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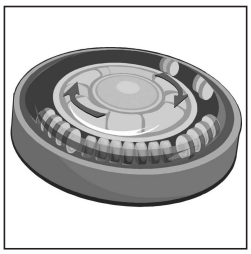

The Oral Contraceptive as Abortifacient: An Analysis of the Evidence

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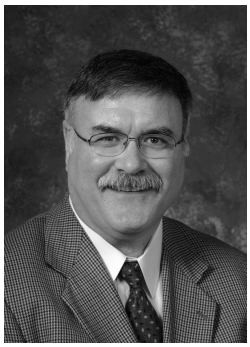
Pro-life Christian ethicists and medical practitioners have been united in their opposition to abortion, but have sometimes been divided in their ethical approach to hormonal contraception. Even though many Christians believe that birth control may be a moral option, some claim that the "Pill" acts, at least some of the time, as an abortifacient. If true, Christians who hold that human personhood begins at conception would be morally opposed to the use of combined oral contraceptives.

This article examines the scientific evidence for an abortifacient effect of such contraceptive agents, and concludes that such an effect is yet unproven. Some of the ethical arguments are also examined, and the author suggests that further research on early pregnancy factor (EPF) may help to resolve this controversial issue.



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As an ethical litmus test, the abortion debate separates large segments of secular and religious communities. Social conservatives have opposed all forms of abortion on absolutist grounds, allowing only rare exceptions where the life of the mother is truly at stake. Furthermore, the pro-life cause has been championed by conservative elements *within* denominations, so that conservative Roman Catholics and conservative Protestants have found common cause. As James Nuechterlein has put it: "Conservative Catholics and Protestants stand together in opposition to their liberal coreligionists."[1]

A major exception to this unified voice is the issue of contraception. The Roman Catholic Church has traditionally opposed artificial birth control, mostly on the ground of natural law, claiming that sexual union must always allow for the possibility of procreation. Protestants, less influenced by natural law (at least in this regard), have held a more permissive view. They have felt that the unitive and procreative aspects of intimacy within marriage may be separated, and thus are open to interventions that prevent the creation of new life.[2]

In all of this, one principle is clear: there are conservative elements in both religious traditions that agree on the sanctity of human life from conception, and therefore oppose abortion. Recently, some pro-life writers have condemned hormone contraceptives as actually causing an early abortion. If this abortifacient action were true, then the Catholic and Protestant sides might join together to condemn such contraceptive methods. Other writers, however, have dismissed the abortifacient evidence as inconclusive, leading to an unresolved debate within the pro-life family about the morality of oral contraceptives. This paper will summarize the available evidence on this question, and will offer a suggestion to help settle the issue.

[There is] an unresolved debate within the pro-life family about the morality of oral contraceptives.

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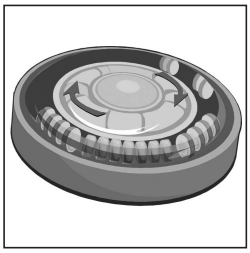


Article

The Oral Contraceptive as Abortifacient: An Analysis of the Evidence

[What] creates a moral issue for some pro-life Christians [is:] If the presence of progestins in COCs [combined oral contraceptives] prevents the endometrium from supporting implantation, then the "Pill" acts as an abortifacient, at least some of the time …

Some Background Physiology

To better understand the issues that surround oral contraceptives, some of the background of the normal uterine cycle and of early pregnancy will be helpful. The uterus lies within the lower abdomen, where it is held in place by suspensory ligaments. The normal uterus is shaped like a small bottle, with the muscular cervix acting as the "bottle neck" where menstrual flow emerges into the vagina, and where sperm night possibly enter the uterus during sexual intimacy. On each upper side of the uterus are the uterine ("Fallopian") tubes. The uterine tubes terminate in the ampulla, a wider area with many finger-like projections that envelop the ovary on each side. The ampulla acts to collect the ovum after ovulation occurs.

