Emergency contraception

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Emergency contraception (**EC**), or **emergency postcoital contraception**, are birth control measures that may be used after sexual intercourse to prevent pregnancy.

Forms of EC include:

- Emergency contraceptive pills (ECPs)—sometimes simply referred to as emergency contraceptives (ECs) or the "**morning-after pill**"—are drugs intended to disrupt or delay ovulation or fertilization, which are necessary for pregnancy (contraceptives).[1][2][3] ECPs and "abortion pills" are not the same. ECPs work by preventing or delaying ovulation and therefore preventing pregnancy, not by abortion.[4]
- Intrauterine devices (IUDs)—usually used as a primary contraceptive method, but sometimes used as emergency contraception.[3]

Background	
Type	Hormonal (progestin or others) or intra-uterine
First use	1970s
Failure rates (per use)	
Perfect use	ECP: see article text IUD: under 1%
Typical use	% (please see Effectiveness of ECPs below)
Usage	
User reminders	Pregnancy test required if no period seen after 3 weeks
Clinic review	Recommended to consider need screen STDs or consider ongoing routine contraceptive options
Advantages and disadvantages	
STD protection	No
Periods	ECP may disrupt next menstrual period by couple days. IUDs may make menstruation heavier and more painful
Benefits	IUDs may be subsequently left in place for ongoing contraception
Risks	As per methods
Medical notes	

Combined estrogrogen/progestin pills of Yuzpe regimen now superseded by better-tolerated and more effective progestin-only pill. Progestin only ECP licensed for use within 3 days of unprotected intercourse, Ulipristal acetate and IUDs within 5 days.

Take 2 times normal dosage birth control pill.

Contents

Emergency contraceptive pills

Emergency contraceptive pills (ECPs) (sometimes referred to as emergency hormonal contraception (EHC)) may contain higher doses of the same hormones (estrogens, progestins, or both) found in regular combined oral contraceptive pills. Taken after unprotected sexual intercourse or contraceptive failure, such higher doses may prevent pregnancy from occurring.[5]

Types of ECPs

Three types of emergency contraceptive pills are available: combined estrogen and progestin pills, progestin-only (levonorgestrel) pills, and antiprogestin (ulipristal acetate or mifepristone) pills.[6] Progestin-only and antiprogestin pills are available as dedicated (specifically packaged for use as) emergency contraceptive pills.[6][7] Combined estrogen and progestin pills are no longer available as dedicated emergency contraceptive pills, but certain regular combined oral contraceptive pills may be used as emergency contraceptive pills.[6]

Progestin-only emergency contraceptive pills contain levonorgestrel, either as a single tablet or as a split dose of two tablets taken 12 hours apart, effective up to 72 hours after intercourse.[6] Progestin-only ECPs are sold under many different brand names.[8][9][10] Progestin-only ECPs are available over-the-counter (OTC) in several countries (e.g. Bangladesh, Bulgaria, Canada, Cyprus, Czech Republic, Denmark, Estonia, India, Netherlands, Norway, Portugal, Romania, Slovakia, South Africa, Sweden, United States), from a pharmacist without a prescription, and available with a prescription in some other countries.[8][9][10]

The antiprogestin ulipristal acetate is available as a micronized emergency contraceptive tablet, effective up to 120 hours after intercourse.[6][7] Ulipristal acetate ECPs developed by HRA Pharma are available by prescription in over 50 countries under the brand names *ellaOne*, *ella* (marketed by Watson Pharmaceuticals in the United States), *Duprisal 30*, *Ulipristal 30*, and *UPRIS*.[8][9][10][11]

The antiprogestin mifepristone (also known as RU-486) is available in five countries as a low-dose or mid-dose emergency contraceptive tablet, effective up to 120 hours after intercourse.[6][7] Low-dose mifepristone ECPs are available by prescription in Armenia, Russia, Ukraine, and Vietnam and from a pharmacist without a prescription in China.[8][9] Mid-dose mifepristone ECPs are available by prescription in China and Vietnam.[8][9]

Combined estrogen (ethinylestradiol) and progestin (levonorgestrel or norgestrel) pills used to be available as dedicated emergency contraceptive pills under several brand names: *Schering PC4*, *Tetragynon*, *Neoprimavlar*, and *Preven* (in the United States) but were withdrawn after more effective dedicated progestin-only (levonorgestrel) emergency contraceptive pills with fewer side effects became available.[6] If other more effective dedicated emergency contraceptive pills (levonorgestrel, ulipristal acetate, or mifepristone) are not available, specific combinations of regular combined oral contraceptive pills can be taken in split doses 12 hours apart (the Yuzpe regimen), effective up to 72 hours after intercourse.[6] The U.S. Food and Drug Administration (FDA) approved this off-label use of certain

brands of regular combined oral contraceptive pills in 1997.[5] As of 2014, there are 26 brands of regular combined oral contraceptive pills containing levonorgestrel or norgestrel available in the United States that can be used in the emergency contraceptive Yuzpe regimen.[6]

