



Emergency Contraception – Not the Best for Adolescents

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ABSTRACT: A policy of either pre-prescribing “emergency contraceptives” to adolescent patients, or making them available without prescription, carries significant medical risk and is counterproductive to the parent-adolescent and patient-physician relationships. The American College of Pediatricians recommends instead that health professionals encourage good adolescent-parental communication, and teach adolescent patients the benefits of delaying sexual activity until marriage and how to avoid early sexual debut.

Some medical organizations are promoting a plan of pre-prescribing “emergency contraceptives” (EC) to all adolescent patients for use “in case” they have unprotected sexual activity.¹ The American College of Pediatricians (*the College*) opposes this practice for the following reasons:

1. The practical effect of availability of EC without restrictions is harmful to adolescents. In England and Wales, rates of sexually transmitted infections (STIs) among teens increased at a faster rate in those areas with free EC for adolescents compared to areas without these pharmacy schemes. In addition, not only was there no decrease in the incidence of teen pregnancies as a result, but the trend was toward an increased rate of teen pregnancies.² As the American Academy of Pediatrics (AAP) states, “no studies have demonstrated that improved access to emergency contraception reduces the pregnancy rate in a population.”^{3,4} Early US studies, including those reviewed by Meyer et al, did not show an increase in the STI incidence, but these studies involved youth (up to age 24) recruited from health clinics, all but one study had poor follow-up participation, and only 2 actually tested for some STIs. These studies show no increase in self-reported “sexual risk taking behaviors” (number of sexual partners, number of episodes of unprotected intercourse, and acquisition of STIs) with increased access to EC, but study participants were not representative of the general population,⁵ coming from groups with higher than average risk. On the contrary, population based studies, both the British study and a new US study from Washington state⁶, show an increase in STI rates with non-prescription pharmacy access. Compared to other studies involving a few thousand teens and young women, with results mainly self-reported, both the Washington state study, and the British study involving the entire teenage population of England and Wales, both of which relied on documented STI rates, are considerably more scientifically rigorous. Easy access did increase use of EC, and those given the tablet to have on hand used it earlier (an average of about 11 hours after intercourse as compared to those with prescriptions or clinic/pharmacy access who used it at 24-36 hours following intercourse). Studies however continue to show similar non-effectiveness in reducing pregnancy⁷ and abortion rates.^{8,9} As Glasier (2006)¹⁰ concludes and Trussell (2012) says, “no published study has yet demonstrated that increasing access to ECPs reduces pregnancy or abortion rates in a population.”¹¹ If EC is effective when taken (as is shown by studies),¹² and it is being taken at a higher rate when supplied by easy access,¹³ why then do pregnancy rates not fall? The possibilities are that self-reports of lack of increased “risky” sexual activity (such as without non-emergency contraception, with more partners, etc.) are inaccurate, or that overall sexual activity is increased.

Thus, increased availability of EC has been shown to be both ineffective in its stated goal of reducing teen pregnancy rates while at the same time increasing harm to adolescents through increased sexual activity and, in the British study, increasing the incidence of sexually transmitted infections. There is also concern that easy access to EC will decrease medical visits where the diagnosis of asymptomatic STIs can be made, thus increasing the risk of future infertility and cancer. Pregnancy and STIs are not the only harms to adolescents from teen sex. Studies have shown that sexually active teens have increased rates of depression and suicide,^{14,15} lower grades (white males),¹⁶ an increased number of lifetime sexual partners,¹⁷ more sexual partners the younger the onset of sexual activity,¹⁸ and an increased divorce rate^{19,20,21} — all of which have negative ramifications both for them and for the lives of their future children, even for those born after adolescence.

2. “Ready access” to EC may place adolescent girls at increased risk for abuse by sexual predators.

Girls who first have sex before they are 16 have sex with a male at least 3 years older (statutory rape in many states) 34% of the time, and with men at least 5 years older 13% of the time; 17 year olds have male partners at least 3 years older 30% of the time.²² Over half of the babies born to 15-17 year olds are fathered by men in their twenties.²³ The College is unaware of any studies investigating a potential relationship between ready access to EC and sexual predation, and given the serious nature of this concern if confirmed, recommends that such studies be undertaken, searching for both positive and null effects.