The two ovaries produce reproductive cells (ova) that a woman releases monthly in the process of ovulation (note: the technical term for a pre-ovulation reproductive cell is *secondary oocyte*, but in the interest of brevity this article will use the more general term ovum). At puberty, the ovaries together contain about 40,000 potential ova, of which about four hundred will mature and be released during a woman's lifetime.[3]

The key endocrine hormones in the female reproductive cycle are GnRH, FSH, LH, estrogen, progesterone, relaxin, and inhibin. Gonadotropin-releasing hormone (GnRH) is made in an area at the base of the brain called the hypothalamus. This hormone controls release of follicle stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary gland. Various forms of estrogen (primarily ß-estradiol) and progesterone are both made by the ovary at various stages of a woman's monthly cycle. Estrogen controls female sexual characteristics and stimulates development of the endometrium, the inner lining of the uterus. Progesterone works with estrogen to stimulate the endometrium and prepares the breasts to secrete milk. Both estrogen and progesterone inhibit (through negative feedback) the release of GnRH and LH, and estrogen also inhibits FSH. The ovary also produces the hormones relaxin and inhibin. Because the role of these last two hormones does not directly impact this discussion, they will not be considered further here.[4]

In the normal twenty-eight days of the female uterine cycle, GnRH stimulates the release of FSH and LH. The release of these hormones, in turn, causes development of ovarian follicles. The follicles are the cell-lined spaces where the ova reside. One dominant ovum tends to suppress the others, so that it becomes larger and larger. As it does so, it secretes more and more estrogen. Estrogen causes development and thickening of the endometrium (this is called the "proliferative phase" of the uterine cycle). The estrogen exerts positive feedback on the hypothalamus, causing an increase in secretion of GnRH. This leads to a sudden increase in LH (called the "LH surge"), which initiates rupture of the follicle and ovulation. The follicular "shell" left over after ovulation, called the corpus luteum, is itself a rich source of hormones. LH causes the corpus luteum to secrete additional estrogen and progesterone. In the last fourteen days of the cycle (under the influence of these hormones), the endometrium becomes thicker, has more blood vessels, and develops secretory glands (this is the "secretory phase" of the uterine cycle).

The secretory phase of the female cycle is the only time that the endometrium is prepared for implantation of a fertilized ovum. If this does not occur, the corpus luteum degenerates, depriving the endometrium of progesterone, which leads to its collapse. The inner layer of the endometrium sloughs, creating the menstrual flow, and a new cycle begins.

Fertilization of an ovum by a sperm cell normally occurs in the uterine tube near the ampulla. The new embryo then travels down the uterine tube, with implantation into the endometrium occurring about six days later, and a new pregnancy is then well established. What happens to the corpus luteum, upon which survival of the inner endometrium depends? If implantation is successful, the developing embryo produces a hormone called human chorionic gonadotropin (hCG). This hormone acts like LH to stimulate the corpus luteum to continue its secretion of estrogen and progesterone. This so-called "rescue" of the corpus luteum allows it to continue to produce progesterone, and the endometrium is maintained, which will eventually develop into the placenta of the developing fetus.[5]

Mechanisms of Hormonal Contraception

The most common oral contraceptive pill used today is a combination of an estrogen, usually ethinyl estradiol but occasionally an analogue called mestranol, plus one of eight possible synthetic progestins (progesterone-like compounds): norethindrone, norethindrone acetate, ethynodiol diacetate, norgestrel, levonorgestrel, desogestrel, gestodene, and norgestimate.[6] This type of pill is often called a combined oral contraceptive (COC). First introduced in the early 1960s, COCs formerly contained much higher doses of both components, but this was associated with higher risks for heart disease, stroke, and venous blood clots. This has led to a reduction in the dose of estrogens and progestins.[7] These newer formulations have not seemingly reduced contraceptive efficacy, but have increased the concern over possible abortifacient effects.[8]

COCs act primarily by inhibiting the release of GnRH from the hypothalamus. This in turn leads to a reduction in levels of LH and FSH. As a result, follicles do not develop in the ovary, and the mid-cycle LH surge is absent, which removes the stimulus for follicle rupture and ovulation. COCs also have a second mechanism: they cause thickening of the cervical mucous, adding an additional barrier to sperm penetration should ovulation occur.[9]

Concern about a third mechanism of action comes from the standard "package insert" that accompanies COCs. Consider, for example, this Web site description from Ortho-McNeil about their popular contraceptive product, Ortho Tri-Cyclin Lo:

> By delivering an adequate amount of progestin and estrogen throughout your body, ORTHO TRI-CYCLEN LO stops ovulation from occurring. ORTHO TRI-CYCLEN LO also thickens the cervical mucus, making it difficult for sperm to enter the uterus, and changes the lining of the uterus to reduce the likelihood of implantation.[10]

It is the last phrase in the description that creates a moral issue for some pro-life Christians. If the presence of progestins in COCs prevents the endometrium from supporting implantation, then the "Pill" acts as an abortifacient, at least some of the time (according to the conception view of human personhood).