Effectiveness

The effectiveness of emergency contraception is presented differently from the effectiveness of ongoing methods of birth control: it is expressed as a percentage reduction in pregnancy rate for a single use of EC. Different ECP regimens have different effectiveness levels, and even for a single regimen different studies may find varying rates of effectiveness. Using an example of "75% effective", an article in *American Family Physician* explains the effectiveness calculation thus:

> ... these numbers do not translate into a pregnancy rate of 25 percent. Rather, they mean that if 1,000 women have unprotected intercourse in the middle two weeks of their menstrual cycles, approximately 80 will become pregnant. Use of emergency contraceptive pills would reduce this number by 75 percent, to 20 women.[12]

The progestin-only regimen (using levonorgestrel) is reported by the U.S. FDA to have an 89% effectiveness. As of 2006, the labeling on the U.S. brand Plan B explained this effectiveness rate by stating, "Seven out of every eight women who would have gotten pregnant will not become pregnant."[13]

In 1999, a meta-analysis of eight studies of the combined (Yuzpe) regimen concluded that the best point estimate of effectiveness was 74%.[14] A 2003 analysis of two of the largest combined (Yuzpe) regimen studies, using a different calculation method, found effectiveness estimates of 47% and 53%.[15]

For both the progestin-only and Yuzpe regimens, the effectiveness of emergency contraception is highest when taken within 12 hours of intercourse and declines over time.[16][17][18] While most studies of emergency contraception have only enrolled women within 72 hours of unprotected intercourse, a 2002 study by the World Health Organization (WHO) suggested that reasonable effectiveness may continue for up to 120 hours (5 days) after intercourse.[19]

For 10 mg of mifepristone taken up to 120 hours (5 days) after intercourse, the combined estimate from three trials was an effectiveness of 83%.[20] A review found that a moderate dose of mifepristone is better than LNG or Yuzpe.[21]

HRA Pharma changed its packaging information for Norlevo (which has dosage and chemical makeup identical to many other EHCs) in November 2013 warning that the drug loses effectiveness in women who weigh more than 165 pounds and is completely ineffective for women who weigh over 176 pounds.[22][23]

History of calculation methods

Early studies of emergency contraceptives did not attempt to calculate a failure rate; they simply reported the number of women who became pregnant after using an emergency contraceptive. Since 1980, clinical trials of emergency contraception have first calculated probable pregnancies in the study group if no treatment were given. The effectiveness is calculated by dividing observed pregnancies by the estimated number of pregnancies without treatment.[24]

Placebo-controlled trials that could give a precise measure of the pregnancy rate without treatment would be unethical, so the effectiveness percentage is based on estimated pregnancy rates. These are currently estimated using variants of the calendar method.[25] Women with irregular cycles for any reason (including recent hormone use such as oral contraceptives and breastfeeding) must be excluded from such calculations. Even for women included in the calculation, the limitations of calendar methods of fertility determination have long been recognized. In their February 2014 emergency review article, Trussell and Raymond note:

> Calculation of effectiveness, and particularly the denominator of the fraction, involves many assumptions that are difficult to validate...The risk of pregnancy for women requesting ECPs appears to be lower than assumed in the estimates of ECP efficacy, which are consequently likely to be overestimates. Yet, precise estimates of efficacy may not be highly relevant to many women who have had unprotected intercourse, since ECPs are often the only available treatment.[6]

In 1999, hormonal assay was suggested as a more accurate method of estimating fertility for EC studies.[26]

Safety

Existing pregnancy is not a contraindication in terms of safety, as there is no known harm to the woman, the course of her pregnancy, or the fetus if progestin-only or combined emergency contraception pills are accidentally used, but EC is not indicated for a woman with a known or suspected pregnancy because it is not effective in women who are already pregnant.[6][27][28][29][30][31][32][33][34]

The World Health Organization (WHO) lists no medical condition for which the risks of emergency contraceptive pills outweigh the benefits.[31] The American Academy of Pediatrics (AAP) and experts on emergency contraception have concluded that progestin-only ECPs may be preferable to combined ECPs containing estrogen in women with a history of blood clots, stroke, or migraine.[6][27][28]