3. Giving adolescents unrestricted access to EC, whether through a prescription that they can later fill themselves or through over the counter availability, bypasses parental involvement.

Research has now documented that the frontal cortex – the important decision-making areas of the human brain – are not fully developed until the mid-twenties.^{24,25,26} The decision to engage in sexual activity as an unmarried adolescent in and of itself demonstrates a lack of mature judgment. If parents do not know that their adolescent is engaging in sexual activity, they cannot adequately assist their child with appropriate guidance, nor can they monitor for complications of sexual activity including side effects of contraceptives (ongoing or EC), pregnancy, STIs, and for emotional or behavioral sequelae. There is no federal law preventing the transport of minors across state lines to procure an abortion in order to circumvent parental consent laws. Consequently, in states such as Massachusetts which have such laws, but are bordered by states without such laws, parental consent laws occasionally move abortions out-of-state.²⁷ However, in states such as Texas where it is not easy for minors to be taken across state lines, parental notification laws have resulted not only in a decrease in the abortion rate for teens, but have also resulted in a greater fall in the birth rate. However among older teens (>18 years) for whom parental notification is not required, abortion and birth rates did not fall.²⁸ Thus parental involvement appears to give adolescents more reason to postpone, or at least engage in “less risky”, sexual activity, resulting in fewer pregnancies yet fewer abortion and births.

4. Potential mode of action of EC includes abortion.

What are the modes of action of “emergency contraception?” Do they act solely by preventing fertilization or do they also act to prevent the survival of an embryo – before, during or after implantation? Sperm are rapid swimmers; some reaching the ampulla of the oviduct within 5 minutes of coitus,²⁹ and actions to prevent ovulation cannot be effective when ovulation has occurred in the 12-24 hours preceding intercourse. EC is widely promoted as not being “abortifacient” (with the term “abortifacient” limited to an agent that interferes with an implanted embryo/established pregnancy.) However, Ulipristol (Ella) is a second generation progesterone antagonist, similar in action to its predecessor, mifepristone, (also known as the abortion pill and used for EC in some other countries) It may have a direct effect on implantation with abortifacient potential^{30,31} ; even the AAP recommends a negative pregnancy test prior to its use.³² Both Mifepristone and Ella are labeled as

pregnancy category X. Levonorgestrel (LNG-EC) (Plan B, Next Choice) has been promoted as not interfering with implantation or disturbing an established pregnancy, however recent studies and critical review of earlier studies offer convincing evidence that LNG-EC taken prior to ovulation prevents ovulation during the following five days (survival time of sperm) only 20% of the time,³³ does not interfere with sperm function at in vivo doses, and consistently results in an inadequate corpus luteum and shortened luteal phase. While it has been theorized that luteal insufficiency makes some ova dysfunctional,³⁴ there is no good evidence to support this theory while there is evidence that luteal insufficiency effectively prevents successful implantation of the embryo resulting in its death.³⁵ Those studying LNG-EC continue to debate the issue. High doses of combined oral contraceptives (Yuzpe method) act primarily by suppressing ovulation but do not do so consistently; it has also been shown to result in endometrial abnormalities;³⁶ whether it has post-fertilization effects is also subject to debate.³⁷ Please see Appendix A for a more thorough discussion of the evidence.

The College opposes any methods of EC whose modes of action include causing the death of a human embryo, whether pre- or post- implantation. The College further recommends that individuals and families considering using EC be fully informed of the possible modes of action of EC including post-fertilization whether pre-/peri-/ or post-implantation.

5. The special situation of sexual assault. Adolescents who have been sexually assaulted need medical and psychological evaluation and treatment, a forensic evaluation, and the support of their parents. Eliminating the need for physician involvement in obtaining EC makes it more likely that adolescents in this situation will receive none of this. Going to an emergency room after sexual assault is both frightening and embarrassing. Ready availability of EC from a pharmacy makes it easier for an adolescent to rationalize avoiding this experience. This increases the possibility that the perpetrator will continue this behavior. In addition, if parents do not know that their daughter has been raped, they cannot offer her the emotional and legal support she needs. Sexual assault teams in many emergency departments are trained to counsel the rape victim, to arrange for ongoing counseling, and to help parents in counseling at a time when the assaulted girl especially requires their love and support.