To be fair to Ortho-McNeil and other companies involved with the manufacture of these drugs, they are trying to reassure their potential customers that their products work well. The key questions for contraceptive users are: "Is it safe?" and "Will it reliably prevent pregnancy?" The lower doses of estrogen and progestins in COCs make the medication relatively safe for women who do not smoke and who do not have a history of heart disease, abnormal clotting, or stroke. As to the second question, the bottom line is the pregnancy rate. To this point, there is a failure rate for contraceptive use: up to 5% for typical users, but dropping to 0.1% for highly compliant use.[11] The manufacturers of oral contraceptives are not necessarily concerned with "fine points" of ethics, so they will understandably make somewhat biased claims to insure a strong market for their products.

The preponderance of evidence shows that COCs work by suppressing ovulation most of the time.[12] As stated earlier, in the rare event that "breakthrough" ovulation occurs, (also called "escape" ovulation or "on-pill" ovulation), COCs also cause thickening of the cervical mucous, making it more difficult for sperm to enter the cervix. Both of the above mechanisms are true *contraceptive* effects, i.e., that prevent fertilization. As to the third possible effect of COCs, this would be an *interceptive* effect, where the action of progestins on the endometrium make it unreceptive for implantation. Despite this theoretical possibility, Keder has said: "There is no direct evidence that this contributes to the effectiveness of oral contraceptives."[13]

The Oral Contraceptive as Abortifacient: The Scientific Debate

As proposed by physician Walter Larimore and popular Christian writer Randy Alcorn, the case against COCs has been dubbed the "hostile endometrium" theory. Larimore and Stanford have presented their scientific argument in a major medical journal[14] and Alcorn eloquently expresses these ideas for a lay readership in booklet form.[15] Their basic premises are analyzed here.

1. *Women who take oral contraceptives have a thinner and less receptive endometrium.*

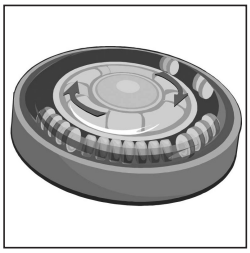
Women who take COCs have a thinner endometrial lining, as well as other biochemical changes, compared with non-Pill users. Larimore and Stanford cite a number of pharmacological and gynecological studies to make this point,[16] and both sides of the debate seem willing to concede this.[17]

2. *A thinner endometrium will decrease the likelihood of successful implantation.*

This is suggested by studies involving embryo transfer during *in-vitro* fertilization (IVF). Noyes and colleagues, for example, retrospectively studied endometrial thickness, as determined by ultrasonography, and concluded that a minimum thickness of 9 mm was needed for success in achieving pregnancy.[18] On the other hand, this idea was tested prospectively in 135 patients in a university setting, and endometrial thickness was *not* predictive of IVF outcomes.[19] Though the clinical evidence is inconclusive, endometrial thickness as a determinant of successful implantation is at least theoretically reasonable, since this assumption affects the practice of embryo transfer in many assisted reproduction clinics.[20]

3. *If breakthrough ovulation occurs, the effects of contraceptives on the endometrium make the embryo less likely to implant.*

This is the highly debated issue. Those who write in support of COCs admit that the endometrium is thinner during non-ovulatory cycles (as is typical with Pill users). For the



To summarize the scientific case indicting COCs as having an abortifacient action [unlike progestin-only contraceptives (POPs), progestin implants (e.g., Norplant), and emergency contraception (EC)], the evidence appears inconclusive at the present time.

purposes of argument, they may even grant that a thinner endometrium may be less hospitable for implantation (though this is not completely clear). However, if ovulation takes place, a completely different hormonal milieu exists. As summarized earlier, ovulation leaves behind the corpus luteum, a rich source of estrogen and progesterone. After the six days required for the embryo to travel down the uterine tube into the uterus, these hormones have transformed the endometrium, which has now become receptive for implantation.[21]

There is no doubt that this is true at least *some* of the time. This should be obvious from the known "failure" rate of the Pill cited earlier (0.1–5%). In other words, some Pill-users get pregnant. The key questions become: How often does the user of COCs ovulate and conceive, only to have such a conception fail to implant? How does this rate compare with non-Pill users?

The baseline failure rate for implantation is an important statistic in this regard. A full 70% of fertilized ova fail to proceed to a full-term pregnancy, with three-fourths of these due to failure of implantation.[22] Against this failure rate, the rarity of breakthrough ovulation makes statistical comparison of Pill-users against non-Pill users difficult. Contraceptive opponents must make a difficult statistical case: (1) In instances of breakthrough ovulation (a rare event), a significant number of sperm must penetrate the thickened cervical mucous (presumably a rare event), thus evading both truly contraceptive effects of COCs; and (2) If fertilization does occur, an embryo must fail to implant in an endometrium at least somewhat prepared for it, or if it implants, fail to continue to term, and this failure rate must be greater than the 70% that occurs naturally.