The AAP, American College of Obstetricians and Gynecologists (ACOG), U.S. Food and Drug Administration, WHO, Royal College of Obstetricians and Gynaecologists, and other experts on emergency contraception state that there are no medical conditions in which progestin-only ECPs are contraindicated.[6][27][28][29][30][31][32] RCOG specifically note current venous thromboembolism, current or past history of breast cancer, inflammatory bowel disease, and acute intermittent porphyria as conditions where the advantages of using emergency contraceptive pills generally outweigh the theoretical or proven risks.[32]

ECPs, like all other contraceptives, reduce the absolute risk of ectopic pregnancy by preventing pregnancies and there is no increase in the relative risk of ectopic pregnancy in women who become pregnant after using progestin-only ECPs.[3][6][27][28][29][30][31][32][34][35][36][37][38]

Interactions

The herbal preparation of St John's wort and some enzyme-inducing drugs (e.g. anticonvulsants or rifampicin) may reduce the effectiveness of ECP, and a larger dose may be required.[35][39]

Side effects

The most common side effect reported by users of emergency contraceptive pills was nausea (50.5% of 979 Yuzpe regimen users and 23.1% of 977 levonorgestrel-only users in the 1998 WHO trial; 14.3% of 2,720 levonorgestrel-only users in the 2002 WHO trial); vomiting is much less common and unusual with levonorgestrel-only ECPs (18.8% of 979 Yuzpe regimen users and 5.6% of levonorgestrel-only users in the 1998 WHO trial; 1.4% of 2,720 levonorgestrel-only users in the 2002 WHO trial).[16][19][35] Anti-emetics are not routinely recommended with levonorgestrel-only ECPs.[35][40] If a woman vomits within 2 hours of taking a levonorgestrel-only ECP, she should take a further dose as soon as possible.[35][41]

Other common side effects (each reported by less than 20% of levonorgestrel-only users in both the 1998 and 2002 WHO trials) were abdominal pain, fatigue, headache, dizziness, and breast tenderness.[16][19][35] Side effects usually do not occur for more than a few days after treatment, and they generally resolve within 24 hours.[6]

Temporary disruption of the menstrual cycle is also commonly experienced. If taken before ovulation, the high doses of progestogen in levonorgestrel treatments may induce progestogen withdrawal bleeding a few days after the pills are taken. One study found that about half of women who used levonorgestrel ECPs experienced bleeding within 7 days of taking the pills.[42] If levonorgestrel is taken after ovulation, it may increase the length of the luteal phase, thus delaying menstruation by a few days.[43] Mifepristone, if taken before ovulation, may delay ovulation by 3–4 days[44] (delayed ovulation may result in a delayed menstruation). These disruptions only occur in the cycle in which ECPs were taken; subsequent cycle length is not significantly affected.[42] If a woman's menstrual period is delayed by two weeks or more, it is advised that she take a pregnancy test.[29] (Earlier testing may not give accurate results.)

Availability by country

Intrauterine device

An alternative to emergency contraceptive pills is the copper-T intrauterine device (IUD) which can be used up to 5 days after unprotected intercourse to prevent pregnancy. Insertion of an IUD is more effective than use of Emergency Contraceptive Pills - pregnancy rates when used as emergency contraception are the same as with normal IUD use. IUDs may be left in place following the subsequent menstruation to provide ongoing contraception (3–10 years depending upon type).[45]

As regular contraception

One brand of levonorgestrel pills was marketed as an ongoing method of postcoital contraception.[46] However, there are serious drawbacks to such use of postcoital high-dose progestin-only oral contraceptive pills, especially if they are not used according to their package directions, but are instead used according to the package directions of emergency contraceptive pills:

- Due to the increasing severity of side effects with frequent use, Postinor is only recommended for women who have intercourse four or fewer times per month.[46][47]
- If not used according to their package directions, but instead used according to the directions of levonorgestrel emergency contraceptive pills (up to 72 hours after intercourse), they would be estimated to have a "perfect-use" (when not used according to their package directions but used as directed on the package directions for levonorgestrel emergency contraception pills) pregnancy rate of 20% per year when used as the sole means of contraception (as compared to a 40% annual pregnancy rate for the Yuzpe regimen).[48] These failure rates would be higher than those of almost all other birth control methods, including the rhythm method and withdrawal.[49]
- Like all hormonal methods, postcoital high-dose progestin-only oral contraceptive pills do not protect against sexually transmitted infections.[50]