6. Violation of conscience. To demand, as some organizations do, that physicians and pharmacists who have moral objections to providing EC refer their patient to someone who has no such objections is a violation of conscience and itself unethical. Aside from differing legal considerations, the ethical equivalent of this is demanding that those who have moral objections to purchasing stolen property refer the seller to someone whom they know has no such moral objections. In both situations, conscientious objectors argue, the individual is an accessory to actions that he or she finds ethically problematic and thus a violation of conscience.

In summary, the American College of Pediatricians opposes a policy of advance prescribing of “emergency contraceptives” to adolescents. Rather than facilitating adolescent sexual activity (and failing to yield any reduction in pregnancy or abortion rates), pediatricians and other health professionals need to facilitate the best for adolescents, encouraging good adolescent-parent communication, teaching adolescents the benefits of delaying sexual activity until marriage, and teaching them how to avoid non-marital consensual sex as well as situations that might result in coerced sex. Pediatricians, other health professionals, parents and educators should also encourage the use of sexual risk elimination education programs.

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The American College of Pediatricians is a national medical association of licensed physicians and healthcare professionals who specialize in the care of infants, children, and adolescents. The mission of the College is to enable all children to reach their optimal, physical and emotional health and well-being.

Appendix

Although IUDs have been used for EC, they are beyond the scope of this paper except to note that if inserted after fertilization, they can act only by destroying the embryo.

Pre-fertilization effectiveness needs to either prevent effective ovulation or prevent capacitation of the sperm. Actions involving thickening or altering the cervical mucus or interfering with sperm transport occur too late to be effective, and have not been shown to occur with levonorgestrel (LNG) EC.³⁸ Furthermore, LNG-EC has no significant effect on sperm function at doses that are achievable in vivo.³⁹ Nor are doses high enough to interfere with sperm-egg binding.⁴⁰ Ova can be fertilized for 12 (at most 24) hours after ovulation.⁴¹ Sperm become less capable of fertilizing an ovum after 48 hours in the female reproductive tract⁴² with much lower pregnancy rates in the succeeding three days.⁴³ Thus the period during which intercourse can result in pregnancy extends from 5 days before through the day of ovulation, with 94% of pregnancies resulting from intercourse within 3 days of ovulation.⁴⁴ Although LNG-EC is quite effective at delaying ovulation if taken prior to this period (in the early to mid-follicular period), it is a moot point since pregnancy would not have occurred regardless. In the pertinent late follicular period, using transvaginal ultrasound plus gonadotropin levels to accurately diagnose ovulation, Noe et al found that 80 - 86% of women ovulated after LNG-EC.^{45, 46} Thus, inhibition of ovulation accounts for at most, 20% of LNG-EC's effectiveness. In these 2 studies, 0 of 13 and 0 of 16 expected pregnancies were found when LNG-EC was taken prior to ovulation, but 6 of 7 and 8 of 8.7 expected pregnancies occurred when it was taken on the day of ovulation. Thus LNG-EC has little or no effectiveness when taken on the day of ovulation.

If LNG-EC does not prevent ovulation (most of the time), and it does not prevent capacitated sperm from reaching and binding with the ovum, then its 100% effectiveness when taken prior to ovulation must either involve altering the ova such that they are incapable of being fertilized, or it must involve effects after fertilization. Studies have repeatedly shown that preovulatory LNG-EC results in a shortened luteal phase.⁴⁷ If given prior to the LH surge, then the LH peak is also blunted. Measurements of progesterone are problematic and inconsistent, and results have varied from low to normal.⁴⁸ Some authors⁴⁹ have theorized that the ova produced in cycles with luteal phases shortened by pre-ovulatory LNG-EC are dysfunctional and incapable of fertilization, however evidence cited to support this theory⁵⁰ is flawed and strong progestins (LNG is a strong progestin) have been shown to speed up oocyte maturation. This casts serious doubt upon this theory. Others have theorized that the shortened luteal phase results in disruption of the endometrium and that this is the primary mode of action of LNG-EC. Most studies are invalid in determining whether pre-ovulation LNG-EC has anti-implantational endometrial effects due to either using higher doses of LNG than that in LNG-EC and/or due to LNG being given after ovulation.⁵¹ Two studies did include biopsies taken after women took LNG-EC 2 days prior to the LH surge (3 of 6 had normal histology)⁵² and 3-4 days prior to the LH surge (initially reported in 2001 as normal histology but re-examined in 2005 with staining for glycodeclin-A, a hormone necessary for implantation, showing significantly lower levels in those women who had taken LNG-EC three or four days prior to the LH surge. The authors commented that "The low staining score for endometrial glycodeclin-A in Group 1 indicates

