


Letters to the editor

Reply

In response to the letter1 from Drs Pittrof, Rubenstein and Sauer we would like to make the following points:

1. There is clear evidence that ulipristal acetate (UPA) is more effective than levonorgestrel (LNG). Biomedical studies have shown that when given at mid-cycle (when risk of pregnancy is greatest) UPA is able to delay ovulation whereas LNG is no better than placebo.2,3 Studies have also demonstrated that UPA has endometrial effects (which may or may not contribute to efficacy) whereas LNG does not.4–5 The recent randomised controlled trial and meta-analysis of studies comparing UPA with LNG for emergency contraception (EC) that we published in the Lancet showed that UPA reduces the risk of pregnancy by almost one half compared to LNG.6

2. A Cochrane review actually concluded that more than 5 milligrams of levonorgestrel (>25 mg) were significantly more effective than LNG for preventing pregnancy when used for EC.7

3. As regards the possible effect of UPA if taken in early pregnancy, we observed in our study that there were pregnancies in women treated with UPA that were judged to have occurred well before treatment, that continued after UPA treatment.4 Furthermore, the miscarriage rate in women who received UPA was similar to that in women who had LNG and no different from that observed in the general population of pregnant women. Whilst there have been a small number of normal births in women who received UPA, clearly UPA is a new drug and so it is only appropriate that a European pregnancy registry has been established to detect any further information on effect on ongoing pregnancy.

4. We discussed the possible interaction of a progestrone receptor modulator (PRM) with hormonal contraceptives in our commentary on this Journal1 and concluded that further research is required, because the requirement to abstain or use barrier methods for the remainder of the menstrual cycle is not based on a reasonable scientific basis.5

5. Drs Pittrof, Rubenstein and Sauer express concern that women who cannot access National Health Service abortion services may try to procure several doses of UPA from sources not commented on in our commentary. We commented in this Journal1 and concluded that further research is required, because the requirement to abstain or use barrier methods for the remainder of the menstrual cycle is not based on a reasonable scientific basis.5

6. Whilst acknowledging that the ideal methodology may not have been possible, we do think the analysis of the self-triage could have been improved. The original power calculation was not included, so it is not clear if the sample is adequate to demonstrate a significant result. This calculation was done for a pilot study, a descriptor for this study that is hidden in the discussion. It is stated that the study was prospective, though the description of the data collection is not adequate to support this. We feel that a study conducted over the Christmas period, when workload is not typical, for such a short period of time may not truly reflect patient flow. In fact the observed improvement may not be related to the change in process at all. Also evaluating such a change immediately is unlikely to record the true effect of the change. Finally, in relation to the methods used in the study, the practices of other sites could be introduced to introduce further bias and complicates the statistics.

In conclusion, we welcome a paper that aims to improve patients’ access to the range of care, studying ways to reduce waiting time, but should guard against overenthusiastic claims.

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References


Combined pill and GTD

I have read the new UK Medical Eligibility Criteria for Contraceptive Use (UKMEC) guidelines1 and am surprised and concerned that the recommendations regarding hormonal contraception, particularly the combined oral contraceptive pill (COC) and gestational trophoblastic disease (GTD), have been changed. It was used to be recommended that the COC was not taken until the beta-huma chorionic gonadotropin (β-hCG) levels had fallen to normal following evacuation of a hydatidiform mole.2 The new (2009) guidelines state the COC can be started whilst the β-hCG levels are decreasing, persistently elevated and in the presence of malignant disease. The accompanying notes suggest that starting the COC in this situation may decrease the requirement for chemotherapy (by promoting a more rapid reduction in β-hCG levels). This advice differs to that given by the Royal College of Obstetricians and Gynaecologists (RCOG), the Patient UK website (a common source of information for both general practitioners and patients) and the Charing Cross Hospital gestational trophoblastic neoplasia (GTN) website, which recommend that hormonal methods [and intrauterine devices (IUDs)] are not used until the β-hCG level has returned to normal.

I am puzzled by the new advice given by UKMEC. The references given in the 2009 guidelines all predate, and are very similar, to those in the 2006 guidelines. Why has the advice changed? I am aware of the paper Contraception3 suggesting that both the COC and IUDs can be used in women with GTN. This paper also quotes some publications suggesting that COC use reduces the risk of women developing post molar trophoblastic disease, however it is not quoted by UKMEC 2009.

