CURRENT OPINION

Drug Safety 2002; 25 (10): 695-706
0114-5916/02/0010-0695/$25.00/0

How Safe is Emergency Contraception?

Abigail Norris Turner[1] and *Charlotte Ellertson*[2]

1 Regional Program Manager, Population Council, Mexico City, Mexico
2 Director of Reproductive Health for Latin America and the Caribbean, Population Council, Mexico City, Mexico

Abstract

Emergency contraception is used to prevent pregnancy after unprotected sex but before pregnancy begins. Currently, women can use emergency contraception by taking higher doses of the active ingredients found in ordinary oral contraceptive pills [either combined estrogen-progestogen (progestin) or progestogen-only formulations], or by having providers insert copper-bearing intrauterine devices (IUDs). The antiprogestogen mifepristone also has an excellent efficacy and safety profile as emergency contraception, but it is currently available for this indication only in China.

Many studies have documented providers' and women's fears about the individual and public health safety risks of emergency contraception. Some of these concerns include potentially increased risks of cardiovascular events (including arterial and venous disease), worries about possible effects on future fertility, feared teratogenic consequences following method failure or inadvertent use during pregnancy, exaggerated or extreme fears of adverse tolerability, and concerns about drug interactions with other medications. Wider public health questions include feared reductions in the use of ongoing, more effective contraception, possible 'abuse' of emergency contraception through overly frequent use, and potential increases in risky sexual encounters (owing to the existence of a back-up, postcoital method) and therefore in rates of sexually transmitted infections, including HIV/AIDS.

These fears can each be generally allayed. Direct and indirect investigations of emergency contraception in the biomedical and social science literature, the extensively documented safety profile of ordinary oral contraceptives, and more than 30 years of clinical experience since hormonal emergency contraception was first described, give strong evidence for its safety. This review confirms declarations by the World Health Organization and the US Food and Drug Administration, and shows that emergency contraception has an excellent safety profile in nearly all women. Finally, emergency contraception allows women a second chance to avoid unwanted pregnancies. Whether pregnancy is carried to term or terminated, the condition has inherent risks that are greater than any posed by emergency contraception.

Emergency contraception is used to prevent pregnancy after unprotected sex but before implantation of a fertilised ovum. Currently, women can use emergency contraception by taking higher doses of the active ingredients in ordinary oral contraceptive (OC) pills [either combined estrogen-progestogen (progestin) or progestogen-only formulations], or by having providers insert copper-bearing intrauterine devices (IUDs). Because it can be created from any of several brands of OCs, emergency contraception is actually available in at least one form in nearly every country in the world, even though knowledge of the option is often scarce. Specially-packaged dedicated emergency contraceptive products containing the same hormonal compounds are also marketed in many areas. An increase in research and advocacy related to emergency contraception in the past decade has led to the introduction of various emergency contraceptive regimens in regions where these methods were previously little known. As providers, legislators, researchers, women's health advocates and potential users have all taken a greater interest in emergency contraception, the safety of these regimens has naturally been a primary concern.

What are the individual and public health safety risks of emergency contraception? Studies investigating emergency contraceptive knowledge and attitudes in different populations list a number of participants' reported fears related to use of emergency contraception. These concerns may sometimes result from a lack of accurate information, and could be effectively addressed with appropriate biomedical and social science literature. Some of the concerns include potentially increased risks of cardiovascular events (including arterial and venous disease), worries about possible effects on future fertility, feared teratogenic consequences following method failure or inadvertent use during pregnancy, exaggerated or extreme fears of adverse tolerability, and concerns about drug interactions with other medications. Wider public health questions include feared reductions in the use of ongoing, more effective contraception, possible 'abuse' of emergency contraception through overly frequent use, and potential increases in risky sexual encounters (owing to the existence of a back-up, postcoital method) and therefore in rates of sexually transmitted infections (STIs), including HIV/AIDS.

Numerous studies have shown that emergency contraception has an excellent safety profile in almost all women. In addition, various medical organisations, including the World Health Organization (WHO) and the American College of Obstetricians and Gynecologists (ACOG), have released statements confirming the safety of emergency contraception and offering guidelines for clinical use.[1,2] The US Food and Drug Administration (FDA) took the unusual step of declaring the safety of emergency contraception in the *Federal Register* in 1997:

'…The Commissioner [of the FDA] has concluded that certain combined oral contraceptives … are safe and effective for use as postcoital emergency contraception… The Commissioner bases this conclusion on the FDA's review of the published literature concerning this use, FDA's knowledge of the safety of combined oral contraceptives as currently labelled, and on the unanimous conclusion that these regimens are safe and effective made by the agency's Advisory Committee for Reproductive Health Drugs at its June 18, 1996 meeting.'[3]

The WHO has also affirmed that there are no absolute contraindications to hormonal emergency contraception (aside from confirmed pregnancy, a state in which no contraceptives are indicated),[1] adding combined estrogen-progestogen emergency contraceptives to its list of essential drugs in 1996 and including progestogen-only emergency contraceptives 2 years later. Finally, regulatory authorities in Sweden and Norway have deemed the levonorgestrel-only emergency contraceptive product NorLevo®[1] safe enough to distribute over the counter, and officials in at least nine other countries allow pharmacists to dispense hormonal

1 Use of tradenames is for identification purposes only and does not imply endorsement.

emergency contraception without a doctor's prescription.[4]

1. Standard Therapies

Three regimens of emergency contraceptives are currently available and widely used clinically. Two are hormonal methods (combined estrogen-progestogen pills and progestogen-only pills), and the third is insertion of copper-bearing IUDs. In addition, the antiprogestogen mifepristone has an extremely good efficacy and safety profile when used as emergency contraception.[5] However, since mifepristone is available for this indication only in China, the majority of this review is limited to the first three methods.

