

# Emergency Contraception

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**E**mergency contraception is used after unprotected intercourse or a contraceptive accident to prevent unwanted pregnancy. It is thought to work by stopping or delaying ovulation or preventing implantation if fertilization has already taken place. Hormonal methods, mifepristone, and intrauterine device insertion are among the methods used worldwide. Combination estrogen-progestin birth control pills are the most commonly used form of emergency contraception in the United States. According to the Yuzpe method, combination pills are taken within 72 hours after intercourse, followed by a second identical dose 12 hours later. With this method, the number of unintended pregnancies is reduced by about 75%. Nausea and vomiting are the most troublesome adverse effects, but these can be controlled with antiemetic medication taken prior to the first dose. The Food and Drug Administration, Washington, DC, has approved an emergency contraception kit consisting of 4 combination pills, a urine pregnancy test, and a patient information book. Most recently, the Food and Drug Administration has approved a progestin-only formulation, which has fewer adverse effects and equal or improved efficacy compared with the combination formula. An intrauterine device can be inserted up to 5 days after unprotected intercourse and is a cost-effective option if it is used as ongoing contraceptive protection. The most readily available form of emergency contraception consists of 2 doses of estrogen-progestin combination birth control pills or 2 levonorgestrel pills taken 12 hours apart. Emergency contraception should not be considered as an alternative to ongoing contraceptive methods, but can prevent unwanted pregnancy.

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Fewer than 1% of women in the United States have ever used emergency contraception (EC), yet this method of preventing pregnancy has been shown to be effective. According to recent data, a pilot program in Washington State that gave patients direct pharmacy access to EC was calculated to have prevented 700 pregnancies. Of these, roughly half would have ended in abortion had EC not been available (Kristin Marciante, e-mail communication, March 15, 2000). Advocates suggest

that EC options be mentioned routinely by physicians, targeting especially those patients most likely to seek EC in the future. These include nulliparous women younger than 25 years who have used some form of contraception in the past.<sup>1</sup>

## DEFINITION AND INDICATIONS

Emergency contraception is any method of contraception that prevents pregnancy after intercourse has occurred. Most commonly, EC involves high-dose combination oral contraceptive (OC) pills, but progestin-only pills, mifepristone (an antiprogesterin), and copper-containing intra-

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uterine devices (IUDs) are also effective. Emergency contraception is indicated after sexual assault, after an episode of unprotected intercourse, or after a contraceptive accident, such as a broken condom.

### MECHANISMS OF ACTION

Emergency contraception does not interrupt an established pregnancy. The mechanism of pregnancy prevention is not clear, but several clinical studies have shown that hormonal methods of EC and mifepristone inhibit ovulation.<sup>2,3</sup> A recent statistical overview suggests that inhibition of ovulation alone cannot account for the efficacy of hormonal treatments.<sup>4</sup> Other mechanisms have also been suggested. These include interference with luteal phase function, alteration of the endometrial lining, creation of an unfavorable cervical mucus, and changes in sperm transport.<sup>2</sup> Thus, numerous factors, including prevention of implantation, may play a role. Emergency contraception is not thought to disrupt pregnancy once implantation has occurred, regardless of method used.

### EFFICACY

Combination contraceptive pills used as EC reduce pregnancy by 75%. This percentage of reduction refers to how many women who would otherwise have become pregnant (if they had used no form of contraception) will avoid pregnancy by using EC. It is estimated that if 100 women have a single episode of unprotected intercourse without particular attention to the timing of the menstrual cycle, 8 of them will become pregnant. With EC (in the form of combination pills), only 2 women will become pregnant.<sup>5</sup> Progestin-only regimens are estimated to be even more effective. Two randomized trials comparing the Yuzpe regimen with 0.75 mg of levonorgestrel showed that the latter regimen prevented