Professionals and patients become confused when contradictory advice is given. As a specialty we should be more aware of this than most following the problems that have arisen after various ‘pill scares’. I would be interested to hear why UKMEC have changed their guidance but
suggest that this was not in the patients' best interests given that it contradicts the advice of the RCOG and the Charing Cross Hospital GTN website.

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References

Resolution of localised lipoatrophy at the site of Implanon®
I have previously reported a 40-year-old woman who had an Implanon® implanted into her right upper arm. At the site of the Implanon in the middle of the inner aspect of her right upper arm it was noticed at the time of implant removal 3 years later that she had a localised area of lipoatrophy extending approximately 2 cm either side of the implant along a length of approximately 15 cm extending above and below the ends of the implant. In this 4 x 15 cm area there was virtually no subcutaneous fat. The lipoatrophy had been asymptomatic and had no effect on the patient who had to have the area of lipoatrophy demonstrated to her.

Six months after removal the area of lipoatrophy had completely resolved and the patient remains asymptomatic. Both arms looked the same with return of the subcutaneous fat on the affected side. It has been suggested 2 the lipoatrophy might have been caused by topical steroids but a review of the patient records shows they have not been prescribed over the last 8 years and the resolution of the lipoatrophy after removal of the implant does not indicate a steroid cause.

I suggest that localised lipoatrophy is added to the rare side effects described for Implanon and that the possibility of it developing, even if it is reversible, further motivates correct placement of the implant.

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References
1 Lindsay P. Localised lipatrophy at the site of Implanon® insertion [Letter]. J Fam Plann Reprod Health Care 2009; 35: 266.

Reply
Dr Lindsay should be commended for reporting1 and following up on this case; 2 indeed all serious events should be followed up and the information collated used to assess causality or the relationship between the drug and the event.

In the case reported by Dr Lindsay, causality cannot be fully established and, as such, the event of localised lipoatrophy cannot be classified as caused by Implanon®. The fact that, at the 6-month follow-up assessment, after implant removal the event had resolved is not enough to establish causality.

When we applied the Naranjo Scale to this case the maximum score we achieved was two out of a possible ten. 3 The Naranjo Scale is a questionnaire designed by Naranjo et al. for determining the likelihood of whether an adverse drug event is actually due to the drug rather than the result of other factors such as pre-existing condition. 4

The score of two suggests the relationship is possible; however, it is too low to classify this event as definite or probable. Therefore Dr Lindsay’s conclusion regarding this event in our opinion is not valid. Furthermore, the patient’s pre-existing autoimmune condition is still a confounding or alternative explanation as previously mentioned in our letter. 4 Excluding the use of steroids is very important in assessing this case, but even with the available information however, the evaluation of all the information gathered so far is not adequate to allow Implanon to be classified as a definite or probable cause of this event.

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Use of an expired Cu-IUD
I was ready to fit an intrauterine device (IUD) in the CASH clinic when the nurse announced that the expiry date of the Flexi-T 300® was 6 months previous. Having already opened the pack, I continued to fit the IUD to save National Health Service money, considering that many years ago at an update conference I had heard an expert panel state that it is safe to use an IUD up to a year after the expiry date. Common sense dictates that an expired Cu-IUD is not the same as expired sandwiches, for example.

Shortly after this episode occurred I was on annual leave. During my holiday, one of my colleagues contacted the patient and subsequently replaced the IUD, informing the patient that there was a risk of pregnancy. I was surprised at this since I am aware that there are a number of problems associated with IUD fitting and removal per se. One could argue that the IUD could have been left in situ for 4.5 years instead of the normal 5 years.

I would be interested to know whether any other Journal readers have used an expired IUD and, if so, what the outcome was. Was my colleague right to replace the IUD on this occasion?

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Reply
I would like to respond to Dr Yadava’s letter on behalf of Williams Medical Supplies, a manufacturer of copper intrauterine devices (IUDs). Most Cu-IUDs have an expiry date of around 4 years. This is to ensure that the sterility can be guaranteed over this time frame. Once the expiry date has passed, the product is no longer guaranteed to be sterile and therefore we would not recommend fitting an expired IUD in a patient because of potential infection concerns. If an expired product is fitted by mistake, then there are two courses of possible action. One would be to undertake close patient observation over an agreed time span to ensure infection has not occurred. The second option would be to remove the IUD and fit a new one that is within its expiry date.

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Reference

Reply
I would like to respond to Dr Yadava’s letter on behalf of the Clinical Effectiveness Unit of the Faculty of Sexual and Reproductive Healthcare. We are not aware of any evidence or