# Letters to the Editor

## Faculty Statement from the CEU and fpa 'Your Guide to the Combined Pill' leaflet, April 2005, based on the WHO's 2004 Guidance re advice for missed COCs

I have researched and reviewed[1] this subject for 25 years, am on the World Health Organization (WHO)'s Selected Practice Recommendations (SPR) Committee and broadly support their latest recommendations.[2] Like so often, though, the devil lies in the detail.

A brief summary of the evidence (for full bibliography see the April issue of the Journal[3]):

- The prime conception risk is after the pill-free interval (PFI) during which, even if it is not lengthened, a consistent minority of users show significant follicular activity.[1–3]
- Lengthening can result from missed pills before or after the PFI, in Week 3 or Week 1, respectively, but
- Pills missed in Week 3 are fully compensated by advice to 'run on' to the next pack – so emergency contraception (EC) is essentially never required.[4]
- If pills are missed only in Week 2 then fertile ovulation is extremely unlikely, because the seven tablets of Week 1 have restored ovarian quiescence. So, again, EC is almost never justified.
- Significant pill omissions in Week 1 produce an ovulation risk.

What more is known about the PFI?

1. *Individual variation in ovarian activity with and without the PFI being extended is much greater than any effect of variation in dose*.[1–3,5] The systematic review for the 2004 WHO meetings identified 11 studies with planned extensions of the PFI, using ultrasound plus and minus progesterone levels as indirect markers of restored fertility. All studies were small, with much between-woman variability, and none had targeted (by preliminary scanning) the crucial vulnerable minority (i.e. those who develop significant follicular activity after seven pill-free days). Small studies could easily fail to recruit such women. Given that fundamental weakness of all available research:
2. *The occurrence in the only 8-day PFI study,[6] of one ovulation and one near-miss among 9/28 volunteers randomised to a 1-day extension to the PFI* – and this was using a 35 μg brand – deserves particular weight. Moreover, in one of the 9-day PFI studies, Creinin *et al*.[7] reported worryingly elevated levels (>3 ng/ml) of progesterone in 2/35 women using a 35 μg brand, and in 3/34 women using a 20 μg product.
3. *True method-failures of the COC exist, despite a normal 7-day PFI* – are these not proxies for other women who might ovulate after 8- or maybe 9-day PFIs?
4. *The mucus back-up mechanism is also weakest after the PFI,* since there have been seven progestogen-free days.[1]

In the **fpa**'s leaflet, 'Your Guide to the Combined Pill' of April 2005,[8] the text on pages 1–11 and 14 onwards is, as usual, excellent. But the flow diagram on pages 12 and 13, to which many pill-users will turn, is disappointing:

- **First, how much simpler to have one scheme, the more cautious one, for all formulations!**

The unhelpful decision for two schemes was by WHO (and I accept my share of responsibility). It was not well founded, given the data: individual variation in ovarian activity is so much greater than any effect of dose.[1–3,5]

However, WHO explicitly states that their SPR document is for local adaptation ("the guidance … is intended for interpretation at country and programmatic levels"[2]). Given that, *much depends on how many advice-avoidable pregnancies are acceptable…* I strongly sense that in the UK this is the fewest possible. So for here, why not make it that "more than one pill missed" triggers 7 days of condom use – for all pills, not just the 20 μg ones? Greater caution, although primarily to help the ovulation-prone minority,[1,5] would not impair anyone's ability to understand the advice.

- **Second, the trigger for extra contraceptive action is imprecise.**

The **fpa** flow diagram says extra precautions are not required for 30–35 μg pills if "up to two" have been missed, but they are if "three or more pills have been missed". "Anything more than two" would be so much better! Superficially these seem synonymous. But consider the following scenario. *A woman is due to start her new packet of Microgynon 30® on Saturday at 7 am. She goes away for the weekend, forgets her packet and omits pills on Saturday and Sunday morning. On Monday at 9 am she takes her Monday pill, then reads her new* ***fpa*** *leaflet. She has missed two pills completely, but the third tablet is only 2 hours late. Should she initiate condom use and ask about EC?*

Since page 10 of the leaflet now defines a missed pill as 24 hours late, hasn't she only 'properly missed' three pills when she has ***three untaken pills sitting in her packet, on Tuesday morning (a 10-day pill-free interval)?*** She and others like her who wake up to their missed-pills status when there are two tablets in their blisters and the third is a little bit late could be unsure whether this counts as missing three tablets. They are in limbo about whether to do anything extra, for almost 24 hours.

Until the flow diagram on pages 12 and 13 is amended (as I hope it soon is) to say *"anything more than x pills missed"*, we will have to spell out (e.g. for 30–35 μg brands) that ***"three missed pills" means two are more than a day late and another has also JUST been missed***.