A distinction is necessary here. This article has focused on COCs, but other types of contraceptives are available. In particular, progestin-only contraceptives (POPs) are attractive because they limit Pill-related side effects. However, their overall efficacy is less, and they statistically increase the likelihood of ectopic (tubal) pregnancy, a dangerous condition that can led to rupture and bleeding, with serious consequences for the mother. This risk is usually expressed as the ectopic/intrauterine pregnancy ratio (E/I ratio).[23] Progestin implants (e.g., Norplant) offer the advantage that compliance is not an issue. They are also more effective than POPs in preventing ovulation.[24] However, for unclear reasons, the ectopic pregnancy rate is also statistically higher when (rarely) breakthrough ovulation does occur. These considerations, according to Crockett and colleagues, present unacceptable added medical risks to women, making both POPs and Norplant undesirable choices.[25] In addition, the higher ectopic rate means that more breakthrough ovulation pregnancies fail to implant, which bolsters the ethical case that these agents are abortifacients.

It is important to be clear on this point. Opponents of *all* hormonal contraceptives have argued that they statistically increase the ectopic pregnancy rate (i.e., they increase the E/I ratio in pregnancies resulting from breakthrough ovulation). However, these writers combined POPs and COCs together in the data pool. If POPs were excluded and the E/I ratio calculated for COCs alone, there would appear to be no specific evidence indicting COCs for the increase in ectopic pregnancies.[26]

There is also an important distinction between COCs and emergency contraception (EC). With EC (sometimes referred to as the "morning-after pill"), a four-times normal dose of a combined oral contraceptive pill is taken over a 12-hour period. Since this regimen is designed to prevent pregnancy after unprotected sexual intercourse, it may act in two ways: (1) by preventing ovulation, or (2) by interfering with implantation if ovulation (and therefore fertilization) had already occurred.[27] Many (including the present author) feel that the supra-physiological dose of hormones used for EC is therefore an abortifacient at least part of the time, though others would dispute this.[28]

Based on this use (and many would say abuse) of oral contraceptives, Wilks has argued that this supports the moral case against them.[29] However, at the very least, the standard use of COCs is not in view here. If it is granted (as it seems reasonable to do) that EC often acts as an abortifacient, it does not follow that the same mechanism applies to the lower dose used in standard contraceptive formulations.

To summarize the scientific case indicting COCs as having an abortifacient action, the evidence appears inconclusive at the present time. Several leading professional organizations have looked at the evidence, and have been unable to reach a consensus. For example, the American Association of Pro-Life Obstetricians and Gynecologists has carefully studied this issue, and has reached the conclusion that "our knowledge of the truth is incomplete."[30] The Christian Medical and Dental Association holds a similar view: "This issue cannot be resolved with our current understanding."[31] While not drafting a position statement on the issue, the Center for Bioethics and Human Dignity has presented both sides of the debate.[32] All of these organizations support the right of conscience for health care providers to not prescribe or dispense these drugs, if such professionals are concerned about a possible abortifacient effect.

The Oral Contraceptive as Abortifacient: Some Ethical Comments

Though this article has focused on the scientific evidence, a few remarks from an ethical perspective are in order. This author holds to the conception view of human personhood, and holds that if a true abortifacient effect were demonstrated for COCs, then the Pill would be an immoral intervention into the reproductive process. However, the evidence is inconclusive. How should Christian health professionals respond?

Larimore and Stanford have cogently argued that the possibility of a post-fertilization effect should be part of informed consent for prescribing oral contraceptives.[33] This seems reasonable where the evidence is clear, as in the case of POPs, or where there are clearly defined other risks, as in the statistically higher possibility of ectopic pregnancy with Norplant. However, since the evidence for COCs is not conclusive, it is not clear what health-care providers should tell their patients. Sherfey has responded in this way:

> Obtaining informed consent of a general medical-legal nature to cover the possible adverse effects and complications of various methods of birth control is already a common practice. Yet to also educate interested patients specifically that there may be postfertilization effects would be a new practice for many physicians and health care providers.[34]

As an added ethical argument against contraceptive use, Larimore has argued that the classic principle of double effect may provide additional guidance.[35] In this principle, a contemplated action (e.g., giving morphine to a terminally ill patient) may have both a good effect (the relief of pain) and a bad effect (hastening death). For an action to be moral, the good effect must be intended, even though the bad effect may be foreseeable.[36]