1.1 Hormonal Emergency Contraception Methods

The ingredients in hormonal emergency contraceptive pills are identical to those in regular OCs. Since OC pills have been in widespread use for more than 40 years, and have been shown repeatedly to be among the world's safest drugs,[6,7] it follows that hormonal emergency contraception should also have a good safety profile in both relative and absolute terms.

1.1.1 Combined Estrogen-Progestogen Emergency Contraceptive Pills

The most commonly used type of emergency contraception is a regimen of pills containing two hormones, estrogen and progestogen. Since the ingredients are identical to those in ordinary combined OCs, women can create the regimen by ingesting the appropriate dose from normal pill packets. This combined therapy, called the Yuzpe regimen after the Canadian physician who first described it in the 1970s,[8] calls for 100μg ethinylestradiol and 500μg levonorgestrel per dose. Many different pill brands can be used to create the Yuzpe regimen (table I). Regardless of brand, women take one dose within 72 hours of unprotected sex and a second identical dose 12 hours later. In the US, the specially-packaged, dedicated combined emergency contraceptive product is Preven®.

Combined estrogen-progestogen pills are at least 75% effective when taken within 72 hours of unprotected sex, meaning that they prevent at least

Table I. Fifteen emergency contraceptive pills available in the US[10]

Pill name	Manufacturer	Pills per dose	Ethinylestradiol per dose (μg)	Levonorgestrel per dose (μg)
Dedicated products				
Plan B®	Women's Capital Corporation	1 white pill	0	750
Preven®	Gynétics	2 blue pills	100	500
Oral contraceptives				
Ovral®	Wyeth-Ayerst	2 white pills	100	500
Ogestrel®	Watson	2 white pills	100	500
Alesse®	Wyeth-Ayerst	5 pink pills	100	500
Levlite™	Berlex	5 pink pills	100	500
Nordette®	Wyeth-Ayerst	4 light-orange pills	120	600
Levlen®	Berlex	4 light-orange pills	120	600
Levora®	Watson	4 white pills	120	600
Lo/Ovral®	Wyeth-Ayerst	4 white pills	120	600
Low-Ogestrel®	Watson	4 white pills	120	600
Triphasil®	Wyeth-Ayerst	4 yellow pills	120	500
Tri-Levlen®	Berlex	4 yellow pills	120	500
Trivora®	Watson	4 pink pills	120	500
Ovrette®	Wyeth-Ayerst	20 yellow pills	0	750

75% of the pregnancies that would otherwise have occurred.[10] For example, if 100 women each had a single act of unprotected intercourse during the second or third week of their cycle, about eight would normally become pregnant. If all 100 women took the Yuzpe therapy, only two would become pregnant, a 75% reduction.[9]

1.1.2 Progestogen-Only Pills

A second hormonal method of emergency contraception consists of progestogen-only pills. Because of the much lower hormone dose per pill, women must often ingest more than 20 progestogen-only pills per dose to reach the recommended progestogen intake for emergency contraception (approximately 750μg levonorgestrel per dose). Progestogen-only dedicated products are registered in some countries; Plan B® is the levonorgestrel-only product in the US. One large recently published trial found the levonorgestrel regimen approximately 85% effective in preventing pregnancy when taken within 72 hours of unprotected sex,[11] although previous research reported a somewhat lower efficacy.[12]

1.1.3 Timing of Hormonal Emergency Contraception

Secondary analyses of emergency contraception efficacy trials have revealed important findings about the timing of hormonal therapies. For example, these methods appear to be more effective the sooner therapy is initiated after unprotected sex,[13] and some providers now give patients advance prescriptions and even advance sets of pills to keep on hand in case of need. Other research has indicated that the method is still somewhat effective, though with reduced efficacy, past the 72-hour cut-off.[14] Women should be aware, therefore, that hormonal emergency contraception could have some effect up to, or even perhaps after, 120 hours from the time of unprotected coitus.

1.2 Copper-Bearing Intrauterine Devices

The copper IUD has an excellent safety profile when used as either emergency or ongoing contraception.[15,16] Used postcoitally to prevent pregnancy, copper-bearing IUDs are 97 to 99% effective when inserted within 5 days of unprotected sex.[17,18] Unfortunately, misconceptions about the method's safety have resulted in limited IUD use by many women.[19] Additionally, numerous service delivery concerns accompany IUD insertion, and these have hampered use in some regions. Some of these obstacles include the need for a trained provider, risk of infection with device insertion, and risk of partial or complete expulsion.[15,20,21] Finally, in some countries the IUD is not cost effective if used only for a short time. Since the method can be used for ongoing contraception for up to 10 years, however, it can become cost effective if left in place after emergency insertion and used for longer-term contraception.[22] As research continues to validate the safety of the IUD, use of this method may increase both for emergency and ongoing pregnancy prevention.

1.3 Mifepristone

A final method with high efficacy for postcoital contraception is the antiprogestogen mifepristone. Mifepristone is sometimes known as RU 486, and is marketed for medical abortion in numerous developed and developing countries. Used widely to terminate early pregnancies, mifepristone is only registered for use as emergency contraception in China, although it is sometimes available elsewhere as emergency contraception under research protocols. Early randomised trials found this method to be exceptionally effective for postcoital contraception, reporting no pregnancies following mifepristone therapy,[23,24] though more recent studies have found slightly higher failure rates.

