

Embracing post-fertilisation methods of family planning: a call to action

Elizabeth G Raymond,¹ Francine Coeytaux,² Kristina Gemzell-Danielsson,³ Kirsten Moore,⁴ James Trussell,⁵ Beverly Winikoff⁶

¹Senior Medial Associate, Gynuity Health Projects, New York, NY, USA

²Project Director, Public Health Institute, Oakland, CA, USA

³Professor, Department of Obstetrics and Gynaecology, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden

⁴Consultant, Reproductive Health Technologies Project, Washington, DC, USA

⁵Professor of Economics and Public Affairs, Office of Population Research, Princeton University, Princeton, NJ, USA and Visiting Professor, The Hull York Medical School, Hull, UK

⁶President, Gynuity Health Projects, New York, NY, USA

Correspondence to

Dr Elizabeth G Raymond, Gynuity Health Projects, 15 East 26th Street, Suite 801, New York, NY 10010, USA; eraymond@gynuity.org

Received 7 June 2013

Revised 5 August 2013

Accepted 15 August 2013

ABSTRACT

Family planning methods that act when administered after fertilisation would have substantial benefits: they could be used longer after sex than current emergency contraceptives, and potentially a woman could use them only on relatively rare occasions when her menstrual period is delayed. Although such methods would displease abortion opponents, they would likely be welcomed by many women. Research to develop post-fertilisation fertility control agents should be pursued.

BACKGROUND

Family planning methods that act after fertilisation have considerable appeal. Compared to currently available contraceptives, which are all designed primarily to keep sperm and egg apart, drugs that would act during or after union of these gametes might offer notable advantages. If used postcoitally, such drugs would be effective later after sex than emergency contraceptives that work only if taken before ovulation,¹ and therefore they could serve more women and provide more benefit at a population level. A woman could potentially use a post-fertilisation method on a planned schedule only once in each menstrual cycle, no matter how many prior coital acts she had had in that cycle. If the drug were effective when administered after implantation of an embryo, timing would be flexible, and she might even be able to limit its use on average to a few times a year when her menstrual period was late. Importantly, post-fertilisation methods would eliminate the conceptual and logistical challenge of needing to obtain and initiate contraception before having sex, which can be daunting for both women and men.

Technically, development of a pharmaceutical regimen that reliably disrupts the pregnancy process after fertilisation,

either before or after implantation or both, might be challenging. Progesterone receptor modulators such as mifepristone, given in adequate doses at certain times in the menstrual cycle, can inhibit endometrial implantation of a blastocyst.²⁻³ Mifepristone, particularly in combination with a prostaglandin, does have the well-established ability to terminate pregnancy when administered after implantation. However, its efficacy very early in gestation is unclear.⁴ Other compounds, in this class of drugs or in others,⁵ may offer more promise. Multidisciplinary research may be needed to define the best option, but given our rapidly increasing understanding of reproductive physiology, ultimate success seems likely.

POLITICAL ASPECTS

The real hurdle is politics. Both the UK and USA governments define pregnancy as beginning at implantation⁶ (US Code of Federal Regulations 45 CFR 46.202), implying that a method that acted after fertilisation but before implantation should not be considered abortifacient. However, not everyone is comfortable with this definition. Interrupting the course of pregnancy *after* implantation is abortion by any definition. In face of the vehement opposition to abortion among some individuals and institutions, development of a method that does not act exclusively before fertilisation would take fortitude.

But support for a post-fertilisation fertility control drug may be substantial. Abortion is legally available in the UK, the USA, Canada, most of Europe, India, China and many other countries with established pharmaceutical industries that are capable of developing and marketing a new drug product. Most of the British and North American public supports access to abortion, particularly in early pregnancy;⁷⁻⁸ indeed, in both England and Wales and in the USA, nearly

To cite: Raymond EG, Coeytaux F, Gemzell-Danielsson K, et al. *J Fam Plann Reprod Health Care* 2013;**39**:244–246.

one-third of women will actually have abortions at some point in their lifetimes.^{9 10} A large body of international data now clearly indicates that abortion is safer the earlier it is performed and that increasing access to legal early medical abortion methods is associated with reduced morbidity and mortality.¹¹ Research from diverse settings has found that many women view medical abortion methods, particularly when used at home, as more natural and more compatible with their religious or ethical views than clinic- or hospital-based surgical procedures.¹² Menstrual regulation – evacuation of uterine contents after missed menses without confirmation of pregnancy – is considered acceptable in some communities where explicit abortion is prohibited.^{13 14} Twenty years ago, a multi-country survey specifically designed to investigate women's feelings about a post-fertilisation contraceptive pill found remarkably high acceptance.¹⁵ We have no evidence that women have changed since then; it is the current political environment that needs refocusing.

