The guidelines include a sample protocol to determine if contraceptive intervention is clinically indicated and to determine that such intervention would be contraceptive and not abortive. It states that if a pregnancy test is positive, no anti-ovulant drugs may be used. If it is negative, then based on menstrual history, hormonal levels determined by a blood test to categorize the timing of ovulation, and results of a urine test, which is reliable to predict ovulation, then the use of EC may be considered. If the urinary ovulation test is negative, then it is presumed that the LH surge has not been initiated, and contraceptive intervention is appropriate. If the urine test is positive, it indicates that hormonal shift toward ovulation has begun. The use of contraceptive intervention could be abortifacient and is therefore not permitted, even though there might be no evidence that conception has occurred. If the patient has just ovulated, anti-ovulant drugs may not be administered. This guideline is referred to as The Ovulation Approach or the Peoria Protocol, first developed in 1995 at Saint Francis Medical Center in Peoria, IL.[42] This protocol emphasizes that the occurrence of ovulation suggests conception may have taken place and this possibility is enough to not offer EC. This method has several drawbacks, including limiting Directive 36, which states women can receive medication to prevent fertilization; the window of time to administer EC is wider than ovulation timing; it gives too much weight to ovulation in setting the moral limits of treatment; and it leans too heavily on the presumption that EC acts as an abortifacient once ovulation has occurred—a fact not supported by research.

An alternative approach is the Pregnancy Approach.[42] In this protocol, after ruling out prior pregnancy, moral certainty exists to justify administering EC at the woman's request, regardless of her ovulation status. This approach is easier to use and supported by several factors. The risk of pregnancy after sexual assault is low. Research has shown that ECPs most likely work by preventing ovulation and do not have any post-fertilization effects to prevent implantation. The intention of giving EC is to prevent conception not inhibit implantation. There is no risk or harm to established pregnancies. And finally, the goal of the medication is to prevent conception from an unjust act of sexual assault, not bringing about the demise of a conceptus. Therefore, a proportionate reason exists for using ECPs: to prevent a pregnancy resulting from the sexual assault.

The courts have even weighed in on this issue. The California Court of Appeals offered opinion in the case Brownfield v. Daniel Freeman Marina Hospital, 256 Cal. Rptr. (1989).[43] In this case, workers in a Catholic hospital refused to inform a rape victim about the morning-after pill despite the victim's mother requesting the information, the possibility of pregnancy, and the need for treatment within 72 hours because such information conflicted with the hospital's religious beliefs. The court initially dismissed the case. Upon appeal, the hospital argued that it was immune under the state's Therapeutic Abortion Act, which excluded religious affiliated hospitals from having to provide abortions. The Appeals Court (208 Cal App 3d 405, 413-14 [1989])[5,43] held that this immunity did not extend to provision of EC, since this treatment constitutes pregnancy prevention.[5] It further stated that a patient has the right to self-determination in his or her treatment, superseding the moral and religious convictions of the hospital, and that medical malpractice would exist in cases where damages have resulted from the failure to provide a patient with information concerning treatment options when another practitioner under similar circumstances would have offered the treatment option. In other words, the court found no duty to provide non-emergency treatment, only a duty to inform the patient about treatment options.

Despite these guidelines and the court opinion, patients still may not receive EC following sexual assault or when the request it following contraceptive failure because of an individual's or institution's beliefs. Some options to assist women in obtaining EC in these situations include: having the medication be provided by an alternative health care provider, referral or transfer of patient to another hospital or women's health center, and having the rape center be separate from such religiously affiliated health care centers.

OTC Status

The FDA currently is evaluating a switch to over-the-counter status for the progestin-only regimen. The ACOG recently recommended that ECPs be available OTC in the United States.[14] The Center for Reproductive Law and Policy has filed a petition with the FDA signed by more than 70 organizations supporting the OTC status.[10] In December 2003, an FDA advisory committee voted 23 to 4 to support a switch for Plan B to OTC. In May 2004, the FDA rejected the application for OTC status, stating that the company had "not provided adequate data to support a conclusion that Plan B can be used safely by young adolescent women for emergency contraception without the professional supervision of a practitioner licensed by law to administer the drug."[44] The biggest concern was that the information provided by Barr Pharmaceuticals did not show that use of Plan B in girls younger than 16 years was safe. Barr Pharmaceuticals has revised

their application and has submitted it to the FDA and is awaiting the FDA decision.[44] Currently, some states allow women to obtain ECPs directly from a pharmacy under "collaborative agreements" with physicians for certain specified conditions, without having to see a physician. These include Alaska, California, Hawaii, New Mexico, and Washington state.[2,45] Planned Parenthood Federation of America has authorized its affiliates to prescribe ECPs via telephone without physical examination.[10]

Hormonal EC is highly suitable for the switch to OTC status. The dose is uniform for everyone, there are no real contraindications to its use, adverse events are rare, and there is no potential for addiction. Repeated use is safe and reasonably effective. Over-the-counter status is unlikely to replace long-term contraception due to expense and side effects such as menstrual changes.

