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Review

The birth control pill, thromboembolic disease, science and the media: a historical review of the relationship

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Abstract

The introduction of the birth control pill (the Pill) in 1960 revolutionized the options for contraception, sparking vibrant discussion in the scientific and social science literature and in the media. Much attention focused on issues of women's rights, including ethics and personal choice. But the Pill also introduced new questions about risk. Shortly after its introduction, the risk of thromboembolic disease was recognized [1]. After more than half a century, controversies about the relationship between the Pill and thromboembolic disease have persisted. The scientific and media communities have been active in the discussion, debate and delivery of information about this risk.

Scientific and public attention to thromboembolism and the Pill has had dramatic consequences, both good and bad. The spotlight on risk has helped to change norms regarding the public's right to know and assess dangers; it has sparked Pill scares linked to increased unplanned pregnancy, birth and abortion rates; and it has led to a change in federally mandated policies regarding how new contraceptive products are studied and brought to market.

This paper charts the narrative of the thromboembolic risk of the Pill from its introduction in 1960 until today and reviews the corresponding media response to this history. How does the story of the thromboembolic risk of the Pill — explored through the lens of science, media and contemporary social dynamics — frame contemporary understanding of risk for researchers, clinicians, individuals and the public?

Keywords: Birth control pill; Media; Thromboembolic disease; Risk; Contraception; Pill scare

1. Introduction

The introduction of the birth control pill (the Pill) in 1960 revolutionized the options for contraception, sparking a vibrant discussion in the scientific and social science literature. Media and medical controversy continues to this day. Although much attention focused on issues of women's rights, the Pill also introduced vexing new questions about risk. Shortly after its introduction, the risk of thromboembolic disease was recognized [1]. After more than half a century, uncertainties about the relationship between the Pill and thromboembolic disease persist. The scientific and media communities remain active in the discussion, debate and communication of information about this risk.

Thromboembolic disease includes blood clots and pulmonary embolism, which can have devastating consequences, including stroke and death. The original case of pulmonary embolism in a woman taking the Pill was reported in *The Lancet* in November 1961 [2]. Subsequent cases reported within the next year fueled media coverage, resulting in contradictory and confusing headlines. On August 4, 1962, *The Los Angeles Times* wrote, "Birth Control Pill Probed in Death of 6" [3] and the next day reported, "Birth Control Pills Cleared in Six Deaths" [4]. A week later, *The Wall Street Journal* reported, "Searle Agrees to Warn Doctors, Pharmacists on Use of Enovid Pill" [5] and the following month ran, "G.D. Searle Asserts Panel Rules Out Enovid as Cause of Blood Clots" [6]. Exactly 1 year later, *The Wall Street Journal* headlines were reassuring: "FDA Says Searle Can Drop Its Warning About Taking Enovid" [7]. The popular journal *Science* captured the situation in which clinicians, policy makers and consumers found themselves on September 6, 1963: "Enovid: Contraceptive Pill and Recent FDA Report Clearing It Stir Continued Medical Dispute" [8].

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The Pill contains two hormones: estrogen and progestin. The role of estrogen in the increased thromboembolic risk was suspected in the 1960s, and its biologic and dose-related role in increasing clotting risk is now well documented [9,10]. More recently, other risk factors such as age, obesity and underlying genetic predisposition to clotting disorders have been elicited [11]. While currently available regimens contain approximately one fifth or less estrogen than the original Enovid, users nonetheless incur a small increased risk of thromboembolism compared to nonusers [12,13]. The role of progestins in the risk is less clear. Newer progestins have been both implicated and exonerated as a possible additional causative factor in thromboembolic risk [14–16]. The challenges in conducting and interpreting epidemiologic studies that adequately address the progestin question, particularly as we account for other known risk factors [11], are complex, fueling heated debate about the safety of the Pill.

