Mechanism of action of emergency contraceptive pills

Like breastfeeding and other forms of hormonal contraception, emergency contraception pills (ECPs) can prevent pregnancy by delaying or inhibiting ovulation. Some of these methods have other established mechanisms of action, and it is possible that all may act after fertilization. The preponderance of research, however, shows that ECPs do not have a major postfertilization mechanism of action. As social conservatives wage a scientifically inaccurate campaign wrongly portraying ECPs as abortifacient, some reproductive rights advocates have responded by asserting that ECPs have no postfertilization effect whatsoever. Healthcare practitioners and their patients alike should be fully informed of the proven and potential mechanisms of action to help increase both knowledge and widespread use of ECPs to prevent unintended pregnancies.

Several clinical studies have shown that combined ECPs containing the estrogen ethinyl estradiol and the progestin levonorgestrel can inhibit or delay ovulation [1-4]. This is an important mechanism of action and may explain combined ECP effectiveness when used during the first half of the menstrual cycle (before ovulation has occurred). Some studies have shown histologic or biochemical alterations in the endometrium after treatment with the regimen, leading to the conclusion that combined ECPs may act by impairing endometrial receptivity to implantation of a fertilized egg [2,5-7]. However, other more recent studies have found no such effects on the endometrium [1,8,9]. Additional possible mechanisms include interference with corpus luteum function; thickening of the cervical mucus resulting in trapping of sperm; alterations in the tubal transport of sperm, egg, or embryo and direct inhibition of fertilization [10-13]. No clinical data exist regarding the last three of these possibilities. Nevertheless, statistical evidence regarding the effectiveness of combined ECPs suggests that there must be a mechanism of action in addition to delaying or preventing ovulation [14]. However, the effectiveness of combined ECPs was probably overestimated in that study, in which the suggestion would be less persuasive [15].

Early treatment with ECPs containing only the progestin levonorgestrel has been shown to impair the ovulatory process and luteal function [16-20]; no effect on the endometrium was found in two studies [17,18], but in another study, levonorgestrel taken before the LH surge altered the luteal phase secretory pattern of glycodelin in serum and the endometrium [21]. Treatment with ECPs containing only levonorgestrel during the luteal phase may fail to inhibit ovulation but, nevertheless, reduce the length of the luteal phase and total luteal phase LH concentrations; this observation suggests a postfertilization contraceptive effect [16]. Levonorgestrel also interferes with sperm migration and function at all levels of the genital tract [22]. Studies in the rat and the Cebus monkey demonstrate that levonorgestrel administered in doses that inhibit ovulation has no postfertilization effect that impairs fertility [13,23,24]. Whether these results can be extrapolated to women is unknown.

Croatto et al. [12,13] have argued that most, if not all, of the contraceptive effect of both combined and levonorgestrel-only ECPs can be explained by inhibited or dysfunctional ovulation. Based on their studies on human and animals, some are tempted to conclude that there is no postfertilization effect [25]. It is unlikely that this question can ever be unequivocally answered, and we therefore cannot conclude that ECPs never prevent pregnancy after fertilization. Even if there were an accurate test for fertilization, a finding that some fertilized eggs do not implant after ECPs ar taken would not mean that ECPs can work after fertilization, since many if not most fertilized eggs naturally do not implant. Nevertheless, even if in some cases ECPs work by inhibiting implantation of a fertilized egg, these probably would be outnumbered by other cases where fertilization of an egg that would not have implanted naturally is prevented because ECPs inhibited ovulation. Therefore, on balance, ECPs probably reduce the incidence of fertilized eggs that do not implant. ECPs do not interrupt an established pregnancy, defined by medical authorities such as the United States Food and Drug Administration/National Institutes of Health [26] and the American College of Obstetricians and Gynecologists [27] as beginning with implantation. Therefore, ECPs are not abortifacient.

Making ECPs widely available is one of the most important steps that can be taken to reduce the unacceptable incidence of unintended pregnancy in the United States [28]. There are 3.0 million unintended pregnancies each year in the United States; half of all pregnancies are

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doi:10.1016/j.contraception.2006.03.028
unintended, and half of all women aged 15−44 years have had an unintended pregnancy [29,30]. Widespread use of ECPs could halve the number of unintended pregnancies and the consequent need for abortion [28]. Yet, only 6% of women at risk of unintentional pregnancy in the United States have ever used ECPs, primarily because awareness of emergency contraception is so low [31]. To avail themselves of this important contraceptive option, therefore, women must be informed that ordinary birth control pills can be taken in higher than usual doses after unprotected intercourse to prevent pregnancy. To make an informed choice, women must know that ECPs — like all regular hormonal contraceptives such as the birth control pill, the progesterin-containing implant and the injectable depot medroxyprogesterone acetate [32], and even breastfeeding [33] — may prevent pregnancy by delaying or inhibiting ovulation, inhibiting fertilization, or inhibiting implantation of a fertilized egg in the endometrium. This information is provided on the Emergency Contraception Web site (www.not-2-late.com) and the Emergency Contraception Hotline (1-888-NOT-2-LATE).

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References