that intake of LNG before the LH surge has endometrial effects that are not identified by normal histology.”⁵³

In summary, LNG-EC is ineffective if take on the day of ovulation or later, but totally effective if taken prior to ovulation. Suppression of rupture of follicles mature enough to release ova within 48 hours occurs no more frequently than 20% of the time and possibly only at a placebo rate.⁵⁴ If it can be shown that ova exposed to an inadequate luteal environment are totally incapable of fertilization, then the mode of action of LNG_EC would not be problematic, but unless this is demonstrated, the insufficient glycodeilin-A (and possibly other hormones) in the endometrium caused by pre-ovulatory LNG-EC is consistent with a post-fertilization mode of action than results in embryonic death.

In addition, several studies of both LNG and of ulipristol have shown remarkably high rates of “spontaneous abortion” or “miscarriage” of pregnancies conceived despite use of EC. While Glasier’s study showed most of the recognized pregnancies being intentionally aborted (many of the US sites were Planned Parenthood Clinics), of the remaining not lost to follow-up, 4 of 4 ulipristol and 4 of 7 LNG pregnancies “miscarried”.⁵⁵ European trials of ulipristol had also shown high rates of “spontaneous” abortion: When given at 50-200 mg, there were 2 normal births, 1 “spontaneous” abortion, and 2 unknown; when given at 10 mg, there were 1 birth, 2 “spontaneous” abortions, and 3 unknown; when given at the currently prescribed dose of 30 mg, there were 6 “spontaneous” abortions, 1 birth, and 5 who intended to continue their pregnancies who were lost to follow-up. One group had a levonorgestrel (Plan B, though dose not specified) control group with 4 “spontaneous” abortions, 1 biochemical pregnancy, and 1 birth.⁵⁶

As mentioned in the body of the paper, although ulipristol inhibits ovulation 60%⁵⁷ of the time, when ovulation does occur ulipristol’s anti-progesterone action can both interfere with implantation and cause early abortion.

More recently, a COX-2 inhibitor, meloxicam, has been suggested for use as EC. When taken at 30 mg daily for 5 days, it inhibits ovulation even after the LH surge when given in the late follicular phase, with normal ovulation in 9%, lack of ovulation in 45% and “dysfunctional” ovulation in the other 45%. Dysfunctional ovulation was defined as delayed ovulation more than 48 hours after the LH surge (about 34%) and as a blunted LH surge (about 11%). But unlike LNG-EC, this blunted LH surge did not result in lowered progesterone levels or a shortened luteal period.⁵⁸ While meloxicam has been shown to lower the pregnancy rate by 80% in non-human primates when used for one-time EC (but not on a monthly basis),⁵⁹ more studies need to be done to determine whether it is embryocidal when ovulation does occur