Other Options

One other option for EC is the copper-bearing intrauterine device (IUD).[45] It can be inserted up to the time of implantation, 5-7 days after ovulation, to prevent pregnancy. Because of the difficulty in determining the day of ovulation, many protocols allow insertion up to 5 days after unprotected intercourse. Use of the copper-bearing IUD is significantly more effective that ECP, reducing the risk of pregnancy by 99%.[46] In addition, a copper-bearing IUD can be left in place to provide ongoing contraception for up to 10 years. One drawback to ED utilization is the need for a gynecologist for its insertion. Another limitation is its cost. The estimated price of the device, not including insertion, is $359.[39] Women at risk for sexually transmitted infections are not good candidates for IUDs because of the risk of pelvic infection leading to infertility.

Another option, more commonly used in other countries, but not in the United States, is mifepristone (RU486), an antiprogesterone. This drug can be used as an abortifacient and, therefore, does not meet the true definition of EC as it has additional post-implantation effects. Studies have shown the drug to be highly effective, and studies have been completed using lower drug dosages to reduce potential side effects. It has been shown that a single 10 mg dose of mifespristone is as effective as 600 mg and levonorgestrel.[46-50] The FDA recently denied approval for over-the-counter EC use of mifepristone in the United States.

Conclusion

With regard to the clinical cases presented in the beginning of the article, both women are in need of and are candidates for EC. Preferred treatment for both women is Plan B administered in the ED. Pre-treatment pregnancy testing is not mandatory. The sexual assault victim needs to receive additional treatment, evidence collection, and sexually transmitted infection prophylaxis in accordance with local policy. The other woman does not need a pelvic examination unless there is a specifically related complaint.

EC is an underused treatment option for women in the event of unprotected sexual intercourse. The currently available treatment options are safe, effective, and well tolerated by patients. Several medical associations and societies advocate their use and support pre-need counseling by primary care physicians and obstetricians-gynecologists. EC also should be provided for all reproductively capable women who are victims of sexual assault. Until EC gains over-the-counter status, emergency physicians will remain an important link in providing this treatment to women who desire or need it.

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Emergency Medicine Reports CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- apply state-of-the-art diagnostic and therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur.

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Physician CME Questions

111. Emergency contraception is defined as:
    A. the morning-after pill.
    B. medical abortion.

C. the use of any drug or device after unprotected intercourse to prevent an unwanted pregnancy.
D. the use of hormone pills to induce abortion.
E. the use of douching following intercourse to prevent pregnancy.

112. The complications of emergency contraception:
A. are usually severe.
B. include hepatitis.
C. can be minimized by using acetaminophen.
D. usually include nausea and vomiting.

113. The risk of ectopic pregnancy following emergency contraception:
A. is high and treatment is contraindicated in women with history of PID.
B. is quite low but patients should be made of aware of signs and symptoms.
C. is most likely due an effect on the uterus lining.
D. is the reason emergency contraception use has been banned in England.
E. is higher in women with a history of endometriosis.

114. The risk of venous thromboembolism from emergency contraception:
A. is much higher than for women using traditional oral contraceptives.
B. is not substantially higher than for women using traditional oral contraceptives.
C. is higher in women who younger than 20 years.
D. can be prevented by using combined ECPs in those patients with risk factors.

115. Side effects from emergency contraception can be minimized by which of the following?
A. Using a high estrogen containing product
B. Taking the pills with a meal
C. Taking the pills with antacid
D. Increasing the time interval between doses
E. Using a progestin-only regimen

116. With regard to the timing and administration of emergency contraception, which of the following statements is true?
A. Studies have suggested that emergency contraception can be given up to 120 hours after intercourse.
B. The earlier it is administered after intercourse, the greater the risk reduction of pregnancy.
C. Emergency contraception pills can be administered intravaginally.
D. All of the above

117. Which of the following is an absolute contraindication to emergency contraception?
A. Ovarian cyst
B. History of pulmonary embolism
C. Smoking
D. None of the above

118. Which of the following statements best represents the Catholic Church's position on emergency contraception?
A. It is abortion and should not be used in any circumstance.
B. Emergency contraception is a viable birth control option and should be offered to women.
C. All women should receive emergency contraception after sexual assault.
D. Emergency contraception is appropriate to use following unprotected intercourse.
E. Emergency contraception is appropriate to use following sexual assault after testing shows no evidence that conception has already occurred.