- **A new problem: advice re emergency contraception.**

The **fpa** flow diagram[8] is not congruent with the WHO or CEU[2,3]: it surprisingly says "seek advice" about EC after missing three or more pills (with sexual exposure) in any week of pill-taking. But EC is redundant in Weeks 2 or 3 (see above).

- **Fourth, "late restarting" by more than x days (I favour "more than one") should be separately highlighted on pages 12 and 13 as the most 'risky' way to miss pills.**

So often women do not see being late in starting a packet as missing pills at all [having just had their (falsely) reassuring 'period]!

In conclusion, all the points detailed above were communicated to those drafting both these UK publications,[3,8] courteously and well in advance. I am intrigued to learn for each point why it has been so comprehensively disregarded.

We must be realistic of course: experience shows that most pill failures occur without any flow diagram being looked at!

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*References*

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2 World Health Organization (WHO). *Selected Practice Recommendations for Contraceptive Use* (2nd edn). Geneva, Switzerland: WHO, 2004. http://www.who.int/ reproductive-health/publications/rhr_02_7/index.htm.
3 Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. Faculty Statement from the CEU on a New Publication: WHO *Selected Practice Recommendations for Contraceptive Use* Update. Missed pills: new recommendations. *J Fam Plann Reprod Health Care* 2005; **31**: 153–155.
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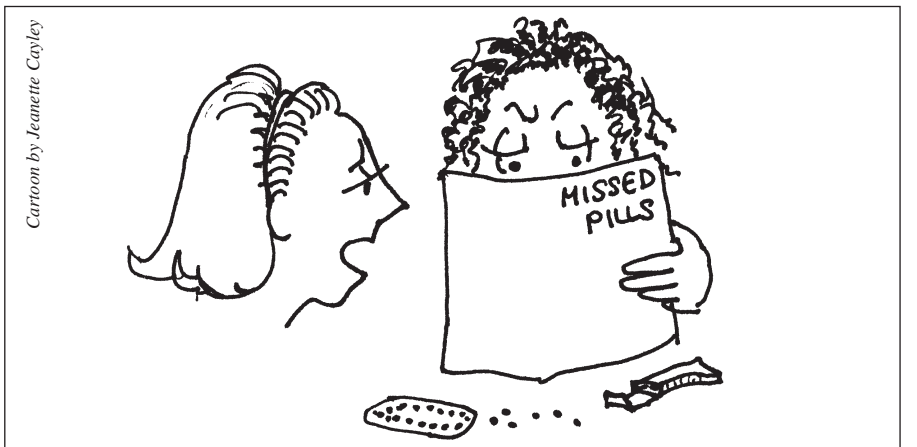
5 Killick SR, Bancroft K, Oelbaum S, Morris J, Elstein M. Extending the duration of the pill-free interval during combined oral contraception. *Adv Contracept* 1990; **6**: 33–40.
6 Hamilton CJ, Hoogland HJ. Longitudinal ultrasonographic study of the ovarian suppressive activity of a low-dose triphasic oral contraceptive during correct and incorrect pill intake. *Am J Obstet Gynecol* 1989; **161**: 1159–1162.
7 Creinin MD, Lippman JS, Eder SE, Godwin AJ, Olson W. The effect of extending the pill-free interval on follicular activity: triphasic norgestimate/35 micro g ethinyl estradiol versus monophasic levonorgestrel/20 micro g ethinyl estradiol. *Contraception* 2002; **66**: 147–152.
8 UK **fpa**. 'Your Guide to the Combined Pill' (patient leaflet). London, UK: Contraceptive Education Service, April 2005.

## Reply

One of the key roles of the Faculty of Family Planning and Reproductive Health Care (FFPRHC) Clinical Effectiveness Unit is to provide objective statements for Faculty members on key publications in the field of family planning and reproductive health. Statements such as 'Missed pill rules: new recommendations'[1] aim to assist Faculty members in applying new evidence to their own clinical practice. The CEU presented this evidence to members in two formats (table and flow chart) to allow individual clinicians and services to use the most appropriate style of presentation in their own clinical practice.[1] In collaboration, the **fpa** (Family Planning Association) have adapted this evidence in their widely used and comprehensive patient information leaflet. It is appropriate that the presentation of information for users may be different from that aimed at health professionals.

The recommendations for missed pills from the World Health Organization *Selected Practice Recommendations for Contraceptive Use* (WHOSPR)[2] were developed by a worldwide Expert Working Group. Systematic methodology and a consensus process were used with evidence identified as fair and indirect (Level I). Following




*Cartoon by Jeanette Cayley*

*"You're a member of MENSA – and* you *don't understand these guidelines?"*