Scientific reports suggesting a possible relationship between the Pill and thromboembolic risk made headlines in the worlds of women's health care, policy and media. At times, this resulted in dramatic responses by both the medical community and users of the Pill. A notable episode unfolded in the United Kingdom in 1995 when the Committee on Safety of Medicines prematurely issued a warning letter to doctors about third-generation birth control pills. It drew widespread media and medical attention, leading to a "Pill scare" — a sudden and dramatic drop in Pill use. Evidence strongly suggests a corresponding increase in unplanned pregnancies, births and abortions in several countries as a result of what some commentators labeled a "panic" [17–20].

This history of debate over thromboembolic risk of the Pill from its introduction in 1960 until today considers not only changes in the nature of the evidence but the corresponding media response to a narrative of contraception and risk. Viewed through the lens of science, media and contemporary social dynamics, the history of the thromboembolic risk of the Pill underscores the ways in which controversy shapes the understanding of risk for researchers, clinicians, individuals and policy makers. Publicity surrounding the Pill contributed to a shift from physician-centered to patient-centered decision making, highlighting the rights of all individuals to decide about risk as a new norm in clinical practice. We have now entered an era of unlimited and often conflicting information. This history underscores, however, that while access to information further complicates decision making, it also presents an opportunity to enhance autonomy, enabling women to achieve the contraceptive goals they desire and deserve.

2. A confused decade

The first decade of the Pill was marked by great enthusiasm, uptake and confusion over the safety of this medical wonder drug. The first Pill, Enovid, was approved in the United States in 1957 for menstrual disorders and for contraception in 1960. The Pill as a contraceptive was rapidly embraced. By the end of 1962, an estimated 1.7 million American women were taking Enovid [21]. The first reported case of thromboembolic disease in 1961 — a bilateral pulmonary embolism with infarction — occurred in a woman taking Enovid for a menstrual disorder, not for contraception. According to the report, Enovid was advised for a nun with recurrent endometriosis [2]. Two deaths from pulmonary embolism in Los Angeles were reported later that year [4].

As rates of use went up, so did episodes of suspected Pill-related thromboembolic events, as reported to both the drug maker, G.D. Searle and Company, and to the Food and Drug Administration (FDA). In response to these episodes, Searle convened 30 experts in gynecology, hematology and epidemiology at the American Medical Association headquarters in 1962, who concluded that, "While more statistics are valuable, there is no real immediate danger involved." [22]. Less than a year later, however, the FDA issued a report warning of an elevated risk in women over 35. But within 5 weeks, that report was revised, citing errors in the statistical calculations [23]. An update was released to the lay press, followed by publication of a brief in *The Journal of the American Medical Association* concluding that, for women of any age, Enovid did not pose a significant increased risk of death. The brief went on to stress the need for further studies. Noting "the controversial nature of the subject," it closed with a statement acknowledging the confusion wrought by the release of the information to the lay press rather than through the associated professions [24].

While the brief did not spell out exactly what those controversies were, it implied a dispute that was about more than just the science; it was a debate about society's willingness to embrace contraception, and women's role in the decision-making process. An article in *Science* in 1963 cited women's reproductive freedom, concerns about overpopulation and the Catholic Church's stance on birth control as just a few of the motivators behind aggressive reactions both for and against the FDA's statement [25]. The question in the medical community was how much risk the clinician considered acceptable. Some physicians opposed oral contraception because of the threat it posed to women's health, drawing on the conflicting FDA reports for support. Others accepted the inevitability of risk, underscoring "that the need for more simple contraceptives is great." Those in this camp reasoned that the lack of consensus indicated, at most, an extremely small risk and that "There would be a greater health risk to those women who, through non-use of any contraceptives, become pregnant." [26].

The controversy continued through the decade. The World Health Organization issued a technical report in 1966 stating that "no cause-and-effect relationship has been established" [27]. The FDA, still smarting from prior criticism, was more cautious. In 1966, it described the data as inadequate "to confirm or refute the role of oral contraceptives in thromboembolic disease" [28]. But by the late 1960s, tenuous scientific consensus began to emerge. In 1968, retrospective data from Britain began to confirm a