One recent trial found that a single 200mg dose of mifepristone administered between 3 and 5 days after unprotected sex prevented 85% of expected pregnancies.[25] Another randomised trial reported that doses of 50mg and 10mg were each as effective as a 600mg dose up to 120 hours (5 days) after unprotected coitus.[26] Researchers also found that mifepristone was more acceptable to women presenting 'late' for emergency contraception (i.e. more than 72 hours after unprotected sex) than the

insertion of a copper-bearing IUD.[25] While the safety of mifepristone as an emergency contraceptive has not been studied extensively, the compound has an excellent safety record when used for other indications.[5]

2. Safety Concerns

Very little research has expressly investigated the safety of different preparations of emergency contraception.[5,27] However, the long-standing epidemiological track record of regular OCs implies a good safety profile for emergency contraception. The primary difference between using hormonal emergency contraception as a back-up contraceptive and using OCs as ongoing contraception is that emergency contraceptive pills are used for a very short period of time, but in a higher dose (approximately four to eight times the typical OC dose in a 24-hour period). Therefore, in addition to recognising that OC pills have a reassuring safety profile, it is necessary to weigh the benefit of a shortened exposure time against the risk of an increased hormone dose.

Available registries of adverse events related to hormonal emergency contraceptive use (for example, The Committee on Safety of Medicines in the UK) list exceptionally few reported adverse events following use of emergency contraceptives (and nearly 40% of recorded events are pregnancies).[5] The WHO guidelines for dispensing hormonal emergency contraceptives do not require extensive screening procedures or a physical exam, further reinforcing the widespread expert agreement about the method's safety.[1] Far from posing dangerous safety hazards, increased availability of emergency contraception will likely save lives by reducing maternal mortality associated with unintended pregnancy and unsafe abortion.[28]

2.1 Venous Disease

Emergency contraceptives containing 'third generation' progestogens [desogestrel, destodene, cyproterone or gestodene, instead of lynestrenol, norethisterone (norethindrone) or levonorgestrel] might be an area of future focus for investigators concerned with the safety of hormonal emergency contraception. Historically, women taking OCs containing third generation progestogens for ongoing pregnancy prevention have been shown to be at higher risk of venous disease, especially deep vein thrombosis, venous thromboembolism and pulmonary embolism.[29,30] There are two important points to consider here. First, all registered formulations of hormonal emergency contraception contain second generation (not third generation) progestogens. Second, only one study has investigated changes in coagulation factors following ingestion of combined estrogen-levonorgestrel emergency contraception. Though small (n =11), this investigation concluded that the combined hormonal regimen had no impact on clotting factors either in the first week following ingestion or during subsequent months of follow-up.[31]

Additionally, there have been almost no reports of venous thromboembolism following use of hormonal emergency contraception. Between 1984 and July 1996, women in the UK took approximately 4 million doses of a dedicated estrogen-levonorgestrel emergency contraceptive product.[5] The Committee on Safety of Medicines recorded only three cases of venous thromboembolism (one fatal) and three cases of cerebrovascular disorders following emergency contraception use. In none of these cases was there a definite association between emergency contraception and the adverse event.[5] Another population-based cohort study found that the risk of venous thromboembolism attributable to hormonal emergency contraception was not substantially higher than the risk of venous thromboembolism with traditional OCs, despite the higher content of both estrogen and progestogen.[32]

Logically, emergency contraceptive use should pose a smaller risk of venous disease than ongoing OC use because of the shorter exposure time (despite the higher peak). Moreover, even the contribution of long-term OC use to venous thromboembolism is smaller than generally perceived owing to media sensationalism. The estimated risk of venous thromboembolism attributable to OC pills is

less than 3 per 10 000 women per year,[33] about half the risk of venous thromboembolism associated with pregnancy.[33,34]

Use of copper IUDs for either emergency or ongoing contraception is not associated with an increased risk of venous disease. Although one contraindication to IUD use is current anticoagulant therapy,[15] and many women take anticoagulants following an incidence of venous disease, this precaution is related to concerns of excessive menstrual bleeding and not to an increased risk of venous disease. The copper IUD does not contain the hormones that are suspected of negatively affecting blood clotting levels, thereby putting prone women at risk for serious venous events.

2.2 Arterial Disease

Another hypothesised safety risk of hormonal emergency contraception derives from the documented association between long-term OC use and increased risk of arterial disease, especially myocardial infarction. Though women's hormonal exposure through emergency contraceptive ingestion is much less than that from long-term OC use, the relationship is important to explore in order to assuage concerns about the safety of emergency contraception.

The link between early formulations of OC pills and heart disease is well documented,[35] particularly among women who are also heavy smokers.[36,37] Early pills were consequently modified to lessen these risks by reducing the dose of estrogen and changing the progestogen. While third generation pills are generally believed to increase the risk of venous disease (as described earlier), they are also thought to decrease the risk of arterial disease owing to a favourable effect on the level of high density lipoprotein-cholesterol.[38] One recent study revealed that while users of any type of OC were roughly twice as likely as nonusers to experience myocardial infarction, risk was greater for first and second generation OC users than for third generation pill users.[35] In contrast, other researchers have postulated that among women who are properly screened before use, there should be no significant increase in the risk of ischaemic stroke or acute myocardial infarction associated with the use of low-dose estrogen OCs.[39]

Neither the IUD nor mifepristone appear to pose any arterial safety risks.

2.3 Future Fertility

Potential users in emergency contraception research trials frequently mention fears about impaired future fertility. Although investigators have studied this topic extensively with regular OCs, no studies have examined return to fertility following the use of hormonal emergency contraception. (Such investigations would be methodologically difficult to conduct, since generally women who take emergency contraception are trying to avoid pregnancy rather than to conceive). Despite initial concerns when OCs were first introduced more than 40 years ago, research shows that OCs do not delay a return to fertility for longer than 1 year (and in most cases, return to fertility is quicker). No studies have linked OCs with long-term fertility problems.[40,41] It follows, then, that hormonal emergency contraception should not have any lasting effect on fertility.