ECPs are generally recommended for backup or "emergency" use, rather than as the primary means of contraception. They are intended for use when other means of contraception have failed—for example, if a woman has forgotten to take a birth control pill or when a condom is torn during sex.[48]

Relationship to high risk sex and abortion

The current (December 2012) American Academy of Pediatrics (AAP) Policy Statement on Emergency Contraception says: "Despite multiple studies showing no increased risk behavior and evidence that hormonal emergency contraception will not disrupt an established pregnancy, public and medical discourse reflects that personal values of physicians and pharmacists continue to affect emergency-contraception access, particularly for adolescents."[51]

The latest (December 2013) review by emergency contraception experts Trussell and Raymond says: "Published evidence would seem to demonstrate convincingly that making ECPs more widely available does not increase risk-taking or adversely affect regular contraceptive use". . . ."However, reanalysis of one of the randomized trials suggests that easier access to ECPs may have increased the frequency of coital acts with the potential to lead to pregnancy."[6] and notes that four randomized controlled trials have found that advanced provision of emergency contraceptive pills did not increase rates of sexually transmitted infections or sexual risk taking.[52][53][54][55] Trussell and Raymond noted that after one of the

four studies had been reanalysed later, the data did show higher sexual risk-taking,[6] specifically substituting in some cases emergency contraceptives for contraceptives such as condoms that are more effective.

In France, Sweden, and Britain—where Yuzpe-regimen EC had been available by prescription for more than a decade and progestin-only EC has been available without a prescription for 8, 6, and 2 years respectively—the abortion rate was stable or higher during that time period.[56] Another study concluded that distribution of free, advance supplies of EC to large numbers of women in Scotland did not reduce abortion rates.[57] A randomized controlled trial of 2000 women in China compared women with advance access to EC to women without access, and noted that the pregnancy rate was the same between the two groups. The study observed that "...providing EC in advance increases use, but there is no direct evidence that it reduces unintended pregnancy" and concluded that EC may not lower abortion rates.[58]

In September 2006, emergency contraception expert Anna Glasier wrote a *BMJ* editorial entitled "Emergency Contraception. Is it worth all the fuss?" that said in closing: "So is emergency contraception worth the fuss? If you are a woman who has had unprotected sex then of course it is, because emergency contraception will prevent pregnancy in some women some of the time—and if you don't want to get pregnant anything is better than nothing. If you are the *CMAJ*'s editor or FDA commissioner then yes, because scientific freedom is worth the fight. If you are looking for an intervention that will reduce abortion rates, emergency contraception may not be the solution, and perhaps you should concentrate most on encouraging people to use contraception before or during sex, not after it."[59]

EC and sexual assault

Before EC was used in the general population or defined as "emergency contraception," it was used, beginning in the 1960s and 70s, specifically as a treatment for victims of sexual assault.[60][61] Pregnancy rates among rape victims of child-bearing age are around 5%; in the U.S., about half of rape victims who become pregnant have abortions.[62] Although EC is commonly used as an option for victims of sexual assault, some researchers believe such use is a public health measure that is not sufficiently widespread.[63]

Mechanism of action

The primary mechanism of action of progestogen-only emergency contraceptive pills is to prevent fertilization by inhibition of ovulation.[3][35][37][64][65][66] The best available evidence is that they do not have any post-fertilization effects such as the prevention of implantation.[3][35][37][64][65][66] The U.S. FDA-approved labels and European EMA-approved labels (except for HRA Pharma's *NorLevo*) levonorgestrel emergency contraceptive pills (based on labels for regular oral contraceptive pills) say they may cause endometrial changes that discourage implantation.[67][68][69] Daily use of regular oral contraceptive pills can alter the endometrium (although this has not been proven to interfere with implantation), but the isolated use of a levonorgestrel emergency contraceptive pill does not have time to alter the endometrium.[67] In March 2011, the International Federation of Gynecology and Obstetrics (FIGO) issued a statement that: "review of the evidence suggests that LNG [levonorgestreol] ECPs

cannot prevent implantation of a fertilized egg. Language on implantation should not be included in LNG ECP product labeling."[67][70] In June 2012, a *New York Times* editorial called on the FDA to remove from the label the unsupported suggestion that levonorgestrel emergency contraceptive pills inhibit implantation.[71] In November 2013, the European Medicines Agency (EMA) approved a change to the label for HRA Pharma's *NorLevo* saying it cannot prevent implantation of a fertilized egg.[72]

