

*Reprinted From The Journal of The American Medical Association
March 11, 1968, Vol. 203, pp. 950-954
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Epidemiological Problems Associated With Studies of the Safety of Oral Contraceptives

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Most segments of American society agree that excessive and disproportionate population growth is a social, economic, and health threat, and there is a consensus, reflected in the stated policy of the federal government¹ that every family should have easy access to family planning information and services so that each may make an intelligent and uninhibited choice concerning the number of children desired. This consensus has increased the need for family planning services and efforts to develop improved techniques of contraception. New methods have been developed because the old ones are not suitable for all populations. It is difficult for a single method to satisfy all the criteria of the ideal contraceptive: efficacy, safety, reversibility, low cost, simplicity, and acceptability.

Advances in reproductive biology supported and conducted by private foundations, industry, and the government have resulted in several unique and effective techniques in the last decade, the most noteworthy being oral contraceptives and intra-uterine devices, and recent reports indicate that other promising new methods are under development.² The new contraceptives have proven to be acceptable in use and in many areas they are rapidly replacing more traditional methods.³ It is estimated, for instance, that in the United States more than 4 million women are now taking oral contraceptives⁴ and throughout the world, according to S. Segal, MD (oral communication, January 1967), more than 5 million women are

using intra-uterine devices. This rapidly increasing use of new methods has occurred despite the warnings by some that they have not been fully tested for safety.

The literature on the effects of oral contraceptives or allied materials on biological systems is large and growing rapidly. Animal work has been conducted extensively for many years, particularly in relation to carcinogenesis, and the work relating to the constituents of oral contraceptives was discussed and summarized recently.⁵ Most reports concerning the apparent effects of these medications on humans concern studies of patients with acute symptoms and are of limited significance, but the variety of presumed reactions which have been reported is remarkable in extent. Indeed, most organ systems have been implicated. Although such studies present useful indicators, few definitive conclusions can be drawn from them and it is clear that carefully designed and conducted epidemiological studies are required in order to ascertain with assurance the safety of these agents.

At present, the potential adverse effects of oral contraceptives are described in four areas.⁶ The first area of concern is the potential effects on the vascular system and blood coagulation. Despite a large literature on the relationship between oral contraceptives and thromboembolism, strong evidence that such a relationship exists was not available until a recent report by the Medical Research Council of England.⁷ Even so, experience is limited to retrospective studies, with little information on the pattern by which risk is increased for women with particular characteristics, such as age, parity, hemoglobin level, blood pressure, and duration of contraceptive use.

The second problem area is the possible relationship between oral contraceptives and carcinoma. It is generally agreed that a large number

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