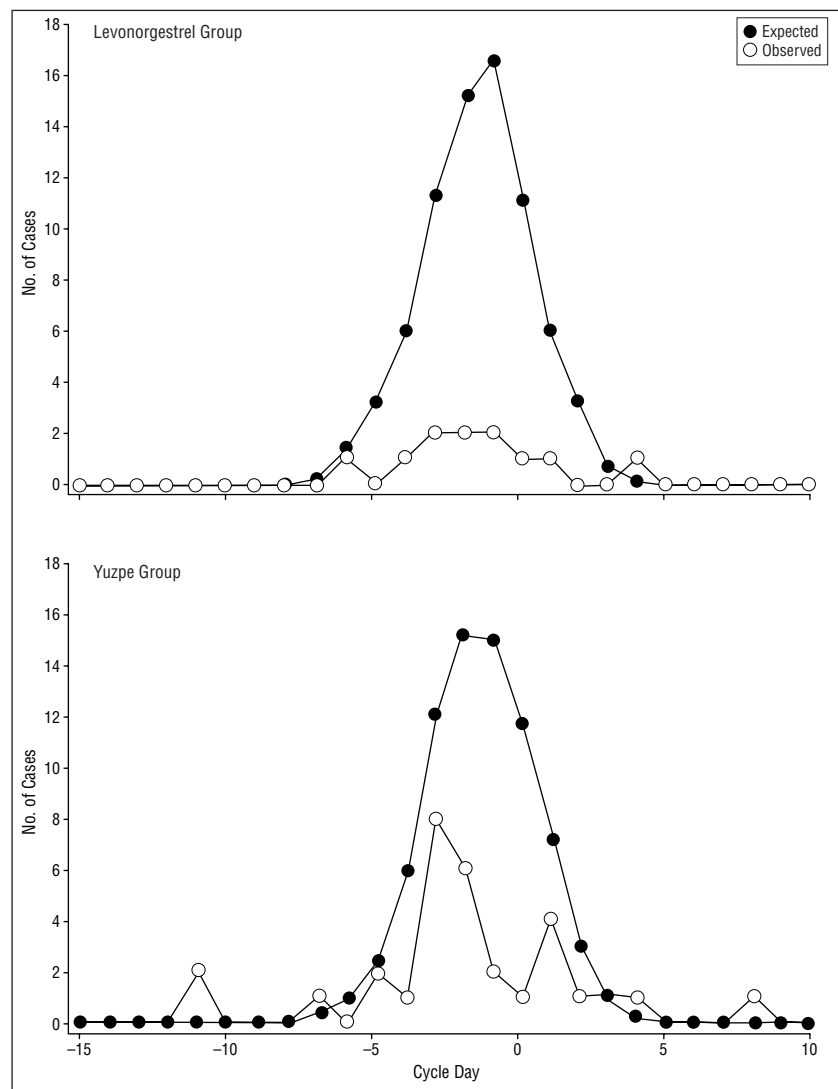
more pregnancies. In one trial, the difference was not statistically significant, but in the other, both the crude and relative efficacy rates were greater for levonorgestrel.<sup>6,7</sup> The copper-bearing IUD is 99% effective.<sup>8</sup>

Although hormonal EC is indicated for up to 72 hours after unprotected intercourse, the sooner the regimen is begun, the more effective it is likely to be. Pregnancy rates increased from 0.5% when treatment was initiated in the first 12 hours after unprotected intercourse to 4.1% when initiated between 61 and 72 hours.<sup>9</sup> **Figure 1**

compares the impact of timing on the efficacy of the Yuzpe vs the levonorgestrel regimens.

### DOSING REGIMENS

The traditional Yuzpe regimen consists of 2 doses of combination contraceptive pills. The first dose is taken within 72 hours after unprotected intercourse and the second is taken exactly 12 hours later.<sup>10</sup> A number of products combining ethinyl estradiol and levonorgestrel (or norgestrel) can be used (**Table 1**). In 1998, the Food and Drug Admin-



**Figure 1.** Observed (open circle) and expected (closed circle) numbers of pregnancies by timing of coitus in relation to predicted ovulation, by treatment group. Reprinted with permission from Lancet (1998;352:428-433). Copyright 1998, the Lancet Publishing Group, London, England, a division of Elsevier Science Ltd.

**Table 1. Hormonal Emergency Contraceptive Regimens**

| Brand         | Pills per Dose | Ethinyl Estradiol per Dose, µg | Levonorgestrel per Dose, mg* |
|---------------|----------------|--------------------------------|------------------------------|
| Plan B†       | 1 White        | 0                              | 0.75                         |
| Preven‡       | 2 Blue         | 100                            | 0.50                         |
| Ovral§        | 2 White        | 100                            | 0.50                         |
| Allesse§      | 5 Pink         | 100                            | 0.50                         |
| Levlite       | 5 Pink         | 100                            | 0.50                         |
| Nordette§     | 4 Light orange | 120                            | 0.60                         |
| Levlen        | 4 Light orange | 120                            | 0.60                         |
| Levora¶       | 4 White        | 120                            | 0.60                         |
| Lo/Ovral§     | 4 White        | 120                            | 0.60                         |
| Low-Ogestrel§ | 4 White        | 120                            | 0.60                         |
| Triphasil§    | 4 Yellow       | 120                            | 0.50                         |
| Tri-Levlen    | 4 Yellow       | 120                            | 0.50                         |
| Trivora¶      | 4 Pink         | 120                            | 0.50                         |
| Ovrette§      | 20 Yellow      | 0                              | 0.75                         |

\*Levonorgestrel is a metabolite of norgestrel. Although some of the compounds listed above (Ovral, Lo/Ovral, Low-Ogestrel, Ovrette) contain norgestrel, their levonorgestrel component is calculated as half the amount of norgestrel.