Progestogen-only emergency contraceptive does not appear to effect the function of the Fallopian tubes or increase the rate of ectopic pregnancies.[73]

The primary mechanism of action of progesterone receptor modulator emergency contraceptive pills like low-dose and mid-dose mifepristone and ulipristal acetate is to prevent fertilization by inhibition or delay of ovulation.[3][35][64][65][66][74] One clinical study found that post-ovulatory administration of ulipristal acetate altered the endometrium, but whether the changes would inhibit implantation is unknown.[3][75] The European EMA-approved labels for ulipristal acetate emergency contraceptive pills do not mention an effect on implantation, but the U.S. FDA-approved label says: "alterations to the endometrium that may affect implantation may also contribute to efficacy."[67][76][77]

The primary mechanism of action of copper-releasing intrauterine devices (IUDs) as emergency contraceptives is to prevent fertilization because of copper toxicity to sperm and ova.[3][35] The very high effectiveness of copper-releasing IUDs as emergency contraceptives means they must also prevent some pregnancies by post-fertilization effects such as prevention of implantation.[3][35][64]

History

In 1966, gynecologist John McLean Morris and biologist Gertrude Van Wagenen at the Yale School of Medicine reported the successful use of oral high-dose estrogen pills as post-coital contraceptives in women and rhesus macaque monkeys, respectively.[78][79] A few different drugs were studied, with a focus on high-dose estrogens, and it was originally hoped that postcoital contraception would prove viable as an ongoing contraceptive method.[80]

The first widely used methods were five-day treatments with high-dose estrogens, using diethylstilbestrol (DES) in the US and ethinylestradiol in the Netherlands by Dr. Haspels.[81][82]

In the early 1970s, the Yuzpe regimen was developed by A. Albert Yuzpe in 1974;[83] progestin-only postcoital contraception was investigated (1975);[84] and the copper IUD was first studied for use as emergency contraception (1975).[85] Danazol was tested in the early 1980s in the hopes that it would have fewer side effects than Yuzpe, but was found to be ineffective.[86]

The Yuzpe regimen became the standard course of treatment for postcoital contraception in many countries in the 1980s. The first prescription-only combined estrogen-progestin dedicated product, Schering PC4 (ethinylestradiol and norgestrel), was approved in the UK in January 1984 and first marketed in October 1984.[87] Schering introduced a second prescription-only combined product, Tetragynon (ethinylestradiol and levonorgestrel) in Germany in 1985.[1]

(http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3774816) By 1997, Schering AG dedicated prescription-only combined products had been approved in only 9 countries: the UK (Schering PC4), New Zealand (Schering PC4), South Africa (E-Gen-C), Germany (Tetragynon), Switzerland (Tetragynon), Denmark (Tetragynon), Norway (Tetragynon), Sweden (Tetragynon) and Finland (Neoprimavlar); and had been withdrawn from marketing in New Zealand in 1997 to prevent it being sold over-the-counter.[2] (http://www.fda.gov/cder/foi/nda/99/21-045_Plan%20B_medr.pdf) [3] (http://www.amwa-doc.org/index.cfm?objectid=1413E9D2-D567-0B25-593F3D9007E7AA63) [4] (http://ec.princeton.edu/questions/dedicated.html) Regular combined oral contraceptive pills (which were less expensive and more widely available) were more commonly used for the Yuzpe regimen even in countries where dedicated products were available.[88]

Over time, interest in progestin-only treatments increased. The Special Program on Human Reproduction (HRP), an international organization whose members include the World Bank and World Health Organization, "played a pioneering role in emergency contraception" by "confirming the effectiveness of levonorgestrel."[89] After the WHO conducted a large trial comparing Yuzpe and levonorgestrel in 1998,[90][91] combined estrogen-progestin products were gradually withdrawn from some markets (*Preven* in the United States discontinued May 2004, *Schering PC4* in the UK discontinued October 2001, and *Tetragynon* in France) in favor of progestin-only EC, although prescription-only dedicated Yuzpe regimen products are still available in some countries.

In 2002, China became the first country in which mifepristone was registered for use as EC.