A potential complication of IUD use is the increased risk of pelvic inflammatory disease and, if untreated, consequent infertility. Women at low risk for STIs may be good candidates for the IUD, and numerous investigations have concluded that in the absence of STIs, the IUD is not linked to future fertility problems.[41-44] One recent publication, however, suggested that increasing duration of IUD use is associated with decreasing fertility in nulliparous women (79% of former IUD users had delivered at 36 months as compared with 91% of former barrier method users); this association remained even after adjusting for maternal age and history of gynaecological illnesses.[45] The results of this study, however, have been seriously questioned because of perceived selection bias and confounding.[46]

No investigations have considered a return to fertility following use of mifepristone for emergency contraception. No such delay follows its use

for medical abortion,[47] however, so compromised fertility following use of mifepristone for emergency contraception is unlikely.

2.4 Potential Teratogenesis

While no studies have directly considered a link between the use of hormonal emergency contraception and fetal malformation (following either failure of emergency contraception or inadvertent use during pregnancy), many studies have investigated the effects of regular OCs (including high dose formulations) used during pregnancy. These have concluded that *in utero* exposure to OCs poses no, or at most, an extremely low, risk of birth defects.[41,48-52] Additionally, hormonal emergency contraceptives are even less likely to be teratogenic because of the timing of administration (typically well before organogenesis begins).[53] For these reasons, it is not necessary to administer a pregnancy test to rule out an existing pregnancy before starting hormonal emergency contraceptive therapy.[54]

Unlike with hormonal emergency contraception, women seeking insertion of a copper IUD should produce a negative pregnancy test first. Because of the IUD's extremely high efficacy, there are only a few reports of women becoming pregnant following emergency insertion. Nevertheless, in cases when the IUD does fail, and a woman wishes to continue the pregnancy, a provider should remove the IUD if a pregnancy is 12 or fewer weeks' gestation. If the pregnancy has progressed past 12 weeks, the IUD can remain safely in place. In both cases, the woman can be reassured that there is no evidence for increased risk of congenital malformation.[15]

As with the IUD, women should take great care to ensure they are not already pregnant before using mifepristone for emergency contraception. Unlike hormonal emergency contraception, mifepristone (in doses as low as 100mg,[55] and perhaps lower) can effectively terminate established pregnancies. If mifepristone emergency contraception fails, or if a woman inadvertently uses it during pregnancy, she should perhaps be encouraged to terminate the pregnancy because of the risk of teratogenesis.[47]

2.5 Other Adverse Effects and Tolerability

Potential users of emergency contraception routinely perceive tolerability concerns as a significant safety problem and a reason for not using the method. Additionally, women and providers often overestimate the prevalence, severity and duration of adverse tolerability. It is important to note that while unpleasant, any adverse tolerability of hormonal emergency contraception does not represent a serious threat to safety. Furthermore, such events are fewer, less severe, and significantly shorter-lived than those typically experienced during pregnancy.

Potential tolerability events with hormonal emergency contraception include nausea, vomiting, headache, menstrual disruption, and less commonly, breast tenderness.[56] Reported events with progestogen-only emergency contraceptives are generally less severe than with combined estrogen-progestogen regimens.[57,58] Nausea and vomiting may be reduced if the non-prescription antinausea drug meclozine (meclizine) is taken 1 hour before emergency contraceptive therapy is initiated; however, this medication must be taken before the onset of symptoms to be useful, and since the risk of drowsiness with meclozine is doubled, many women may opt not to use it.[59] If vomiting occurs within 2 hours after taking either dose, women may consider repeating that part of the therapy.[9] In addition, though some women report affected bleeding patterns and other menstrual disturbances, research is not conclusive as to whether hormonal emergency contraceptive accelerates or delays a women's normal menstrual cycle.

Adverse events of the IUD include potential discomfort during insertion and the possible introduction of an existing bacterial infection into the upper genital tract. Such infection can put the user at risk of pelvic inflammatory disease, and untreated pelvic inflammatory disease can lead to infertility, as described in section 3.3.[15,60] Many users also experience increased menstrual bleeding

and pain, and intermenstrual spotting.[15] These effects can be severe enough to warrant discontinuation of the method as ongoing contraception in 4 to 11% of women.[15,17]

When used as emergency contraception, mifepristone has the same potential tolerability concerns as hormonal methods, though events are generally less severe.[23,24]

2.6 Drug-Drug Interactions

Providers and pharmacists must always remind their patients to consider potential drug interactions when taking any new medication. Known interactions are described below, but while these drug-drug reactions may reduce the efficacy of emergency contraception, they do not pose dangerous safety hazards.