†Women's Capital Corp, Seattle, Wash.

‡Gynetics Inc, Somerville, NJ.

§Wyeth-Ayerst Laboratories, Philadelphia, Pa.

||Berlex Laboratories Inc, Wayne, NJ.

¶Oclassen Pharmaceuticals Inc, San Rafael, Calif.

**Table 2. Advantages and Disadvantages of Emergency Contraceptive Options**

| Method                         | Advantage                                                                                              | Disadvantage                                                                                                    |
|--------------------------------|--------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------|
| IUD                            | Can be inserted up to 5 days after unprotected intercourse<br>Can continue for long-term contraception | IUD limitations*<br>Requires office visit                                                                       |
| Estrogen-progestin combination | Established safety and efficacy<br>Can continue as regular contraceptive                               | Nausea and vomiting common<br>72-h window                                                                       |
| Progestin only                 | Well tolerated                                                                                         | 72-h window                                                                                                     |
| Mifepristone                   | Highly efficacious and well tolerated<br>Can be used up to 5 days after unprotected intercourse        | Not available in United States†<br>Disrupts established pregnancy at high doses (higher than those used for EC) |

\*Intrauterine devices (IUDs) should not be used in women with recent (eg, within the last 3 months) or recurrent pelvic infection, women with anatomical distortion, women who are immunocompromised, have undiagnosed genital bleeding, or who have had previous problems with an IUD.<sup>13</sup> Given that any woman needing emergency contraception (EC) may be at increased risk of sexually transmitted diseases, her situation should be reviewed thoroughly before considering IUD insertion.

†Even when mifepristone is approved by the Food and Drug Administration, Washington, DC, it will be marketed in a 200-mg dose, whereas EC requires as little as a single 10-mg dose.

istration (FDA), Washington, DC, approved an EC kit (Preven; Gynetics Inc, Somerville, NJ), which consists of a patient information book, a urine pregnancy test, and 4 pills, each containing 0.25 mg levonorgestrel and 50 µg ethinyl estradiol.<sup>11</sup>

A levonorgestrel-only product (Plan B; Women's Capital Corp, Seattle, Wash) has just been ap-

proved by the FDA. Levonorgestrel alone is better tolerated than combination OCs.<sup>4,6</sup> However, until recently, it was available only in the form of a low-dose progestin (Ovrette; Wyeth-Ayerst Laboratories, Philadelphia, Pa) requiring 20 pills per dose when used as EC. Now that a progestin-only pill can be taken as a single tablet per

dose, this may become a preferred method of EC.<sup>12</sup>

A copper-containing IUD is also highly effective. It must be inserted within 5 days after unprotected intercourse. Intrauterine devices are generally not suited for use in women at risk for sexually transmitted diseases.<sup>13</sup> Because of its expense and the requirement of proper insertion, this method is only practical in settings in which a patient has easy access to a health care center. Its advantages include high efficacy, the 5-day window for insertion, and ongoing contraceptive benefit if the IUD remains in place.

Finally, mifepristone has been studied using single doses as low as 10 mg.<sup>14</sup> Mifepristone is considered to be at least as effective as the Yuzpe regimen with fewer adverse effects. An additional benefit is that mifepristone is effective up to 5 days after unprotected intercourse. The only considerable adverse effect is delayed onset of menses, which is consistent with one of the drug's mechanisms of action since the drug interferes with ovulation. This effect seems to be dose related. As EC, mifepristone is given in much lower doses than would induce abortion, but its associated use as an abortifacient may prevent its acceptance in the United States for use as EC. Advantages and disadvantages of each method are given in **Table 2**.