United States

DES

- In 1971, a *New England Journal of Medicine* editorial calling attention to previously published studies on the use of DES as a postcoital contraceptive at Yale University, and a large study published in *JAMA* on the use of DES as a postcoital contraceptive at the University of Michigan, led to off-label use of DES as a postcoital contraceptive becoming prevalent at many university health services.[92][93]
- In May 1973, in an attempt to restrict off-label use of DES as a postcoital contraceptive to emergency situations such as rape, a *FDA Drug Bulletin* was sent to all U.S. physicians and pharmacists that said the FDA had approved, under restricted conditions, postcoital contraceptive use of DES.[94] (In February 1975, the FDA Commissioner testified that the only error in the May 1973 *FDA Drug Bulletin* was that the FDA had **not** approved postcoital contraceptive use of DES.)[95]
- In September 1973, the FDA published a proposed rule specifying patient labeling and special packaging requirements for any manufacturer seeking FDA approval to market DES as a postcoital contraceptive, inviting manufacturers to submit abbreviated new drug applications (ANDAs) for that indication, and notifying manufacturers that the FDA intended to order the withdrawal of DES 25 mg tablets (which were being used off-label as postcoital contraceptives).[96][97][97][98]

- In late 1973, Eli Lilly, the largest U.S. manufacturer of DES, discontinued its DES 25 mg tablets and in March 1974 sent a letter to all U.S. physicians and pharmacists telling them it did not recommend use of DES as a postcoital contraceptive.[95]
- Only one pharmaceutical company, Tablicaps, Inc., a small manufacturer of generic drugs, ever submitted (in January 1974) an ANDA for use of DES as an emergency postcoital contraceptive, and the FDA never approved it.[95][99]
- In February 1975, the FDA said it had not yet approved DES as a postcoital contraceptive, but would after March 8, 1975 permit marketing of DES for that indication in emergency situations such as rape or incest *if* a manufacturer obtained an approved ANDA that provided patient labeling and special packaging as set out in a FDA final rule published in February 1975.[100] To discourage off-label use of DES as a postcoital contraceptive, in February 1975 the FDA ordered DES 25 mg (and higher) tablets removed from the market and ordered the labeling of lower doses (5 mg and lower) of DES still approved for other indications be changed to state: "THIS DRUG PRODUCT SHOULD NOT BE USED AS A POSTCOITAL CONTRACEPTIVE" in block capital letters on the first line of the physician prescribing information package insert and in a prominent and conspicuous location of the container and carton label.[97][101]
- In March 1978, a *FDA Drug Bulletin* was sent to all U.S. physicians and pharmacists which said: "FDA has not yet given approval for any manufacturer to market DES as a postcoital contraceptive. The Agency, however, will approve this indication for emergency situations such as rape or incest if a manufacturer provides patient labeling and special packaging. To discourage 'morning after' use of DES without patient labeling, FDA has removed from the market the 25 mg tablets of DES, formerly used for this purpose."[102]
- In the 1980s, off-label use of the Yuzpe regimen superseded off-label use of DES for postcoital contraception.[99][103][104]
    - DES is no longer commercially available in the U.S.; Eli Lilly, the last U.S. manufacturer, ceased production in spring 1997.[105]

Preven

- On February 25, 1997, the FDA posted a notice in the *Federal Register* saying it had concluded that the Yuzpe regimen was safe and effective for off-label use as postcoital EC, was prepared to accept NDAs for COCPs labeled as ECPs, and listed 6 then available COCPs (there are now 22) that could be used as ECPs.[5]
- On September 1, 1998, the FDA approved the prescription Yuzpe regimen Preven Emergency Contraception Kit (which contained a urine pregnancy test and 4 COCPs).[106] Preven was discontinued in May 2004.[107]

Plan B

- On July 28, 1999, the FDA approved the prescription progestin-only Plan B (two 750 µg levonorgestrel pills) emergency contraceptive.[108]
- On August 24, 2006, the FDA approved nonprescription behind-the-counter access to Plan B from pharmacies staffed by a licensed pharmacist for women 18 or older; a prescription-only form of Plan B was made available for younger females aged 17 and younger.[109]

- On November 6, 2006, Barr Pharmaceuticals announced that its subsidiary, Duramed Pharmaceuticals, had initiated shipment of dual-label Plan B OTC/Rx and it would be available in pharmacies across the U.S. by mid-November 2006.[110]
- On March 23, 2009, a US judge ordered the FDA to allow 17-year-olds to acquire Plan B without a prescription.[111] This now changes the August 24, 2006 ruling and Plan B is now available "behind the counter" for men and women. There is a prescription method available for girls under 17.
- On April 30, 2013, the FDA approved (with three-year marketing exclusivity) Teva Pharmaceutical Industries Plan B One-Step for sale without a prescription to anyone age 15 or over who can show proof of age such as a driver's license, birth certificate, or passport to a drug store retail clerk.[112] Generic one-pill levonorgestrel emergency contraceptives and all two-pill levonorgestrel emergency contraceptives will remain restricted to sale from a pharmacist—without a prescription to anyone age 17 or over who can show proof of age.[112]
- On June 10, 2013, the Obama administration ceased trying to block the over-the-counter availability the pill for all women and girls. With this reversal it means that any woman or girl will be able to purchase the Plan B One-Step without a prescription.[113]