REFERENCES

- ¹ American Academy of Pediatrics. Emergency Contraception COMMITTEE ON ADOLESCENCE. Pediatrics Web site. <http://pediatrics.aappublications.org/content/130/6/1174>. Accessed April 29, 2013.
- ² Girma S, Paton D. The impact of emergency birth control on teen pregnancy and STIs. *J Health Economics*. 2011; 30(2):373-380. <http://www.sciencedirect.com/science/article/pii/S0167629610001505>. Accessed on March 17, 2012.
- ³ Raymond EG, Stewart F, Weaver M, Monteith C, Van der Pol B. Impact of increased access to emergency contraceptive pills: a randomized controlled trial. *Obstet Gynecol*. 2006; 108(5):1098–1106. <http://pediatrics.aappublications.org/content/early/2012/11/21/peds.2012-2962.full.pdf+html>. Accessed on March 18, 2013.
- ⁴ Raymond EG, Trussell J, Polis CB. Population effect of increased access to emergency contraceptive pills: a systematic review. *Obstet Gynecol*. 2007; 109(1):181–188.
- ⁵ Meyer JL, Gold MA, Haggerty CL. Advance provision of emergency contraception among adolescent and young adult women: a systematic review of literature. *J Pediatr Adolesc Gynecol*. 2011; 24(1):2-9.
- ⁶ Durrance CP. The effects of increased access to emergency contraception on sexually transmitted disease and abortion rates. *Economic Inquiry*. 2012; 10: 1465-7295.
- ⁷ Raine TR, Harper CC, Rocca CH, et al. Direct access to emergency contraception through pharmacies and effect on unintended pregnancy and STIs: a randomized controlled trial. *JAMA*. 2005; 293:54-62.
- ⁸ Durrance CP. The effects of increased access to emergency contraception on sexually transmitted disease and abortion rates. *Economic Inquiry*. 2012; 10: 1465-7295.
- ⁹ Glasier A, Fairhurst K, Whyke S, et al. Advanced provision of emergency contraception does not reduce abortion rates. *Contraception*. 2004; 69: 361-366.
- ¹⁰ Glasier A. Emergency contraception: is it worth all the fuss? [editorial]. *BMJ*. 2006; 333:560-561.
- ¹¹ Trussell J, Raymond EG. Emergency contraception: a last chance to prevent unintended pregnancy. Princeton University Web site. <http://ec.princeton.edu/questions/ec-review.pdf>. Published September 2012.
- ¹² Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and meta-analysis. *Lancet*. 2010; 375(9714):555-562.
- ¹³ Meyer JL, Gold MA, Haggerty CL. Advance provision of emergency contraception among adolescent and young adult women: a systematic review of literature. *J Pediatr Adolesc Gynecol*. 2011 Feb; 24(1):2-9.
- ¹⁴ Hallfors DD, Waller MW, Bauer D, Ford CA, Halpern CT. Which comes first in adolescence—sex and drugs or depression? *Amer J of Prev Med*. 2005; 29:163-170.
- ¹⁵ Rector RE, Johnson KA, et al. Sexually active teenagers are more likely to be depressed and to attempt suicide. Washington, DC: The Heritage Foundation; 2003: CDA03-04. This study analyzed data from Carolina Population Center, National Longitudinal Survey of Adolescent Health, Wave II, 1996. 123 W Franklin St, Chapel Hill, NC 27516-3997.
- ¹⁶ Billy JO, et al. Effects of sexual activity on adolescent social and psychological development. *Soc Psych Qtrly*. 1988; 151: 190-212.