The ethinylestradiol component of combined estrogen-progestogen emergency contraception may interfere with the metabolism of other compounds, either through its absorption, metabolism or excretion, or because of competition for metabolic pathways.[61] Theoretically, the effectiveness of both estrogen-progestogen and progestogen-only pills is reduced by hepatic enzyme-inducing drugs such as anticonvulsant agents (phenytoin, primidone, barbiturates, carbamazepine, ethosuximide and methosuximide), antituberculosis drugs such as rifampicin (rifampin), and antifungal drugs such as griseofulvin.[61,62] Ethinylestradiol can also inhibit microsomal enzymes, possibly slowing the metabolism of other drugs [e.g. analgesic antiinflammatories such as phenazone (antipyrin), antidepressants, cyclosporin, theophylline and alcohol (ethanol)] and increasing the possibility of side effects.[61]

Researchers have not found conclusive evidence of interactions between broad-spectrum antibacterials and combined OCs,[62,63] though simultaneous use may result in decreased contraceptive efficacy for ongoing OC use. No studies have considered the effects of concurrent use of hormonal emergency contraception and broad-spectrum antibacterials, though some clinicians recommend doubling the first emergency contraceptive dose to compensate for potentially reduced efficacy.[4] In recent years, speculation has also arisen about possible interactions between hypericum (extract of St John's wort), an over-the-counter, herbal antidepressant, and OCs. Some women report intermenstrual bleeding when using this herbal treatment concomitantly with OCs.[64] In addition, recent evidence of an interaction between hypericum and the HIV medication indinavir may have consequences for other medications metabolised through a similar pathway, including OCs.[65] As yet, however, no studies have considered whether hypericum decreases the efficacy of hormonal emergency contraception.[66]

There are no known drug interactions with copper-bearing IUDs, though women with an allergy to copper should not use this method of emergency contraception.

Owing to its metabolism by cytochrome P450 (CYP)3A4, mifepristone's effectiveness could possibly be inhibited by various compounds, including ketoconazole, itraconazole, erythromycin and grapefruit juice. In addition, rifampicin, dexamethasone, hypericum, and certain anticonvulsants (phenytoin, phenobarbital, carbamazepine) may interfere with mifepristone metabolism.[67] Finally, coadministration of mifepristone may lead to an increase in serum levels of drugs that are CYP3A4 substrates, including some agents used during general anaesthesia.[67]

3. Public Health Concerns

Much of the research focusing on emergency contraception has considered the public health consequences of use instead of the medical safety of different regimens. Indeed, both providers and potential users repeatedly cite concerns that wider availability of emergency contraception will lead to numerous negative outcomes. The most commonly expressed fears are that expanded access to emergency contraception will cause women to abandon their more effective, ongoing contraception, that some users will 'abuse' the method through repeat use, and that STI rates will increase following more frequent unprotected sex.[68-73]

3.1 Abandonment of Ongoing Contraception in Favour of Emergency Contraception

Numerous studies have investigated whether increased access to emergency contraception will lead some users to reject their more effective, long-term contraception in favour of this back-up method.[71-73] In fact, reported behaviour of study participants in many cases shows the opposite to be true; that is, coming to a clinic for emergency contraception provided some women a point of entry into the healthcare system, and reported rates of more effective, long-term contraceptive use actually increased.[74] Another randomised study considering two groups of women, one given emergency contraceptive supplies in advance and one required to come to the clinic to request emergency contraception when needed, found no difference in type and effectiveness of chosen contraception at follow-up.[75] Still another study found contradictory results: while women with advance emergency contraceptive supplies did not report higher frequencies of unprotected sex, they were more likely than those in the control group to report using less effective contraception at follow-up than at enrolment.[76] One possible explanation for the decline in use of more effective contraception methods is that women with greater emergency contraceptive access (representing an effective back-up pregnancy prevention method) may have begun using condoms for STI protection.

Finally, one study that asked women (n = 295) to ingest a single 750μg dose of levonorgestrel immediately after intercourse reported that use of that regimen (half the dose recommended for emergency contraception) for ongoing contraception was generally unsuitable to women, further emphasising that women are unlikely to chose to use emergency contraception on a regular basis in place of more effective methods of long-term contraception.[77]

3.2 Repeat Use

As more providers consider giving their patients advance emergency contraceptive prescriptions or pills before a need for the method arises, research has considered whether such advance provision will encourage women to use emergency contraception repeatedly or to 'take chances' with their normal contraception. Aside from intuitive reasons discouraging repeat use (including potential adverse tolerability and lower efficacy than long-term contraceptive methods), these studies have concluded without exception that greater availability of emergency contraception does not result in the method's misuse.[74,75,78] Repeat use was low (or nonexistent) in all studies. One study reported no repeat use in either study arm,[78] and another found equal rates of repeat use between women who had advance supplies of emergency contraception and women who had to come to the clinic to request it.[75] A large cohort study reported that only 4% of the study population (n = 95 007) ever used emergency contraception more than once in a given year.[74] As further encouragement for advance provision of emergency contraception, another project found reduced rates of unintended pregnancy among women who were given emergency contraception in advance of need when compared with women who were required to come to the clinic to request it.[75] The same study also found that only 2% of women reported that having access to emergency contraception encouraged them to 'take more risks' with their normal contraception.[75]

3.3 Increase in Sexually Transmitted Infections/HIV Rates

Critics of increased access to emergency contraception have postulated that greater availability will lead to more 'promiscuous' sex and therefore increased rates of STIs. No good studies have compared STI rates between populations with varying access to emergency contraception to determine whether increased availability leads to riskier sex and higher rates of STI transmission. Nevertheless,

at least two published studies report that when emergency contraception is more available, women are more likely to use it when needed, but that their incidence of unprotected sex does not increase.[76,78] Therefore, while there is no direct evidence to refute a link between increased access to emergency contraception and increased rates of STIs, an unchanged rate of unprotected sex independent of access to emergency contraception indicates that such availability probably has little or no effect on STI rates.

STIs are of special concern with IUD users, though not for reasons related to emergency contraception. In a woman using an IUD, ordinary STIs are more likely to lead to pelvic inflammatory disease,[15] and untreated disease may lead to infertility. Though the increased risk is small,[79,80] the severity of associated consequences of pelvic inflammatory disease have convinced some providers that the IUD is not the best emergency contraceptive method for adolescents (who are more likely to have multiple partners and be at higher risk of STIs).[81] Because of important timing considerations for effective use of the IUD as emergency contraception, it is not reasonable to require a full STI screening before insertion. Women should, however, be informed of the possible complications resulting from STI infection and encouraged to think about whether, given their personal level of risk, the IUD is their best emergency contraceptive option.