See also

- Rape crisis center
- Ulipristal acetate - Another emergency contraceptive, marketed as *Ella*, was approved in the U.S. in 2010, and is effective up to five days after sex
- Reproductive Health Supplies Coalition

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Mechanism of action
Copper-releasing IUCs
When used as a regular or emergency method of contraception, copper-releasing IUCs act primarily to prevent fertilization. Emergency insertion of a copper IUC is significantly more effective than the use of ECPs, reducing the risk of pregnancy following unprotected intercourse by more than 99%.[2,3] This very high level of effectiveness implies that emergency insertion of a copper IUC must prevent some pregnancies after fertilization.
Emergency contraceptive pills
To make an informed choice, women must know that ECPs—like the birth control pill, patch, ring, shot, and implant,[76] and even like breastfeeding[77]—prevent pregnancy primarily by delaying or inhibiting ovulation and inhibiting fertilization, but may at times inhibit implantation of a fertilized egg in the endometrium. However, women should also be informed that the best available evidence indicates that ECPs prevent pregnancy by mechanisms that do not involve interference with post-fertilization events.

ECPs do not cause abortion[78] or harm an established pregnancy. Pregnancy begins with implantation according to medical authorities such as the US FDA, the National Institutes of Health[79] and the American College of Obstetricians and Gynecologists (ACOG).[80]

Ulipristal acetate (UPA). One study has demonstrated that UP can delay ovulation.[81]... Another study found that UPA altered the endometrium, but whether this change would inhibit implantation is unknown.[82]
p. 122:
Progestin-only emergency contraceptive pills. Early treatment with ECPs containing only the progestin levonorgestrel has been show to impair the ovulatory process and luteal function.[83–87]
p. 123:
Combined emergency contraceptive pills. Several clinical studies have shown that combined ECPs containing ethinylestradiol and levonorgestrel can inhibit or delay ovulation.[107–110]

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> How does EC work?
>
> In 2002, a judicial review ruled that pregnancy begins at implantation, not fertilisation.[8] The possible mechanisms of action should be explained to the patient as some methods may not be acceptable, depending on individual beliefs about the onset of pregnancy and abortion.
> Copper-bearing intrauterine device (Cu-IUD). Copper is toxic to the ovum and sperm and thus the copper-bearing intrauterine device (Cu-IUD) is effective immediately after insertion and works primarily by inhibiting fertilisation.[9–11] A systematic review on mechanisms of action of IUDs showed that both pre- and postfertilisation effects contribute to efficacy.[11] If fertilisation has already occurred, it is accepted that there is an anti-implantation effect,[12,13]
> Levonorgestrel (LNG). The precise mode of action of levonorgestrel (LNG) is incompletely understood but it is thought to work primarily by inhibition of ovulation.[16,17]
> Ulipristal acetate (UPA). UPA's primary mechanism of action is thought to be inhibition or delay of ovulation.[2]

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> Can LNG ECPs cause an abortion?
>
> LNG ECPs do not interrupt an established pregnancy or harm a developing embryo.[15] The evidence available to date shows that LNG ECP use does not prevent a fertilized egg from attaching to the uterine lining. The primary mechanism of action is to stop or disrupt ovulation; LNG ECP use may also prevent the sperm and egg from meeting.[16]