119. From studies, it appears that the most plausible mechanism of action of emergency contraception is:
A. prevention of fertilization.
B. sperm immobilization.
C. blockade or delay of ovulation.
D. endometrial changes preventing implantation.

120. Which of the following statements is true concerning emergency contraception?
A. The progestin-only regimen causes less nausea and vomiting than the Yuzpe method.
B. A single dose of the progestin-only regimen has a higher incidence of failure.
C. The progestin-only regimen is less effective than the Yuzpe method.
D. The progestin-only regimen is teratogenic, and pregnancy must be ruled out prior to its use.
E. EC has a high incidence of side effects that limits it use.

CME Answer Key

111. C; 112. D; 113. B; 114. B; 115. E; 116. D; 117. D; 118. E; 119. C; 120. A

In Future Issues: **Influenza**

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion.* When your evaluation is received, a certificate will be mailed to you.

Emergency Medicine Reports
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Emergency Contraception

Oral Emergency Contraception Options Available in the United States

BRAND	DISTRIBUTOR	PILLS PER DOSE+	ETHINYL ESTRADIOL PER DOSE (MCG)	LEVONORGESTREL PER DOSE (MG)†
Plan-B	Duramed	1 white	NA	0.75
Preven	Gynetics	2 blue	100	0.50
Alesse	Wyeth	5 pink	100	0.50
Aviane	Barr	5 orange	100	0.50
Cryselle	Barr	4 white	120	0.60
Enpresse	Barr	4 orange	120	0.50
Lessina	Barr	5 pink	100	0.50
Levlen	Berlex	4 light orange	120	0.60
Levlite	Berlex	5 pink	120	0.50
Levora	Watson	4 white	120	0.60
Lo/Ovral	Wyeth	4 white	120	0.60
Low-Ogestrel	Watson	4 white	120	0.60
Nordette	Wyeth	4 light orange	120	0.60
Ogestrel	Watson	2 white	100	0.50
Ovral	Wyeth	2 white	100	0.50
Ovrette	Wyeth	20 yellow	0	0.75
Portia	Barr	4 pink	120	0.60
Seasonale	Barr	4 pink	120	0.60
Tri-Levlen	Berlex	4 yellow	120	0.50
Triphasil	Wyeth	4 yellow	120	0.50
Trivora	Watson	4 pink	120	0.50

*Plan-B and Preven are the only dedicated products specifically marketed for EC. The remaining have been declared safe and effective.[10]

+Treatment schedule is 1 dose within 120 hours after unprotected intercourse and another dose 12 hours later. See text for updated dosing information.

† The progestin in Ovral, Lo/Ovral, Low-Ogestrel, Cryselle, and Ovrette is norgestrel, which contain 2 isomers, only 1 of which (levonorgestrel) is bioactive; the amount of norgestrel in each tablet is twice the amount of levonorgestrel.

EC Resources for Physicians and Patients

- Consortium for Emergency Contraception: www.cecinfo.org
- Emergency Contraception Web Site: http://not-2-late.com
- Emergency Contraception Hotline: 1-888-NOT-2-LATE
- ARHP EC Train-the-Trainer PowerPoint slide set: http://www.arhp.org/ec/
- Emergency Contraceptive Pills: Common Legal Questions about Prescribing, Dispensing, Repackaging, and Advertising. New York: The Center for Reproductive Law and Policy; 1999. To order, call 212-514-5534.
- Emergency Contraception: Resources for Providers. Seattle (WA): Program for Appropriate Technology in Health, 1997. To order, call 1-800-669-0156
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- Expanding Global Access to Emergency Contraception. Consortium for Emergency Contraception. 2000. To order, www.path.org/cec/.
- Emergency Contraception (AP114) [patient education pamphlet]: American College of Obstetrics and Gynecologists. To order, call 1-800-763-2264, ext 830.
- Planned Parenthood, www.plannedparenthood.org .

