A study on the first combined oral contraceptive pill: Enovid

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Enovid, the first combined oral contraceptive pill (COCP) was composed of mestranol and norethynodrel. The United States Federal Drug Administration (FDA) approved it in 1960 for use to prevent contraception[1]. The launch of this medication "marked the beginning of a relatively long period of controversy surrounding the use of 'the Pill'. The controversy comprised various social influences including legal, religious, and feminist issues, as well as health concerns"[2].

Enovid was initially approved in 1957 to treat disturbances and suppress menstruation by targeting hormonal pathways of the menstrual cycle[3] because "socially, legally, and politically, contraception was taboo"[4]. Effectively, discussion of contraception in the public as well as contraceptive research were prohibited by the US Comstock law.[4] Similarly, any discussion of contraception or prescription of hormones for any reason pertaining to birth control were considered illegal and punishable under the 1982 Criminal Code of Canada.[4] In 1968, the Catholic Church took official position on the oral contraceptive and condemned it as a sinful act.[4] Therefore, in many societies birth control was regarded as a "criminal act, against the values of society and against divine will"[5]. However, the use of contraceptives proved to be a fight for women's sexual and reproductive rights. The sexual revolution of the 1960s had been launched and women were being regarded as being as "sexually free" as men.[4] The drug stirred fear of encouraged sexual promiscuity amongst females as well as a perceived "sexual anarchy"[4]. In reality, oral contraceptives promised control for women over their own bodies.[4] It allowed women control of their reproductive health in a way that was "easy to handle, independent of men's control, and discrete"[5].

The concept of contraception began in the 1920s when two doctors, Dr. Haberlandt and Dr. Fellner, reported separately that experimental animals could be rendered infertile following transplantation of ovarian tissue as well administration of estrogen extracts[6]. In the 1930s, other scientists confirmed that estrogen and progestogen[6] as well as high-dose progesterone could arrest ovulation in animal experiments[7]. The concept of cessation of ovulation in women only became a reality in the late 1940s when Dr. Djerassi synthesized progestin from an extract of wild yam root.[4] The basic composition of all later oral contraceptives included a combination of estrogen, which has an anti-ovulatory effect by suppressing the rise of FSH and follicular growth, as well as progestin which suppresses the ovulatory LH surge, thickens the cervical mucus and exercises an antiproliferative effect on the endometrium[7].

In an ironic turn of events, two devout Catholics, Dr. John Rock and Margaret Sanger were the pillars behind the clinical investigation of the oral contraceptive. They began an early trial of the oral contraceptive in Boston, Massachusetts under "the guise of a fertility study"[4]. Because of US laws this proved to be difficult so in 1956 the study was moved to Puerto Rico where over 200 women participated.[4] "They were given little information about the safety of the product, as there was none to give, and no one thought that it might be necessary to provide such information"[4]. That was the standard of the day. The Searle Corporation received approval for Enovid in 1957 for the treatment of menstrual disorders and in 1960 as a contraceptive.[8] During the early clinical studies, Enovid proved to have 100% efficacy but the recipients of the drug fell victim to many side effects[1]. In a study conducted in Puerto Rico, it was found that 17% of the women taking Enovid experienced stomach irritation, vomiting, headaches, nausea and dizziness[1]. "In 1961, the Lancet reported the death of a woman from thrombosis who was taking the pill [and] in less than a year, the FDA had received reports of 6 deaths and 20 non-fatal cases

of thromboembolism"[1]. Despite the evident positive effects of Enovid, it's history is "marked by a lack of consent, a lack of full disclosure, a lack of true informed choice, and a lack of clinically relevant research regarding risk"[4]. "By 1965, the year in which the Supreme Court struck down the Connecticut laws prohibiting the use of birth control, more than 6 million American women were using oral contraception"[8].

The first marketed oral contraceptive, Enovid 10, "contained 9.85 mg of the progestin norethynodrel and 150 μg of the estrogen mestranol"[4]. Today's pills contain much lower levels of hormones, normally resting around doses of "0.1 to 3.0 mg of modern progestins and 20 to 50 μg of estrogens"[4]. The progestins used in the modern versions of oral contraceptives are much more specific in terms or their target and in terms of their effect.[4] Oral contraceptives are now being seen to employ low doses of ethinyl estradiol in combination with other progestins since combined oral contraceptives have been proven safe and effective[9]. Modern COCs normally follow a 28-day cycle, thus 21 active pills and a pill-free interval of 7 days or a placebo interval of 7 days to improve compliance.[1] The past 10 years has also seen the introduction of the extended cycle COC which contains 3 or 4 months of active pills and a 7-day pill-free interval.[1] Furthermore, the prevention of pregnancy isn't the only benefit to using oral contraceptives. Studies have shown that ever users of the pill have a 40% decrease in the risk of ovarian cancer and the protective effects continue up to 10 years after discontinuation.[8] Similarly, there is a 50% decrease in the risk of endometrial cancer.[8] Additionally, the pill decreases acne severity, reduces dysmenorrhea and decreases overall blood loss during menstruation.[8] Consequently, "in 2009, COC represented 8.8% of contraceptive prevalence. More than 100 million women used COCs"[1].

The introduction of the oral contraceptive into society over 50 years ago marks a monumental event in human history.[10] "The large-scale use of contraceptives triggered the most powerful social revolution of a century in reproductive health and gender equity"[9]. A lasting impact on many aspects of social life can be observed, such as changes to "women's careers, health, fertility trends, laws and policies, religion, interpersonal relationships and family roles, feminist issues, and gender relations, as well as sexual practices among both adults and adolescents"[2]. Many long-standing societal beliefs, especially regarding the control of women's fertility, were tested and has forced society to reexamine said beliefs.[2] Although, the impact of oral contraception on society must be noted, it is important to understand the impact it has had more specifically for the individual woman who is using it, from both perspectives: effectiveness and health benefits.[2] Consequently, the most notable social significance of the oral contraceptive is that it allows women everywhere a sense of "worth and dignity"[5].

To conclude, modern day scientists are now challenged by an unfinished research agenda.[9] The story of the oral contraceptive has been a viable source of learning for the medical community and has proven to be a driving force behind optimal sexual and reproductive health for women.[5] Now, further research must be conducted to better understand method failures of COCs, to weigh the risks versus the benefits of COCs as well as to discover new and more effective molecules.[1] Finally, COCs have provided an excellent method of contraception for women but there is a present need for research and development of male contraceptives, better emergency contraceptives, improved vaginal microbicides as well as female and male condoms.[9]

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