

Oral contraceptives for older women

The Fertility and Maternal Health Drugs Advisory Committee of the US Food & Drug Administration (FDA) recently (October 1989) decided to remove the upper age limit in the USA on oral contraceptive use for healthy, non-smoking women. A year earlier, the American College of Obstetricians & Gynecologists (ACOG) also decided that the Pill was safe for healthy non-smokers up to the age of 45.

History of Pill side-effects

Although it is widely believed that the FDA imposed age restrictions on Pill use, this is not exactly the case. In 1975, Mann and his colleagues published two articles^{1,2} which reported an increased risk of both fatal and non-fatal cardiovascular events (primarily myocardial infarction) in Pill users, especially older ones. (A later article by the same research group reported a relative risk of 3 in women over 40,³ which was lower than earlier reported.) The FDA then recommended (via the *FDA Drug Bulletin*, July 1975) that Pill users over 40 be made aware of the increased risk and be urged to use other forms of contraception. This became the first *de facto* age limit imposed on oral contraceptive users by the FDA.* The age limit was included in *Contraceptive Technology* (8th edition, 1976).

In 1977, the FDA Advisory Committee recommended that labelling be revised to reflect variable risks for smokers and non-smokers. In January 1978, package inserts for users started to include the statement "Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke." This labelling remains in place today.* Age as a contra-indication to Pill use was rigorously implemented by many providers, including the Planned Parenthood Federation of America.

The increased risks of myocardial infarction (MI) and of stroke were the first serious side-effects of oral contraception to be identified.⁴ The association is attributed to the effect of oestrogen increasing clotting factors, and to the atherogenicity of the progestagen. Three cohort studies and many case-control studies have confirmed this increase in risk which applies to all age groups, but is greater for older women. For women of 40 years and over who take the Pill, the risk of MI is three to four times greater and the risk of stroke is about five times greater than for women who do not take oral contraceptives.⁵ And not only is the *relative* risk higher for older women who take the Pill, but the *absolute* risk also increases rapidly with age (Table I).

Changed decision on Pill-taking

Why then, in spite of this knowledge, did the ACOG

TABLE I. AGE-SPECIFIC ACUTE MYOCARDIAL INFARCTION (ICD 410) MORTALITY RATES (PER 100,000 WOMEN), USA, 1965-1985

Year	Age in years				
	30-34	35-39	40-44	45-49	50-54
1965†	4.2	11.1	24.3	52.0	102.9
1970	3.3	7.5	16.0	36.3	70.7
1975	2.0	5.9	14.2	29.4	58.0
1980	1.3	3.4	10.4	23.6	44.4
1985	1.1	3.0	8.3	17.1	37.5

Source: Vital Statistics of the USA.
† 'Acute myocardial infarction' had no ICD code in 1965. The 1965 rates shown are for 'arteriosclerotic heart disease'.

*Ridgely C. Bennett. Remarks to the Fertility and Maternal Health Drugs Advisory Committee, 26 October 1989.

For three quite independent reasons:

- The Pill has changed
- Pill prescribing practices have changed
- Women's health risks have changed.

The change in Pill composition

Studies showing an increased risk were all done on women who were taking higher-dose Pills than are available today. Low-dose Pills (with 50 µg of oestrogen) were in common use in the UK by 1973, and in the rest of Europe at about the same time. While high-dose Pills had almost disappeared from use by 1973, Mann's 1975 publications reported on non-fatal MIs occurring from 1968 to 1970, and fatal MIs in 1970, when those formulations were still widely used. The trend to lower doses occurred slightly later in the USA; low-dose Pills were first introduced in 1973. High-dose Pills (i.e. with 50 µg of oestrogen) were not removed from the USA market until 1988. After low-dose Pills were introduced, the speed with which the transition took place also differed between the USA and the UK. In the USA, older women were often the last to switch to the newer formulations.⁶

Intuitively, the lower dose carries less risk, but few studies have been done to demonstrate this. An ongoing study by Vessey and his colleagues in the UK is showing that the relative risk of MI in Pill users is certainly less than 1.5, and virtually all events occur in smokers.* This study, however, excluded women over 40 because of low OC use prevalence in this age-group.

Changes in Pill prescribing

The prescribing of oral contraceptives has become more sophisticated. The epidemiological studies that evaluated the several benefits and risks of oral contraceptive use also identified groups of women who would be better off using other methods of contraception. In the early days of the Pill, almost any woman who wished to take them was given a prescription.

Today Pills are rarely prescribed for women with any of several diseases, ranging from cancer to diabetes. Also excluded are women with risk factors for heart attacks or strokes — women who smoke, are hypertensive or obese, have high cholesterol levels or a history or family history of cardiovascular events. The risk of MI in women with multiple risk factors (three or more) is more than 100 times higher than for women with no risk factors. Regardless of whether low-dose Pills are themselves safer, improved prescribing would mean fewer heart attacks and strokes.

Change in women's health risks

The incidence of both heart attacks and strokes has declined quite dramatically in the last 20 years in both men and women. This change is attributed to improved eating habits, increased exercise, and a decrease in smoking. Table I shows that, since the mid-1970s when the age limit for Pill use was first imposed, the incidence of acute myocardial infarction has declined by almost half among women aged 40-49. And since 1965 when Pill use first began to be significant, the incidence of myocardial infarction has decreased by about two-thirds in the age groups of interest. The incidence of strokes has shown a similar dramatic decline.

Again, regardless of whether low-dose Pills are safer, there will be fewer heart attacks and strokes today than when age restrictions were first imposed, simply because women (and men) have a lower total risk of these diseases today than they had in the 1960s and 70s.

World-wide implications of the change

Both the FDA and the ACOG decisions are directed

*M. Thompson. Personal communication, March 1990.

towards family planning practice in the USA. What are the implications of this policy change for other countries? This question has two aspects: are the risks of cardiovascular events likely to be the same elsewhere? How do contraceptive choices vary among countries?

Risks of cardiovascular events vary substantially among countries. The risk of MI is typically low in many Asian countries (probably because of lifestyle differences), intermediate in Africa and Latin America, and highest in the developed countries.⁷ Thus the adverse consequences of OC use for cardiovascular disease are less in many (but not all) developing countries than in the USA.

The range of contraceptive options varies among countries. Two methods which are perhaps ideal for older women — Depo-Provera and Norplant — are not available in the USA. Safe abortion is not available in many developing countries, perhaps leading to a greater demand for highly effective contraceptive methods. In the USA, and in many other countries, both developing and developed, sterilization is the most popular method of family planning among older women. Whether the method is popular for its own sake, or as a response to a perceived lack of options, is not known. Experience in providing family planning services tells us that the greater the range of options, the greater the proportion of women who will choose to use contraception.

Conclusion

Finally, it is important to keep in mind that the risks associated with pregnancy are far higher for older women than for younger ones. Older women are more likely than younger ones to choose abortion which, in countries where it is not legal, carries a high risk of morbidity and mortality. The increased risk of congenital malformations in the fetus is well known. Even in developed countries with a low overall obstetric risk, the risk of maternal death is up to 10 times higher for women in their 40s than it is for younger women. In many developing countries the risk of death associated with pregnancy is a very significant one, and must be weighed against any risks associated with contraception.

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