Indications for Use of Emergency Contraception

- Sexual assault
- Lack of contraceptive use during coitus
- Mechanical failure of male condom (breakage, slippage, or leakage)
- Dislodgment, breakage, or incorrect use of diaphragm, cervical cap, or female condom
- Failure of spermicide tablet or film to melt before intercourse
- Error in practicing withdrawal (coitus interruptus)
- Missed combined oral contraceptives (any two consecutive pills)
- Missed progestin-only oral contraceptives (one or more)
- Expulsion or partial expulsion of an intrauterine device
- Exposure to potential teratogen while not using effective contraception
- Late injection of injectable contraceptive (> 2 weeks late for progestin-only formulation or > 3 days late for a combined estrogen plus progestin formulation)

Strategies to Reduce the Risk of Nausea Following EC

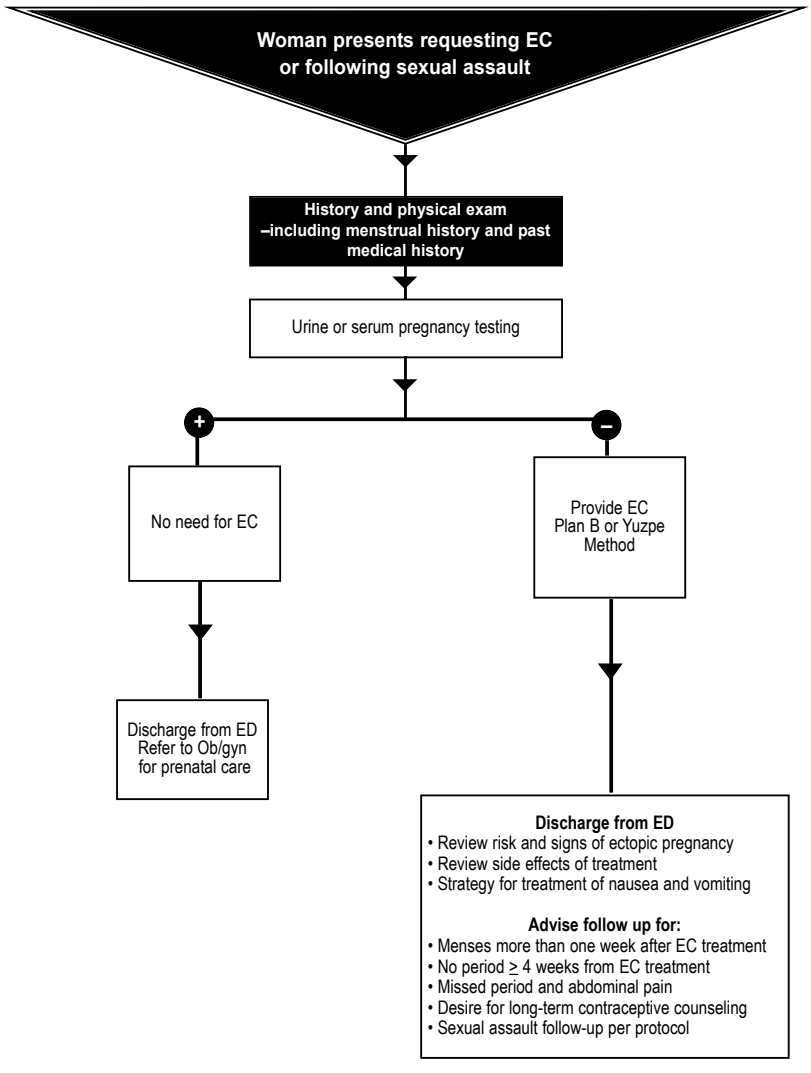
OTC

- 2 meclizine hydrochloride (Antivert, Bonine) 25-mg tablets 1 hour before first ECP dose
- 1-2 diphenhydramine hydrochloride (Benadryl) 25-mg tablets 1 hour before each ECP does; repeated as needed every 4-6 hours
- 1-2 dimenhydrinate (Dramamine) 50-mg tablets or 4-8 teaspoons 30-60 minutes before each ECP dose; repeat as needed every 4-6 hours

PRESCRIPTION

- 2 meclizine hydrochloride 25-mg tablets 1 hour before the first ECP dose
- 1 trimethobenzamide hydrochloride (Tigan) 250-mg tablet or 200-mg suppository 1 hour before each ECP dose; repeat as needed every 6-8 hours
- 1 promethazine hydrochloride (Phenergan) 25-mg tablet or suppository 30-60 minutes before each ECP dose, repeat as needed every 8-12 hours

ED Strategy for EC Administration



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