

## How do contraceptives work?

By John Guillebaud [Emeritus Professor of Family Planning]

When do you consider life to start? Is it at fertilisation? Does it start later: before, during or even after implantation? Most Christian doctors have a personal opinion; though this varies, they are united in being unwilling to prescribe a contraceptive drug or device that acts after implantation, but many are unsure about the time between fertilization and that point. It is also an important issue for many couples when deciding on their own method. I have argued elsewhere<sup>1</sup> that theists, whether providers or users of contraceptives, should be comfortable with the view that conception is a process initiated by fertilization but not completed till implantation. Hence contraceptive mechanisms up to the time of implantation are not abortifacient. But I am happy to “agree to differ” with those who do not accept this.

**We need to be armed with the facts. Yet, partly because non-Christian - or non-theist - colleagues and researchers rarely share our concerns, accurate scientific information can be hard to obtain.** Two classic review articles are worth considering.<sup>2,3</sup> The take-home message is that human chorionic gonadotrophin (hCG) is first measurable in the maternal circulation *shortly after the time of implantation*.<sup>4</sup> Hence, research showing no hCG or other known embryo-specific substances in the maternal blood during contraceptive use, only tells us that it does not operate after implantation. At least on some occasions, it might operate after fertilisation, by prevention of implantation or direct destruction of the blastocyst. Clearly, any method linked with the presence of serum hCG would be off-limits to someone requiring a contraceptive that only operated before fertilisation.

### Intrauterine contraceptive devices (IUCDs)

The following table summarises the interesting results of a study.<sup>5</sup>

Population	Sample size	Percentage of sample with hCG increase
Control (sexually active without contraception)	22	32
Inert IUCDs	40	20
Copper IUCDs	41	4
Levonorgestrel-IUS ( <i>Mirena</i> )	19	0

On this evidence, both copper and inert devices sometimes operate after fertilisation. The findings regarding *Levonorgestrel-intrauterine systems (LNG-IUSs)* are compatible with absent fertilisation, either through the levonorgestrel effect on cervico-uterine mucus blocking sperm migration or anovulation in a proportion of cycles. Yet unfavourable cervical mucus is not always observed and we know that ovulation still occurs in most cycles.<sup>6</sup> Is the levonorgestrel effect on sperm migration within the uterine fluid always enough to stop the sperm reaching any egg? Although there are no direct data, the very rare cases of ectopic pregnancy in women using this method provide indirect evidence that fertilisation can occur. If so in other cases (non-ectopic), intrauterine pregnancy in a user of this method might sometimes be being prevented by the blocking of implantation.

Several studies have demonstrated that hCG is not the earliest signal of pregnancy. Although not testable in clinical laboratories, Early Pregnancy Factor (EPF) is part of the materno-

embryonic immunomodulatory interaction. It appears two to six days earlier than hCG and can occur two to seven days after ovulation in women who have conceived.<sup>7</sup> In fact, EPF is detectable in maternal serum in some cases within 24-48 hours of fertilisation.<sup>8</sup> However, the vast majority of research using EPF has been for detecting very early pregnancy in subfertile women, not for aiding our understanding of the exact modes of action of various contraceptives. More research is needed in this area. So, as there is no routinely testable biological marker of the time between fertilisation and implantation, we must remain unsure also that the Levonorgestrel intrauterine systems (IUSs) never operate post-fertilisation.

### **Systemically applied hormonal methods**

With the notable exception of the desogestrel-containing progestogen-only pills (POPs) such as *Cerazette*<sup>®</sup>, or *Cerelle*<sup>®</sup>], POPs probably do sometimes act post-fertilisation.<sup>9</sup> Except *if the woman is breastfeeding* (see below), non-desogestrel POPs permit ovulation in many cycles. Reduced sperm-penetrability of cervico-uterine mucus is unlikely to explain all the failures to conceive in the presence of ovulation. As with intrauterine devices, the occurrence of ectopic pregnancies provides further evidence, though not proof, of this. Importantly, *any* well-taken POP in combination with the so-called Lactational Amenorrhoea Method (LAM)<sup>10</sup> equates to an anovular method, not acting after fertilization. LAM - in which there is full breastfeeding plus amenorrhoea plus baby not yet more than 6 months of age - already has 98% efficacy, so the combination is essentially 100% effective, and by pre-fertilisation mechanisms.

### **What about the combined oral contraceptive (COC)?**

Obviously a *forgetful* COC user, particularly if taking the lowest dose UK products with the currently-marketed pill-free interval (PFI) of 7 days between packs, might risk ovulation and yet not conceive. That regimen is now outdated<sup>10-13</sup>, since hormonal and ultrasound data show that such a long PFI permits the suppressed ovary to regain ovulatory potential. It is the lengthening of the PFI, which after all is a *contraceptive-free* interval, that causes nearly all pill-failure pregnancies and ‘near-misses’ (the mechanism of the latter being our concern here). With or in fact *even without* lengthening of the pill-free time beyond 7 days, if ovulation occurred without conception it still does not follow that the COC necessarily acted post-fertilisation:

1 First, the sperm might have been blocked by the progestogen contained in COC’s, that well-known effect on the mucus, as with POPs. Moreover:

2 Most authorities express the view that if the COC effect is too weak to prevent ovulation, then it will also be too weak to suppress endogenous hormones sufficiently to imperil an embryo. Indeed the risk of pregnancy-loss, always real through a range of causes, should be no higher than background through the COC because:

(i) recently the view has grown that in *ovulatory* cycles, if LH is present in sufficient amounts to trigger ovulation then it will also produce a surge of hormones from the corpus luteum, hence sufficient luteinising effect in the endometrium to allow implantation. Therefore if fertilisation has taken place the endometrium will be sufficiently prepared to enable successful implantation despite the administered artificial hormones, ie eliminating any abortifacient effect. Indeed:

(ii) obstetricians often describe the embryo as a “perfect parasite”. It seems to modify the intrauterine environment in its own favour very quickly, regardless of almost all other factors. These points 1-4 apply also to desogestrel POPs, or any POP during full breastfeeding.