Larimore lays out five conditions for proper application of this principle, including the condition that there exists no other way to produce the good effect. He rightly argues that there is indeed an alternative to oral contraception, that of natural family planning, a sophisticated modern option that has little resemblance to the "rhythm method" of twenty years ago. On this basis, he argues that the rules for applying the principle of double effect are not fulfilled, and therefore this principle cannot be an ethical justification for oral contraceptive use.[37]

Yet surely Larimore commits, at least in part, the *petitio principii* fallacy, where he implicitly assumes as true that which he would prove. In the case of morphine in terminal patients or other applications of the principle of double effect, the contemplated intervention has known "bad" consequences (such as the inhibition of respiratory drive with morphine). In the case of COCs, the "bad effect" is unknown or unclear. The principle of double effect is simply not applicable here.

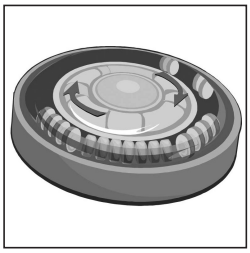
The Oral Contraceptive as Abortifacient: The Future of the Debate

Many writers on this issue would abandon COCs as a moral option if COCs truly could be shown to be abortifacient. The problem has been to precisely define *when* breakthrough ovulation occurs during COC use, and *when* fertilization occurs. Armed with this information, the rate of implantation can then be statistically compared with the natural rate, and conclusions can be drawn.

Standard pregnancy tests depend upon the presence of hCG in maternal blood, which does not rise to measurable quantities until well after implantation. Until recently, there has not been a maternal test that could reliably diagnose fertilization prior to implantation. Australian researcher Alice Cavanagh has worked extensively with a maternal protein called early pregnancy factor (EPF), first described in 1974 by Morton and colleagues.[38] Cavanagh describes EPF in this way:

> Prevailing orthodoxy held that maternal recognition of pregnancy did not occur until implantation; prior to this, the embryo was thought to be merely a silent passenger in the maternal reproductive tract. It is now known that there is extensive cross-talk between mother and embryo throughout the pre-implantation period. However, EPF is still one of the earliest manifestations of this changed physiological status of the mother, opening a unique diagnostic window on this stage of pregnancy.[39]

In passing, it is worth noting that the above is an eloquent rebuff to those who would claim that "pregnancy" begins with implantation, a euphemistic justification for early abortion, human embryonic stem cell research, and other morally problematic practices.[40] Cavanagh goes on to say



Ethical decisions should be based on personal convictions combined with the best possible scientific evidence … Scripture would call on all participants in this discussion to mutual respect and peace, and to apply the principles of Romans 14 as a guide to disputable matters.

that "EPF could be valuable in discriminating between failure to fertilize and failure to implant."[41] In other words, this is exactly the test that will help to answer the question posed in the oral contraceptive discussion.

What is the function of EPF? The embryo, as an immunologically distinct foreign entity, nonetheless is not rejected by the mother's immune system. One of the intriguing roles of EPF may be to suppress the mother's immune system, in order to allow pregnancy to proceed.[42]

One of the problems with EPF is that it exists in such minute quantities. In the past, it has only been detectable by a complex and indirect bioassay called the rosette inhibition test. In recent years, this molecule has been purified and characterized further, and appears to be similar in form to the mitochondrial matrix protein chaperonin 10.[43] As a therapeutic agent, this chemical messenger may be useful for its immunosuppressive effects, and has already been used in an animal model for this purpose.[44] Nonetheless, further research on EPF as a diagnostic tool may ultimately help to unravel the abortifacient question as it relates to hormonal contraceptives.

Conclusion

This article should not be construed as an unqualified endorsement of hormonal methods of birth control. Indeed, there are many methods (e.g., POPs, Norplant) that raise serious medical and ethical questions for pro-life health care providers. Moreover there are reliable alternatives to hormonal contraceptives, such as barrier methods, natural family planning, and abstinence. However, ethical decisions should be based on personal convictions combined with the best possible scientific evidence. To fail to use a potentially useful intervention because of minimal evidence or theoretical concerns is not how health practitioners should live their ethical lives.

Scripture would call on all participants in this discussion to mutual respect and peace, and to apply the principles of Romans 14 as a guide to disputable matters. Though this author would not wish to minimize the importance of this issue, it remains a debate "within the family." There are other pressing moral concerns before us, concerns about which we will have much broader agreement. As Christians in the health professions, we must remain united in the defense of the sanctity of human life, as under the authority of our Sovereign Lord.

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