## ADVERSE EFFECTS

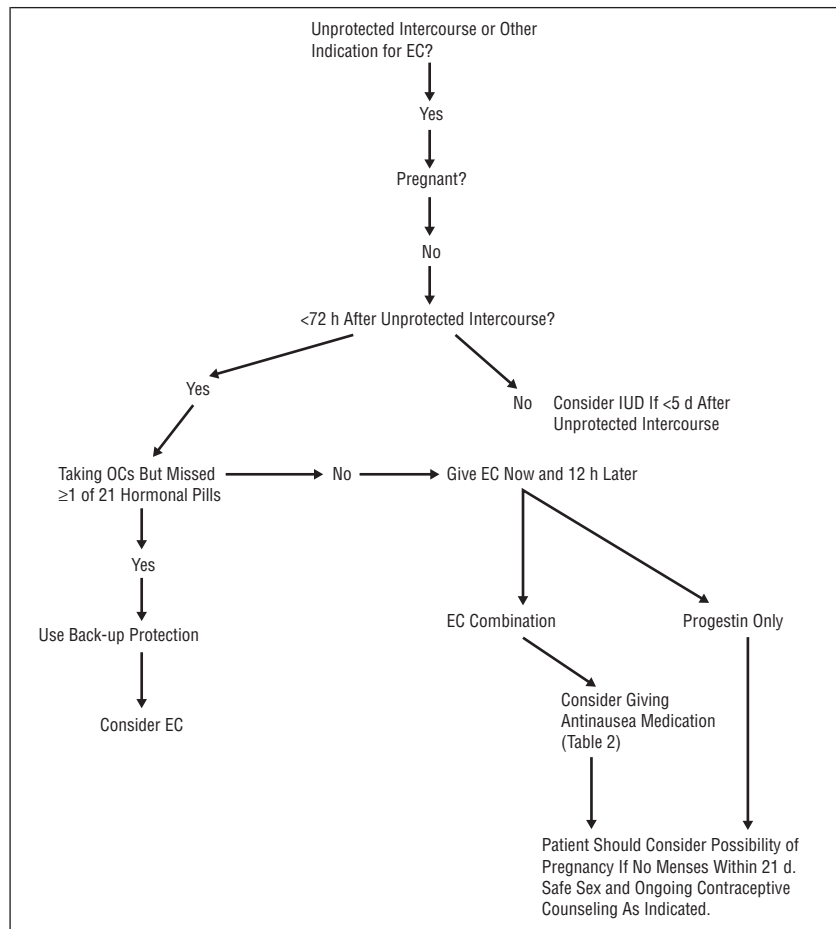
Adverse effects of combination OCs include nausea (50%) and vomiting (20%).<sup>1</sup> These symptoms are not only unpleasant but raise the issue of what to do if a woman vomits after ingesting the pills. Some physicians recommend taking an additional dose 1 to 3 hours after vomiting; others assume that vomiting indicates systemic absorption of the pills and that additional doses are therefore not required.<sup>13</sup> Anti-nausea medications, such as meclizine hydrochloride, taken 1 hour be-

fore the first dose may reduce the severity of symptoms (**Table 3**).<sup>13</sup> With levonorgestrel-only pills, nausea and vomiting have been shown to be significantly reduced (23% and 6%, respectively).<sup>6,7</sup> Other adverse effects of both regimens include dizziness, breast tenderness, and fatigue. Withdrawal bleeding occurs within 21 days of using EC and indicates that the patient is not pregnant. If no withdrawal bleeding occurs, a pregnancy test should be performed.

Women who have a known pregnancy or who are experiencing active migraine with focal neurologic deficit should not use combination estrogen-progestin EC. Migraine is not a contraindication for progestin-only EC. Other contraindications that usually apply to OCs are less of a concern with EC because EC is used only within a 24-hour time frame. However, there are no studies directly comparing short- and long-term use of OC. It may be prudent to use a progestin-only preparation for EC if the patient has important contraindications to OCs, such as a history of thromboembolic disease. The Plan B package insert lists only pregnancy, hypersensitivity to the drug, and unexplained genital bleeding as contraindications to its use.<sup>15</sup>

## COUNSELING AND FOLLOW-UP

Given FDA approval of EC as an indicated use of hormonal contraceptive pills, this method is likely to gain increasing favor as a means of preventing unwanted pregnancies. Because contacting a physician after unprotected intercourse can be a major inconvenience, physicians should consider giving patients a prescription to fill when needed. Hormonal EC may become widely available without a physician's prescription. Programs in various stages of implementation are evaluating the feasibility of direct dispensing of EC by



**Figure 2.** Algorithm for administering emergency contraception. EC indicates emergency contraception; IUD, intrauterine device; and OC, oral contraceptive. Unprotected intercourse or other indication for EC indicates a contraceptive accident, missed contraceptive pills, sexual assault, or exposure to a potential teratogen. New guidelines will not require follow-up with a clinician if there is no menses at 21 days; alternatives include home pregnancy testing or further waiting.