4. Benefits of Emergency Contraception

Emergency contraception has a positive reproductive health consequence that should not be underestimated: the method allows women a second chance to avoid unwanted pregnancies. Numerous reports have explored the harmful consequences of unwanted pregnancy, particularly in developing countries, where poor sanitation, lower education, malnutrition and insufficient access to safe abortion can make the condition even life-threatening. The detrimental social and health outcomes for women faced with unintended pregnancies have also been well-documented.[28,82-86] Whether pregnancy is carried to term or terminated, the condition has inherent risks that are greater than any posed by emergency contraception.

5. Conclusion

Both direct and indirect evidence reinforce the individual and public health safety of available regimens of emergency contraception. Declarations from the WHO and the US FDA reinforce these findings to make a compelling case for the safety of the three regimens used in clinical practice today. The health consequences of unintended pregnancy are far greater than any individual health risk posed by emergency contraception. All efforts to increase emergency contraception's availability and use should be encouraged.

Acknowledgements

The authors have no personal financial interest in the commercial success or failure of emergency contraception. Both are employed by the Population Council, a not-for-profit research organisation that receives royalties on sales of the copper-T intrauterine device.

References

1. World Health Organization. Emergency contraception: a guide for service delivery. Geneva: World Health Organization, 1998
2. American College of Obstetricians and Gynecologists. ACOG practice bulletin: emergency oral contraception. No. 25. Washington, DC: ACOG, 2001 Mar
3. Food and Drug Administration. Prescription drug products: certain combined oral contraceptives for use as postcoital emergency contraception. Fed Regist 1997; 62: 8610-2
4. Princeton University Office of Population Research. The emergency contraception website [online]. Available from URL: http://not-2-late.com [Accessed 2002 Apr 16]
5. Glasier A. Safety of emergency contraception. J Am Med Womens Assoc 1998; 53 (5 Suppl. 2): 219-21
6. Kubba AA. Contraception: a review. Int J Clin Pract 1998; 52 (2): 102-5
7. Shulman LP. Oral contraceptives: risks. Obstet Gynecol Clin North Am 2000; 27 (4): 695-704
8. Yuzpe AA, Thurlow HJ, Ramzy I, et al. Post coital contraception: a pilot study. J Reprod Med 1974; 13 (2): 53-8
9. Ellertson C, Trussell J, Stewart F, et al. Emergency contraception. Semin Reprod Med 2001; 19 (4): 323-30
10. Trussell J, Rodriguez G, Ellertson C. New estimates of the effectiveness of the Yuzpe regimen of emergency contraception. Contraception 1998; 57 (6): 363-9
11. Task Force on Postovulatory Methods of Fertility Regulation. Randomised controlled trial of levonorgestrel versus the Yuzpe regimen of combined oral contraceptives for emergency contraception. Lancet 1998; 352 (9126): 428-33