- ¹⁷ Abma JC, Chandra A, MosherWD, et al. Fertility, family planning, and women's health: new data from the 1995 National Survey of Family Growth. *Vital Health Stat.* 1997; 23(19). http://www.cdc.gov/nchs/data/series/sr_23/sr23_019.pdf. Accessed March 18, 2013.
- ¹⁸ Martinez G, Copen CE, Abma JC. Teenagers in the United States: sexual activity, contraceptive use, and childbearing, 2006–2010. *Vital Health Stat.* 2011; 23(31).http://www.cdc.gov/nchs/data/series/sr_23/sr23_031.pdf. Accessed July 21, 2012.
- ¹⁹ Heaton TB. Factors contributing to increasing marital stability in the United States. *J of Fam Iss.* 2002; 23: 392-409.
- ²⁰ J.R. Kahn, K.A. London. Premarital sex and the risk of divorce. *J of Mar Fam.* 1991; 53:845-855.
- ²¹ Janus SS, Janus CL. *The Janus Report on Sexual Behavior.* New York: John Wiley & Sons, Inc.; 1993:175-176.
- ²² Abma JC, Chandra A, MosherWD, et al. Fertility, family planning, and women's health: new data from the 1995 national survey of family growth. *Vital Health Stat.* 1997; 23(19).http://www.cdc.gov/nchs/data/series/sr_23/sr23_019.pdf. Accessed March 18, 2013.
- ²³ Saul R. Using—and misusing—data on age differences between minors and their sexual partners. The Guttmacher Report on Public Policy. <http://www.guttmacher.org/pubs/tgr/02/4/gr020410.pdf>. 1999. Accessed on March 18, 2013.
- ²⁴ Giedd JN. Structural magnetic resonance imaging of the adolescent brain. *Ann NY Acad Sci.*2004; 1021:77-81.
- ²⁵ NIH. Teenage brain: A work in progress: A brief overview of research into brain development during adolescence. 2001. Publication No. 01-4929.
- ²⁶ Sowell ER, Thompson PM, Holmes CJ, et al. In vivo evidence for post-adolescent brain maturation in frontal and striatal regions. *Nature Neuroscience.* 1999; 2(10):859-61.
- ²⁷ Cartoof V, Klerman L. Parental consent for abortion: Impact of the Massachusetts law. *Am J for Pub Health.* 1986; 76(4):397–400.
- ²⁸ Joyce T, Kaestner R, Coleman S. Changes in abortions and birth and the Texas parental notification law. *New Eng J of Med.* 2006; 354(10):1031-1038.
- ²⁹ Moore KL. *The Developing Human.* 8th ed. Philadelphia, PA: Saunders; 2008:29.
- ³⁰ Assessment Report for Ellaone. CHMP ASSESSMENT REPORT. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/001027/WC500023673.pdf. 2009. Accessed February 24, 2012.
- ³¹ US Food and Drug Administration. Ella (ulipristal acetate) tablet prescribing information. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022474s000lbl.pdf. November 26, 2012.
- ³² American Academy of Pediatrics. Emergency Contraception COMMITTEE ON ADOLESCENCE. *Pediatrics.* 2012; 130(1174).http://www.sbp.com.br/pdfs/POLICY_STATEMENT_Emergency_Contraception.pdf . Published online November 26, 2012.
- ³³ Noé G et al., é et al., “Contraceptive Efficacy of Emergency Contraception with Levonorgestrel Given Before or After Ovulation,” *Contraception* 84.5 (November 2011):, 488. (cited in ncb...p.21)
- ³⁴ H. B. Croxatto et al., “Pituitary–Ovarian Function following the Standard Levonorgestrel Emergency Contraceptive Dose or a Single 0.75-mg Dose Given on the Days Preceding Ovulation,” *Contraception* 70 (2004):

442–450; W. M. Verpoest et al., “Relationship between Midcycle Luteinizing Hormone Surge Quality and Oocyte Fertilization,” *Fertility and Sterility* 2373.1 (January 2000): 75–77.

³⁵ Peck R and Velez JR. The Postovulatory Mechanism of Action of Plan B: A Review of the Scientific Literature” *The National Catholic Bioethics Quarterly* □ Winter 2013. 1-35. <http://ncbcenter.org/document.doc?id=584> accessed Jan 23, 2014.

³⁶ E. G. Raymond et al., “Effect of the Yuzpe Regimen of Emergency Contraception on Markers of Endometrial Receptivity,” *Human Reproduction* 15.11 (November 2000): 2351–2355.

³⁷ Refs: Kahlenborn C et al. Postfertilization effect of hormonal emergency contraception. *Annals Pharm* 36(3) march 2002: 465-470.; Crockett SA, Harrison D DeCook J. Harsh C. Hormone contraceptives: controversies and clarifications. April 1999 available by emailing prolifeob@aol.com

³⁸ Trussell J, Raymond EG. Emergency contraception: a last chance to prevent unintended pregnancy. Princeton University Web site. <http://ec.princeton.edu/questions/ec-review.pdf>. Published September 2012.

³⁹ The studies showing no LNG-EC effect on sperm at doses found in vivo are do Nascimento JA et al., “In Vivo Assessment of the Human Sperm Acrosome Reaction and the expression of glycodeilin-A in human endometrium after levonorgestrel-emergency contraceptive pill administration. *Human Reproduction* 22.8 (Aug 2007); W. S. Yeung et al., “The Effects of Levonorgestrel on Various Sperm Functions,” *Contraception* 66.6 (December 2002): 453–457; and Hermanny et al., “In Vitro Assessment of Some Sperm Function.” Cited in ncb p. 6.