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> Emergency postcoital contraception
> Levonorgestrel
> Mechanism and efficacy
> There is strong evidence that treatment with emergency contraception acts primarily by preventing or delaying ovulation and by preventing fertilization.[22–26] Studies have indicated that emergency contraception does not prevent implantation.[27–29] Experiments in monkeys and rats could detect no effect of a high dose of levonorgesterel administered postcoitally once fertilization had occurred.[30,31] The evidence indicates that a postfertilization effect does not contribute to the efficacy of emergency contraception.[25,30–33] Clinicians, pharmacists, and patients can be reassured that treatment with emergency contraception is not an abortifacient.
> p. 157:
> The use of progesterone receptor modulators for emergency contraception
> Mifepristone. In randomized trials, 10 mg mifepristone was as effective as 25, 50, or 600 mg. preventing about 80-85% of expected pregnancies (the same efficacy and side effects as with the levonorgestrel method), with a slight decrease in efficacy when treatment was delayed to 5 days after intercourse.[16,52–54]
> Ulipristal Acetate. Ulipristal acetate (ellaOne) has similar biologic effects as mifepristone and is approved for emergency contraception in Europe and is expected to become available in the U.S.in a single oral dose of 30 mg. Randomized trials demonstrated that ulipristal acetate is slightly more effective than the single 1.5 mg dose of levonorgestrel when used within 72 h after sexual intercourse and even between 72 h and 120h.[55,56] … Progesterone receptor modulators like ulipristal acetate and mifepristone suppress ovarian follicular growth and also delay endometrial maturation, manifested in a delay in menstruation after treatment. Ovulation can be temporarily postponed.
> Other methods
> Another method of emergency contraception is the insertion of a copper IUD, anytime during the preovulatory phase of the menstrual cycle and up to 5 days after ovulation. The failure rate (in a small number of studies) is very low, 0.1%.[34,35] This method definitely prevents implantation, but it is not suitable for women who are not candidates for intrauterine contraception, e.g., multiple sexual partners or a rape victim. The use of a copper IUD for emergency contraception is expensive, but not if it is retained as an ongoing method of contraception.

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Emergency contraception
It is believed that the main mechanism of action of high-dose progestin emergency contraception is inhibition of ovulation, but other mechanisms may be involved... Taken together, these data are highly supportive of the concept that levonorgestrel emergency contraception has little or no effect on postovulation events but is highly effective when taken before ovulation. Levonorgestrel emergency contraception does not affect implantation and is not abortifacient.
Intrauterine insertion of a copper IUD within 5 to 10 days of midcycle coitus is a very effective method of preventing continuation of the pregnancy… The LNG-IUS should not be used for emergency contraception.
A study by the WHO reported that use of a single tablet of 10 mg of mifepristone was an effective emergency contraceptive with a pregnancy rate of 1.2%.
Ulipristal, also known as CDB-2914, has been studied as an emergency contraceptive pill… In 2009, European regulatory approval was granted for a 30-mg tablet of ulipristal (under the brand name of EllaOne) as an emergency contraceptive pill for use up to 5 days after unprotected intercourse. An application for approval in the United States is under review.

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Levonorgestrel-only emergency contraceptive pills:
• Interfere with the process of ovulation;
• May possibly prevent the sperm and the egg from meeting.
Implications of the research:
• Inhibition or delay of ovulation is LNG ECPs principal and possibly only mechanism of action.
• Review of the evidence suggests that LNG ECPs cannot prevent implantation of a fertilized egg. Language on implantation should not be included in LNG ECP product labeling.
• The fact that LNG ECPs have no demonstrated effect on implantation explains why they are not 100% effective in preventing pregnancy, and are less effective the later they are taken. Women should be given a clear message that LNG ECPs are more effective the sooner they are taken.
• LNG ECPs do not interrupt a pregnancy (by any definition of the beginning of pregnancy). However, LNG ECPs can prevent abortions by reducing unwanted pregnancies.

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of ovulation; however, alterations to the endometrium that may affect implantation may also contribute to efficacy... The pharmacodynamics of ulipristal acetate depends on the timing of administration in the menstrual cycle. Administration in the mid-follicular phase causes inhibition of folliculogenesis and reduction of estradiol concentration. Administration at the time of the luteinizing hormone peak delays follicular rupture by 5 to 9 days. Dosing in the early luteal phase does not significantly delay endometrial maturation but decreases endometrial thickness by 0.6 ± 2.2 mm (mean ± SD)."

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External links

- The Emergency Contraception Website (not-2-late.com) (http://ec.princeton.edu) – by the Office of Population Research at Princeton University and the Association of Reproductive Health Professionals. Information for women who need emergency contraception now.
- Planned Parenthood web site. (http://www.plannedparenthood.org/health-topics/emergency-contraception-morning-after-pill-4363.asp) Educational web site with information for women who need emergency contraception now.
- International Consortium for Emergency Contraception (http://www.cecinfo.org/) Policy-oriented web site directed at professionals.
- Emergency contraception (http://www.acsa-caah.ca/Portals/0/Member/PDF/en/documents/emergcontra.pdf) by the Adolescent Medicine Committee, Canadian Pediatric Society (CPS), *Paediatrics and Child Health* ACSA-CAAH
- Use of Emergency Contraception Among Women Aged 15-44, United States, 2006-2010 (http://purl.fdlp.gov/GPO/gpo41799) National Center for Health Statistics

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