**Crucially, even if any pill regimen truly has the capacity to block implantation, this does not of necessity mean that it ever needs to operate by the use of that mechanism. Incontrovertibly, if ovulation never occurs in the user, none of the above discussion on**

**the (unproven) possibility of post-ovulatory contraceptive effects of pills even applies.** Therefore, if a couple hold the view that blocking implantation is a form of abortion - despite my arguments elsewhere against that being a necessary view for theists,<sup>1</sup> anyway - and are worried that their pill-taking might ever entail that mechanism, they should take steps to ensure no escape ovulations ever occur. This means not taking the COC by the ‘outdated’ 21/7 regimen but instead use what I term the 21<sup>st</sup> century way, taking it continuously 365/0. This avoids the “unsuppressing” of the COC-suppressed ovaries by the licensed and established but wrong routine, of omitting pills to produce the regular 7-day contraceptive-free interval. There is clear evidence that this time without taking the contraceptive is too long for some women.<sup>10,11</sup> Continuous pill-taking so strengthens the anovulation mechanism as to allow at least 4 pills to be omitted at any time, whether inadvertently or at the woman’s choice, with zero need for extra precautions! The *continuous-flexible* or *tailored* regimen is often ideal, in which the woman has discretion, on her own “say-so”, to try the effect of a 4-day break if she has unacceptable bleeding.<sup>10-13</sup> See the latest UK patient information leaflet from Sexwise/fpa.<sup>13</sup>

### **Other methods**

Subdermal implants (eg Nexplanon<sup>®</sup>), and injectables (depot medroxyprogesterone acetate, DMPA) given as *Depo-Provera*<sup>®</sup> im or *Sayana Press*<sup>®</sup> sc are brilliantly effective anovulants. They must be injected accurately up to every 13 weeks. For someone with the concern here regarding modes of action, there is the good option of having their injection every ten weeks. This gives added confidence that ovulation is always blocked, with the to-them unacceptable back-up anti-implantation mechanism never being required.

### **Summary**

Assuming perfect compliance to regimens, with the above adjustments, I feel one could be confident that, even after say 20 years’ perfect use of the COC, the desogestrel POP, a subdermal implant or DMPA, there would not have been a single occasion when a post-fertilisation mechanism would have been utilised. *Moreover, having done everything possible in the light of the best available scientific data, might not a believer legitimately ask her omnipotent Lord to ensure that this would be so for her?*

After prayerful consideration, my own personal view remains unequivocally, anyway, that implantation is the biological event that separates family planning from abortion<sup>1</sup>. That said, I conclude by listing a range of methods that are entirely secure for those who hold the absolutist ethical position that blocking implantation is a form of abortion:

- **Male and female sterilisation.**
- **The combined oral contraceptive pill (COC) - and the combined hormonal vaginal ring and cutaneous patch -** provided always that one of the preferred continuous regimens with no 7-day contraceptive-free intervals is used.<sup>10-13</sup>
- **The desogestrel POP,** since it is a POP that is as effective as the 21/7 COC at blocking ovulation, plus it has the strong back-up of blocking fertilization by the mucus effect. Moreover, it is taken 365 days a year and so does not have the 21/7 COC’s weakness of regular 7-day breaks from its actions. Additionally points 1-2(ii) above re the improbability of post-ovulation contraceptive effects apply here as to COCs.
- **Any POP during total breastfeeding,** including of course a desogestrel one, since this is supplementing the lactational amenorrhoea method (LAM)<sup>13</sup>. With the old-type POP which is less strongly anovulant, there could be a slight risk of breakthrough ovulation (and hence the back-up anti-implantation mechanism being used) during weaning. Therefore as soon as the baby was not obtaining 100 percent of its nutrition from breast-

feeding, the woman should change to another method in this list or use additional barrier contraception.

- **Nexplanon**<sup>®</sup>, a subdermal implant whose anovulant and sperm-blocking mucus-barrier actions are exceptionally strong. It should be replaced no later than every three years.
- **Depo-Provera**<sup>®</sup> and **Sayana Press**<sup>®</sup> are two versions of DMPA, another anovulant method. If the up to 13-week injection interval is never exceeded, it is not thought that they would ever use a post-fertilisation mechanism. Those wanting even greater confidence on that point could be offered injections every 10 weeks.
- **Male and female barrier methods** and all **spermicides**, though the latter used alone have a high failure rate.
- **All fertility awareness methods.**
- **Coitus interruptus.**

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See pp 2-4 for COC Summary and pp 5-11 re continuous use regimens.
  - 13 Sexwise-fpa [www.sexwise.fpa.org.uk/sites/default/files/resource/2019-03/the-combined-pill-your-guide.pdf](http://www.sexwise.fpa.org.uk/sites/default/files/resource/2019-03/the-combined-pill-your-guide.pdf)
- Note: Refs 1 and 11 are available at [www.ecotimecapsule.com](http://www.ecotimecapsule.com)