⁴⁰ Chui PC et al, Cumulus oophorus-associate glycodeilin-C displaces sperm-bound glycodeilin-A and –F and stimulates spermatozoa-zona pellucida binding. *J Bio. Chem* 282.8 (feb 12, 2007:5378-5388, cited in Durand m et al Hormonal evaluation and midcycle detection of intrauterine glycodeilin in women treated with levonorgestrel as in emergency contraception,. *Contraception* 82.6 (dec 2010) 532. Cited in ncb p.10.

⁴¹ Moore KL. *The Developing Human*. 8th ed. Philadelphia, PA: Saunders; 2008:29.

⁴² *Ibid.*, 31.

⁴³ Wilcox, AJ, Weinberg CR, Baird DD. Timing of sexual intercourse in relation to ovulation. *N Eng J Med*. 1995; 333(23): 1517-1521.

⁴⁴ *Ibid.*

⁴⁵ Noé G et al., é et al., “Contraceptive Efficacy of Emergency Contraception with Levonorgestrel Given Before or After Ovulation,” *Contraception* 84.5 (November 2011):, 488.

⁴⁶ Noé Get al., “Contraceptive Efficacy of Emergency Contraception with Levonorgestrel Given Before or After Ovulation,” *Contraception* 81.5 (May 2010): 417; (cited in ncb...p. 20-21)

⁴⁷ Peck,pp 10-35

⁴⁸ Peck p 26

⁴⁹ Durand M et al. Hormonal evaluation and midcycle detection of intrauterine glycodeilin in women treated with levonorgestrel as in emergency contraception. 82.6 (Dec 2010) 531

⁵⁰ Peck pp 17

⁵¹ Peck pp 30-35

⁵² Marions Emergency contraception with mifepristone 69

⁵³ Durand M et al. Late follicular phase administration of levonorgestrel as an emergency contraceptive changes the secretory pattern of glycodeilin in serum and endometrium during the luteal phase of the menstrual cycle. *Contraception* 71.6(June 2005) , 456. Cited in Peck p. 34

⁵⁴ von Hertzen H, Piaggio G, Peregoudov A, et al. Loq soaw midwpristone and two regimens of levonorgestrel for emergency contraception: a WHO multicenter randomized trial. *Lancet* 2002;360:1803-10 cited in Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and meta-analysis. *Lancet*. 2010; 375(9714):555-562.

⁵⁵ Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and meta-analysis. *Lancet*. 2010;375(9714):555-562

⁵⁶ CHMP ASSESSMENT REPORT "Assessment Report for Ellaone".Procedure No. EMEA/H/C/001027; Doc.Ref.: EMEA/261787/2009 EMA. 2009:37 http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Public_assessment_report/human/001027/WC500023673.pdf Retrieved Feb 24, 2012

⁵⁷ Glasier AF, Cameron ST, Fine PM, et al. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomized non-inferiority trial and meta-analysis. *Lancet*. 2010;375(9714):555-562

⁵⁸ JesamC et al. Suppression of follicular rupture with meloxicam, a cyclooxygenase-2 inhibitor: potential for emergency contraception *Human Reproduction*, Vol.25, No.2 pp. 368-373, 2010Advanced Access publication on November 19, 2009 doi:10.1093/humrep/dep392Accessed at <http://ec.princeton.edu/news/Meloxicam.pdf> on Jan 24, 2014

⁵⁹ [McCann NC](#), [Lynch TJ](#), [Kim SO](#), [Duffy DM](#) The COX-2 inhibitor meloxicam prevents pregnancy when administered as an emergency contraceptive to nonhuman primates. *Contraception*. 2013 Dec;88(6):744-8. doi: 10.1016/j.contraception.2013.09.006. Epub 2013 Sep 13 accessed at <http://www.ncbi.nlm.nih.gov/pubmed/24120248> on Jan 24, 2014