

Postfertilization Effects of Oral Contraceptives and Their Relationship to Informed Consent by
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Summary for non-medical persons by Sister Marie Paul Lockerd RSM, DO

(For all references please read the complete article)

The primary mechanism of oral contraceptives is to inhibit ovulation. However, it is possible for a woman to ovulate on oral contraceptives. This is called breakthrough ovulation. Breakthrough ovulation rates vary by the different preparations and the dose of the oral contraceptives. Breakthrough ovulation is more likely with lower doses of estrogen and with women who miss one or more days of taking the pill. The research for the rate of ovulation varies greatly, but the main point is that ovulation and conception does happen on oral contraceptives.

This article presents the research for the mechanisms of birth control pills for preventing a live birth after ovulation that results in fertilization (conception). It is documented in the *physician' Desk Reference, in Drug Facts and Comparisons*, and in most standard gynecological, family practice, nursing, and public health textbooks that birth control pills prevent pregnancy not only by preventing conception but also by preventing implantation after conception. In this regard the term "birth control pills" is a more precise term than "contraceptive pills" because at least some of the time the live birth is prevented by mechanisms other than preventing ovulation.

The authors use the Academy of Obstetrics and Gynecology definitions for the following: *Fertilization* is when the sperm enters the ovum. *Preembryo* includes the human developmental stages that occur after fertilization but prior to the appearance of the primitive streak which is about 14 days after fertilization. *Embryo* is the term used after the primitive streak until the end of the eighth week after fertilization. *Implantation* is the process whereby the preembryo attaches to the endometrial lining of the uterus. This process begins 5-7 days after fertilization and may last for several days. *Postfertilization effects* include any mechanism of action that operates after fertilization that prevents a viable pregnancy.

The article discusses postfertilization effects of oral contraceptives which could involve any one or more mechanisms of action:

1. There could be a slower transport of the preembryo through the fallopian tube which could result either in an ectopic pregnancy in which the preembryo implants in the

fallopian tube, or the preembryo does not survive because of the need to implant in the uterus within a certain number of days.

2. There can be an alteration in the endometrium such that the preembryo that reached the uterus was unable to successfully implant in the endometrial lining because of the changes in the endometrium caused by the oral contraceptive hormones.
3. It is possible that a preembryo or an embryo that was successful in implanting in the endometrial lining of the uterus would be unable to maintain itself because the alteration in the endometrial lining from the oral contraceptives was unfavorable for maintaining the pregnancy.

The authors of this article give detailed research regarding the changes that occur in the endometrial lining. The research in the area of in-vitro fertilization demonstrates that decreased thickness of the endometrium decreases the likelihood of implantation. Furthermore, when the endometrial lining becomes too thin, then implantation does not occur. The minimal endometrial thickness required to maintain a pregnancy in patients undergoing in-vitro fertilization has been reported to range from 5mm to 9mm to 13mm. Whereas, the average endometrial thickness in women taking oral contraceptives is 1.1 mm.

This data helps to explain why the Food and Drug Administration's approved product information for oral contraceptives in the *Physicians' Desk Reference* states:

"Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus, which increases the difficulty of sperm entry into the uterus, and changes in the endometrium, which reduce the likelihood of implantation."

Other research regarding the receptivity of the uterine lining for implantation involves a family of cells called *Integrins*. Integrins are accepted as markers of uterine receptivity for implantation. These cells are absent in different causes of infertility. Integrins have been compared using endometrial biopsy specimens from normally cycling women and women taking oral contraceptives. In most oral contraceptive users, the normal patterns of expression of the integrins are grossly altered leading one researcher to conclude that oral contraceptive effects include integrin changes which have significant evidence of reducing endometrial receptivity to implantation of an embryo or preembryo.

These authors also evaluated research that considered the rate of ectopic pregnancy in women who conceived on oral contraceptives. The conclusion was that both combined oral contraceptives and progesterone only contraceptives were associated with an increased risk of ectopic implantation compared to the rate of ectopic pregnancies in woman not using contraceptives. Because ectopic pregnancy involves a substantial risk to the woman this is significant research.

In summary, this article found a reasonable likelihood that there are unrecognized spontaneous abortions with the use of oral contraceptives. It is a measurable fact that women conceive on oral contraceptives. The rate of conception analyzed in the scientific literature has many variables including “perfect use” of birth control pills verses “typical use” which is a range of patterns of how women really take birth control. Reported rates of pregnancy in woman using oral contraceptives that does not take into consideration unreported elective abortions is “1.0 per 100 woman-years in perfect use and 3 per 100 woman-years in the first year of typical use.” One national analysis that accounted for the underreporting of elective abortions estimated that the unintended pregnancy rates during the first year of using oral contraceptives was 4% for “good compliers”, 8% for “poor compliers” and up to 29% for some time users.

The documented rate of conceptions on birth control pills has a wide range, but the rate of conceptions resulting in unrecognized spontaneous abortions is even more difficult to measure. The evidence based research demonstrating the postfertilization effects of oral contraceptives were evaluated in this article. These effects include thinning of the endometrial lining and abnormal endometrial integrins both of which decrease the receptivity of the endometrial lining to implantation of the preembryo or the embryo. In addition if implantation occurs there is a greater chance of the endometrial lining not being able to sustain the embryo. Furthermore, there is evidence that women who conceive on oral contraceptives have an increased risk of ectopic pregnancy.

The authors conclude that the postfertilization effects of oral contraceptives have implications for informed consent. “Physicians should understand and respect the beliefs of patients who consider human life to be present and valuable from the moment of fertilization.” “Failure to disclose information that might lead a patient to choose a different method of treatment is generally considered to be unethical. Therefore, it seems clear to us that failure to inform patients of a possible postfertilization mechanisms of an oral contraceptive is a failure to provide informed consent.”