pharmacists. A patient can obtain EC by going to a participating pharmacy where the pharmacist prescribes and dispenses the medication under an agreement with a licensed nurse practitioner or medical doctor. One such program in Washington State seems to have been successful in improving patient access to EC.<sup>16</sup>

Studies thus far have not supported concerns that EC self-administration promotes contraceptive carelessness.<sup>17</sup> Patient education materials accompanying packaged pills emphasize that EC is not to be used as a regular means of contraception since its cumulative efficacy is low. Women who obtain their EC in the physician's office should first be

tested for pregnancy. If the patient is going to use combination or progestin-only pills, she should be told what dosage to take: all hormonal EC methods start with the first dose taken within the first 24 hours and the second taken 12 hours later. If a dedicated packet is not available, any contraceptive brand can be used, but in multiphase OCs or those with 7 placebo pills, care must be taken to use the appropriately colored pills only (Table 1). Most physicians will recommend starting a new pack of combination OCs the day after the second EC dose, with additional pregnancy protection used the first 7 days.

The patient's next menses may come early or late (depending on

Table 3. Antinausea Medications\*

| Trade Name                      | Brand Name | Dosage                                                                                                               | Comments                        |
|---------------------------------|------------|----------------------------------------------------------------------------------------------------------------------|---------------------------------|
| Meclizine hydrochloride         | Antivert†  | 25 mg: 1-2 tablets 1 h before first EC dose; repeat once as needed in 24 h                                           | 25-100 mg daily                 |
| Diphenhydramine hydrochloride   | Benadryl‡  | 25 mg: 1-2 tablets 1 h before first EC dose; repeat as needed every 4-6 h                                            | ...                             |
| Dimenhydrinate                  | Dramamine§ | 50 mg: 1-2 tablets 30-60 min before first EC dose; repeat as needed every 4-6 h                                      | Do not exceed 8 tablets in 24 h |
| Cyclizine hydrochloride         | Marezine   | 50 mg: 1 tablet 30 min before first EC dose; repeat as needed every 4-6 h                                            | Do not exceed 200 mg daily      |
| Trimethobenzamide hydrochloride | Tigan¶     | 250 mg: 1 tablet 1 h before first dose; repeat as needed every 4-6 h<br>200 mg: 1 suppository; same dosage as tablet | ...                             |
| Promethazine hydrochloride      | Phenergan# | 25 mg: 1 tablet or suppository 30-60 min before first EC dose; repeat as needed every 4-6 h                          | ...                             |

\*EC indicates emergency contraception; ellipses, not applicable.

†Roerig, New York, NY.

‡Parke-Davis, Morris Plains, NJ.

§Pharmacia & Upjohn Inc, Kalamazoo, Mich.

||Himmel, Lake Worth, Fla.

¶Roberts Pharmaceutical Corp, Eatontown, NJ.

#Wyeth-Ayerst Laboratories, Philadelphia, Pa.

where she was in her cycle when she took EC), but if she has not had menses after 21 days, she should return to the physician's office for a pregnancy test. Women should be told that EC will not prevent pregnancy if unprotected intercourse occurs after treatment.

Follow-up is not absolutely required but is important to rule out pregnancy if the patient has not experienced bleeding. It also provides an opportunity for counseling the patient on ongoing contraception and safe sex. Oral contraception, IUDs, and barrier methods such as condoms or diaphragms are options for continuing contraception with varying efficacy. Implants and injectable forms of contraception can be given within 7 days of the start of the next menstrual cycle or sooner if results from a pregnancy test are negative. An algorithm for administration of EC is provided in **Figure 2**.

Updated information on guidelines and availability of EC

can be obtained from the following resources:

| Resource                          | Web Address or Telephone Number                                         |
|-----------------------------------|-------------------------------------------------------------------------|
| Office of Population Research     | <a href="http://opr.princeton.edu/ed/">http://opr.princeton.edu/ed/</a> |
| Program for Technology and Health | <a href="http://www.path.org">http://www.path.org</a>                   |
| Emergency Contraception Hotline   | 1-888-NOT-2-LATE                                                        |

Plan B will not reach pharmacies until the FDA extends the shelf life (currently, approximately 8 months). It can be ordered from a drug distribution house or by qualified providers at 1-800-330-1271 or by faxing 1-973-822-1444.

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