12. Ho PC, Kwan MS. A prospective randomized comparison of levonorgestrel with the Yuzpe regimen in post-coital contraception. Hum Reprod 1993; 8 (3): 389-92
13. Piaggio G, von Hertzen H, Grimes DA, et al. Timing of emergency contraception with levonorgestrel or the Yuzpe regimen. Task force on postovulatory methods of fertility regulation. Lancet 1999; 353 (9154): 721
14. Rodrigues I, Grou F, Joly J. Effectiveness of emergency contraceptive pills between 72 and 120 hours after unprotected sexual intercourse. Am J Obstet Gynecol 2001; 184 (4): 531-7
15. Kishen M. Intrauterine contraceptive devices. In: Glasier A, Gebbie A, editors. Handbook of family planning and reproductive healthcare. 4th ed. London: Churchill Livingstone, 2000: 105-26
16. Ramirez Hidalgo A, Pujol Ribera E. Use of the intrauterine device: efficacy and safety. Eur J Contracept Reprod Health Care 2000; 5 (3): 198-207
17. Liying Z, Bilian X. Emergency contraception with multiload Cu-375 SL IUD: a multicenter clinical trial. Contraception 2001; 64 (2): 107-12
18. Trussell J, Ellertson C. Efficacy of emergency contraception: topical reviews. Fert Control Rev 1995; 4 (2): 8-11
19. Cheng D. The intrauterine device: still misunderstood after all these years. South Med J 2000; 93 (9): 859-64
20. Reuter S. Barriers to the use of IUDs as emergency contraception. Br J Fam Plann 1999; 25 (2): 61-8
21. Borgatta L. Managing clinical complexities of long-term contraception. Medscape Womens Health 1998; 3 (1): 3
22. Trussell J, Leveque JA, Koenig JD, et al. The economic value of contraception: a comparison of 15 methods. Am J Public Health 1995; 85 (4): 494-503
23. Glasier A, Thong KJ, Dewar M, et al. Mifepristone (RU 486) compared with high-dose estrogen and progestogen for emergency postcoital contraception. N Engl J Med 1992; 327 (15): 1041-4
24. Webb AM, Russell J, Elstein M. Comparison of Yuzpe regimen, danazol, and mifepristone (RU486) in oral postcoital contraception. BMJ 1992; 305 (6859): 927-31
25. Ashok PW, Wagaarachchi PT, Flett GM, et al. Mifepristone as a late post-coital contraceptive. Hum Reprod 2001; 16 (1): 72-5
26. Comparison of three single doses of mifepristone as emergency contraception: a randomised trial. Task Force on Postovulatory Methods of Fertility Regulation. Lancet 1999; 353 (9154): 697-702
27. Webb A. How safe is the Yuzpe method of emergency contraception? Fert Control Rev 1995; 4 (2): 16-8
28. World Health Organization. Unsafe abortion: global and regional estimates of incidence of and mortality due to unsafe abortion, with a listing of available country data. Geneva, Switzerland: World Health Organization, 1998, WHO/RHT/MSM/97
29. Jick H, Kaye JA, Vasilakis-Scaramozza C, et al. Risk of venous thromboembolism among users of third generation oral contraceptives compared with users of oral contraceptives with levonorgestrel before and after 1995: cohort and case-control analysis. BMJ 2000; 321 (7270): 1190-5
30. Vasilakis-Scaramozza C, Jick H. Risk of venous thromboembolism with cyproterone or levonorgestrel contraceptives. Lancet 2001; 358 (9291): 1427-9
31. Webb A, Taberner D. Clotting factors after emergency contraception. Adv Contracept 1993; 9 (1): 75-82
32. Vasilakis C, Jick SS, Jick H. The risk of venous thromboembolism in users of postcoital contraceptive pills. Contraception 1999; 59 (2): 79-83
33. Pymar HC, Creinin MD. The risks of oral contraceptive pills. Semin Reprod Med 2001; 19 (4): 305-12
34. Burkman RT, Collins JA, Shulman LP, et al. Current perspectives on oral contraceptive use. Am J Obstet Gynecol 2001; 185 Suppl. 2: S4-12
35. Tanis BC, van den Bosch M, Kemmeren JM, et al. Oral contraceptives and the risk of myocardial infarction. N Engl J Med 2001; 345 (25): 1787-93
36. Rosenberg L, Palmer JR, Rao RS, et al. Low-dose oral contraceptive use and the risk of myocardial infarction. Arch Intern Med 2001; 161 (8): 1065-70
37. Shapiro S, Slone D, Rosenberg L, et al. Oral-contraceptive use in relation to myocardial infarction. Lancet 1979; 1 (8119): 743-7
38. Godsland IF, Crook D, Simpson R, et al. The effects of different formulations of oral contraceptive agents on lipid and carbohydrate metabolism. N Engl J Med 1990; 323 (20): 1375-81
39. Heinemann LA. Emerging evidence on oral contraceptives and arterial disease. Contraception 2000; 62 Suppl. 2: 29S-36S
40. Burkman RTJ. Noncontraceptive effects of hormonal contraceptives: bone mass, sexually transmitted disease and pelvic inflammatory disease, cardiovascular disease, menstrual function, and future fertility. Am J Obstet Gynecol 1994; 170 (5 Pt 2): 1569-75
41. Huggins GR, Cullins VE. Fertility after contraception or abortion. Fertil Steril 1990; 54 (4): 559-73
42. Skjeldestad F, Bratt H. Fertility after complicated and noncomplicated use of IUDs: a controlled prospective study. Adv Contracept 1988; 4 (3): 179-84
43. Gupta BK, Gupta AN, Lyall S. Return of fertility in various types of IUD users. Int J Fertil 1989; 34 (2): 123-5
44. Van Os WA, Edelman DA. Fifteen years' experience with the Multiload IUD. Adv Contracept 1988; 4 (3): 165-78
45. Doll H, Vessey M, Painter R. Return of fertility in nulliparous women after discontinuation of the intrauterine device: comparison with women discontinuing other methods of contraception. Br J Obstet Gynaecol 2001; 108 (3): 304-14
46. Grimes DA. Intrauterine devices and infertility: sifting through the evidence. Lancet 2001; 358 (9275): 6-7
47. Stewart FH, Wells ES, Flinn SK, Weitz TA. Early medical abortion: issues for practice. San Francisco: UCSF Center for Reproductive Health Research & Policy, 2001
48. Simpson JL, Phillips OP. Spermicides, hormonal contraception and congenital malformations. Adv Contracept 1990; 6: 141-67
49. Harlap S, Shiono PH, Ramcharan S. Congenital abnormalities in the offspring of women who used oral and other contraceptives around the time of conception. Int J Fertil 1985; 30 (2): 39-47
50. Savolainen E, Saksela E, Saxen L. Teratogenic hazards of oral contraceptives analyzed in a national malformation register. Am J Obstet Gynecol 1981; 140 (5): 521-4
51. Vessey M, Meisler L, Flavel R, et al. Outcome of pregnancy in women using different methods of contraception. Br J Obstet Gynaecol 1979; 86 (7): 548-56
52. Raman-Wilms L, Tseng AL, Wighardt S, et al. Fetal genital effects of first-trimester sex hormone exposure: a meta-analysis. Obstet Gynecol 1995; 85 (1): 141-9
53. Glasier A. Emergency contraception. In: Glasier A, Gebbie A, editors. Handbook of family planning and reproductive healthcare. 4th ed. London: Churchill Livingstone, 2000: 201-13
54. Grimes DA, Raymond EG. Bundling a pregnancy test with the Yuzpe regimen of emergency contraception. Obstet Gynecol 1999; 94 (3): 471-3