FUTURE STRATEGIES

One strategy that we could implement immediately is to refrain from extolling pre-fertilisation mechanisms of action to justify the legitimacy of existing contraceptives. Such conduct implicitly stigmatises post-fertilisation mechanisms as illicit. This behaviour has been particularly pronounced recently in efforts to defend access to hormonal emergency contraception (EC), which has been relentlessly attacked as a supposed form of early abortion. In fact, considerable data now indicate that the most widely used EC regimen containing levonorgestrel acts primarily, and probably exclusively, by disrupting ovulation.^{1 16} Certainly legislators and policymakers need to understand this evidence in order to avoid bad decisions based on misinformation. But women do not use EC to disrupt ovulation or another physiological event; they use it to avoid having babies. Indeed, the essential value of this method lies precisely in the attributes it shares with abortion: it is an efficacious, extremely safe, easily administered, postcoital means for reducing the serious medical and personal risks associated with unintended pregnancy.

Furthermore, we should openly acknowledge that some of the most effective standard contraceptive methods probably act, at least in part, after fertilisation. Both copper-bearing and hormone-releasing intrauterine devices are more likely to prevent intrauterine than ectopic pregnancies, which suggests that these devices sometimes disrupt embryo attachment to the endometrium.¹⁷ The near-perfect efficacy of the copper-bearing device for EC also indicates a post-ovulation effect.¹⁸ Chronic use of most hormonal contraceptives causes profound histological and biochemical changes to the endometrium;¹⁹ these changes have been postulated to diminish receptivity to implantation in any cycles in

which ovulation and subsequent fertilisation occur. Oral EC products containing mifepristone or the related compound ulipristal are more effective than the levonorgestrel regimen;^{20 21} as noted above, mifepristone, at least, can affect pregnancy development after ovulation. Even breastfeeding, which is widely used for contraception in the first 6 months postpartum, has been postulated to impair implantation by altering hormone levels in ovulatory cycles.²² Although the precise role of these post-fertilisation mechanisms is unknown, they should certainly be celebrated, because without them the methods would not provide as much benefit as they do.

THE WAY FORWARD

Most importantly, we should get to work! Nothing is as compelling as success: given the importance of fertility control to women, an effective, safe method that fills gaps in the array of existing contraceptives will undoubtedly attract support regardless of its mechanism. Scientists and advocates are ready; they just need funding. Despite the political climate, surely intrepid donors exist who will step up to the mark. To meet the challenges of our increasingly complicated world, women deserve all possible options for controlling and preserving their reproductive health and lives.

Acknowledgements The authors are grateful to Raffaella Schiavon MD, Ipas Mexico for her helpful insights.

Funding James Trussell's work on this paper was supported by the Eunice Kennedy Shriver National Institute of Child Health and Human Development grant for Infrastructure for Population Research at Princeton University (Grant R24HD047 879).

Competing interests None.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Noe G, Croxatto HB, Salvatierra AM, *et al.* Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. *Contraception* 2011;84:486–492.
- 2 Lalitkumar PG, Lalitkumar S, Meng CX, *et al.* Mifepristone, but not levonorgestrel, inhibits human blastocyst attachment to an in vitro endometrial three-dimensional cell culture model. *Hum Reprod* 2007;22:3031–3037.
- 3 Gemzell-Danielsson K, Swahn ML, Svalander P, *et al.* Early luteal phase treatment with mifepristone (RU 486) for fertility regulation. *Hum Reprod* 1993;8:870–873.
- 4 Swahn ML, Bygdeman M, Chen JK, *et al.* Once-a-month treatment with a combination of mifepristone and the prostaglandin analogue misoprostol. *Hum Reprod* 1999;14:485–488.
- 5 Shi L, Shi SQ, Given RL, *et al.* Synergistic effects of antiprogesterins and iNOS or aromatase inhibitors on establishment and maintenance of pregnancy. *Steroids* 2003;68:1077–1084.
- 6 British Medical Association (BMA). *The Law and Ethics of Abortion*. London, UK: BMA, 2007.
- 7 AngusReid Global. Britons think NHS should only fund abortions in emergency cases. 20 March 2012. <http://www.angusreid.com>