55. Creinin MD, Pymar HC, Schwartz JL. Mifepristone 100 mg in abortion regimens. Obstet Gynecol 2001; 98 (3): 434-9
56. Trussell J, Ellertson C, Stewart F. The effectiveness of the Yuzpe regimen of emergency contraception. Fam Plann Perspect 1996; 28 (2): 58-64
57. Cheng L, Gulmezoglu AM, Ezcurra E, Van Look PF. Interventions for emergency contraception. Available in The Cochrane Library [database on disk and CD ROM]. Updated quarterly. The Cochrane Collaboration; issue 2. Oxford: Update Software, 2000: CD001324
58. Sanchez-Borrego R, Balasch J. Ethinyl oestradiol plus dl-norgestrel or levonorgestrel in the Yuzpe method for postcoital contraception: results of an observational study. Hum Reprod 1996; 11 (11): 2449-53
59. Raymond EG, Creinin MD, Barnhart KT, et al. Meclizine for prevention of nausea associated with use of emergency contraceptive pills: a randomized trial. Obstet Gynecol 2000; 95 (2): 271-7
60. McMillan A. Sexually transmitted infections. In: Glasier A, Gebbie A, editors. Handbook of family planning and reproductive healthcare. 4th ed. London: Churchill Livingstone, 2000: 281-313
61. Gynétics. Preven™ Emergency Contraceptive Prescribing Information [online]. Available from URL: http://www.preven.com/prodinfo/prescinfo.asp [Accessed 2002 Apr 16]
62. Women's Capital Corporation. Plan B Patient information [online]. Available from URL: http://www.go2planb.com/consumers_guide/patient_info.html#IndicationsAndUsage [Accessed 2002 Apr 16]
63. Weaver K, Glasier A. Interaction between broad-spectrum antibiotics and the combined oral contraceptive pill: a literature review. Contraception 1999; 59 (2): 71-8
64. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: a systematic review. Drugs 2001; 61 (15): 2163-75
65. Piscitelli SC, Burstein AH, Chaitt D, et al. Indinavir concentrations and St John's wort. Lancet 2000; 355 (9203): 547-8
66. Does St. John's Wort decrease OC efficacy? Contraceptive Technology Update 2001; 22 (2): 15-7
67. Danco Laboratories. The Early Option Pill (Mifeprex): product labeling [online]. Available from URL: http://www.earlyoptionpill.com/hcp_labeling.php3. [Accessed 2002 Apr 16]
68. Harper C, Ellertson C. Knowledge and perceptions of emergency contraceptive pills among a college-age population: a qualitative approach. Fam Plann Perspect 1995; 27 (4): 149-54
69. Langer A, Harper C, Garcia-Barrios C, et al. Emergency contraception in Mexico City: what do health care providers and potential users know and think about it? Contraception 1999; 60 (4): 233-41
70. Muia E, Ellertson C, Lukhando M, et al. Emergency contraception in Nairobi, Kenya: knowledge, attitudes and practices among policymakers, family planning providers and clients, and university students. Contraception 1999; 60 (4): 223-32
71. Golden NH, Seigel WM, Fisher M, et al. Emergency contraception: pediatricians' knowledge, attitudes, and opinions. Pediatrics 2001; 107 (2): 287-92
72. Ziebland S, Graham A, McPherson A. Concerns and cautions about prescribing and deregulating emergency contraception: a qualitative study of GPs using telephone interviews. Fam Pract 1998; 15 (5): 449-56
73. Ziebland S, Maxwell K. Not a 'proper' solution? The gap between professional guidelines and users' views about the safety of using emergency contraception. J Health Serv Res Policy 1998; 3 (1): 12-9
74. Rowlands S, Devalia H, Lawrenson R, et al. Repeated use of hormonal emergency contraception by younger women in the UK. Br J Fam Plann 2000; 26 (3): 138-43
75. Glasier A, Baird D. The effects of self-administering emergency contraception. N Engl J Med 1998; 339 (1): 1-4
76. Raine T, Harper C, Leon K, et al. Emergency contraception: advance provision in a young, high-risk clinic population. Obstet Gynecol 2000; 96 (1): 1-7
77. United Nations Development Programme. Efficacy and side effects of immediate postcoital levonorgestrel used repeatedly for contraception. Contraception 2000; 61 (5): 303-8
78. Ellertson C, Ambardekar S, Hedley A, et al. Emergency contraception: randomized comparison of advance provision and information only. Obstet Gynecol 2001; 98 (4): 570-5
79. Shelton JD. Risk of clinical pelvic inflammatory disease attributable to an intrauterine device [letter]. Lancet 2001; 357 (9254): 443
80. Grimes DA. Intrauterine device and upper-genital-tract infection. Lancet 2000; 356 (9234): 1013-9
81. Foran T. Contraception in general practice before teenage pregnancy: intrauterine device may not be suitable method of contraception for teenagers. BMJ 2001; 322 (7282): 363-4
82. Klima CS. Unintended pregnancy: consequences and solutions for a worldwide problem. J Nurse Midwifery 1998; 43 (6): 483-91
83. Population Crisis Committee. Policymaker's chartbook on world population issues. Washington, DC: Population Crisis Committee, 1992
84. International Planned Parenthood Federation. Family planning for the underserved: an IPPF perspective. In: Family planning, health and family well-being. Proceedings of the United Nations Expert Group Meeting on Family Planning, Health and Family Well-Being; New York, NY. United Nations, Department for Economic and Social Information and Policy Analysis, Population Division, 1996
85. Women's Studies Project. Egypt: the social and behavioral outcomes of unintended pregnancy. Research Triangle Park, North Carolina: Family Health International, 1998
86. Adetunji JA. Unintended childbearing in developing countries: levels, trends, and determinants. DHS Analytical Reports no 8. Calverton (MD): Macro International, 1998

Correspondence and offprints: *Abigail Norris Turner*, Population Council, Regional Office for Latin America and the Caribbean, Escondida #110, Colonia Villa Coyoacán, Mexico. E-mail: anorristurner@hotmail.com