- angusreidglobal.com/polls/44442/britons-think-nhs-should-only-fund-abortions-in-emergency-cases/ [accessed 5 June 2013].
- 8 PollingReport.com. Abortion and birth control. <http://www.pollingreport.com/abortion.htm> [accessed 5 June 2013].
 - 9 Royal College of Obstetricians and Gynaecologists (RCOG). *The Care of Women Requesting Induced Abortion*. Evidence-based Clinical Guideline Number 7. London, UK: RCOG Press, 2011.
 - 10 Jones RK, Kavanaugh ML. Changes in abortion rates between 2000 and 2008 and lifetime incidence of abortion. *Obstet Gynecol* 2011;117:1358–1366.
 - 11 Sedgh G, Singh S, Shah IH, *et al*. Induced abortion: incidence and trends worldwide from 1995 to 2008. *Lancet* 2012;379:625–632.
 - 12 Lie ML, Robson SC, May CR. Experiences of abortion: a narrative review of qualitative studies. *BMC Health Serv Res* 2008;8:150.
 - 13 Benson J, Andersen K, Samandari G. Reductions in abortion-related mortality following policy reform: evidence from Romania, South Africa and Bangladesh. *Reprod Health* 2011;8:39.
 - 14 Alam A, Bracken H, Johnston HB, *et al*. Acceptability and feasibility of mifepristone-misoprostol for menstrual regulation in Bangladesh. *Int Perspect Sex Reprod Health* 2013;39:79–87.
 - 15 Rimmer C, Horga M, Cerar V, *et al*. Do women want a once-a-month pill? *Hum Reprod* 1992;7:608–611.
 - 16 Gemzell-Danielsson K. Mechanism of action of emergency contraception. *Contraception* 2010;82:404–409.
 - 17 Backman T. Benefit-risk assessment of the levonorgestrel intrauterine system in contraception. *Drug Saf* 2004;27:1185–1204.
 - 18 Cleland K, Zhu H, Goldstick N, *et al*. The efficacy of intrauterine devices for emergency contraception: a systematic review of 35 years of experience. *Hum Reprod* 2012;27:1994–2000.
 - 19 Sherman ME, Mazur MT, Kurman RJ. Benign diseases of the endometrium (Chapter 10). In: Kurman RJ (ed.), *Blaustein's Pathology of the Female Genital Tract* (5th edn). New York, NY: Springer, 2010;420–467.
 - 20 Cheng L, Gulmezoglu AM, Piaggio G, *et al*. Interventions for emergency contraception. *Cochrane Database Syst Rev* 2008;8:CD001324.
 - 21 Glasier AF, Cameron ST, Fine PM, *et al*. Ulipristal acetate versus levonorgestrel for emergency contraception: a randomised non-inferiority trial and meta-analysis. *Lancet* 2010;375:555–562.
 - 22 Diaz S, Cardenas H, Brandeis A, *et al*. Relative contributions of anovulation and luteal phase defect to the reduced pregnancy rate of breastfeeding women. *Fertil Steril* 1992;58:498–503.

Embracing post-fertilisation methods of family planning: a call to action

Elizabeth G Raymond, Francine Coeytaux, Kristina Gemzell-Danielsson, Kirsten Moore, James Trussell and Beverly Winikoff

J Fam Plann Reprod Health Care 2013 39: 244-246
doi: 10.1136/jfprhc-2013-100702

Updated information and services can be found at:
<http://srh.bmj.com>

These include:

Supplementary Material

Supplementary material can be found at:
<http://jfprhc.bmj.com/content/suppl/2013/10/16/jfprhc-2013-100702.DC1>

References

This article cites 16 articles, 0 of which you can access for free at:
<http://srh.bmj.com#ref-list-1>

Email alerting service

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>