

Age-Related Fertility Decline

Committee on Gynecologic Practice

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American Society for Reproductive Medicine



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ABSTRACT: Age is a significant factor influencing a woman's ability to conceive. Social trends have led to deferred childbearing, and an increasing number of women are experiencing age-related infertility and pregnancy loss. Women older than 35 years should receive expedited evaluation and treatment after 6 months of failed attempts to conceive, or earlier if clinically indicated.

The number of oocytes in the ovaries declines naturally and progressively through the process of atresia. The maximum complement of oocytes is 6–7 million and exists at 20 weeks of gestation in the female fetus. The number of oocytes decreases to approximately 1–2 million oocytes at birth; 300,000–500,000 at puberty; 25,000 at age 37 years; and 1,000 at age 51 years, the average age of menopause in the United States (1–3). Fecundity declines gradually but significantly beginning approximately at age 32 years, and decreases more rapidly after age 37 years, reflecting primarily a decrease in egg quality in association with a gradual increase in the circulating level of follicle-stimulating hormone (3). The mechanisms involved are poorly understood, but appear to include multiple factors encoded by genes on both the X chromosome and the autosomes (4).

Age alone has an impact on fertility. Historical data suggest that among populations that do not use contraception, fertility rates decrease with increasing age of women (Fig. 1). Because sexual activity also declines with age, it is difficult to separate out the effects of sexual behavior from age. However, a classic French study was able to separate behavioral and age effects by studying normal women with azoospermic husbands undergoing donor insemination. The study found that pregnancy rates decreased progressively with increasing age of the recipient female (5). The cumulative pregnancy rate observed across up to 12 insemination cycles was 74% for women younger than 31 years and decreased to 62% for women aged 31–35 years and to 54% for women older than 35

years (5). A similar trend has been observed in analyses of data derived from in vitro fertilization (IVF) embryo transfer programs in the United States. For the year 2006, the percentage of embryo transfers resulting in live births decreased progressively from 44.9% in women younger than 35 years to 37.3% for women aged 35–37 years, 26.6% for women aged 38–40 years, 15.2% for women aged 41–42 years, and 6.7% for women aged 43–44 years (6). By contrast, in cycles using eggs obtained from healthy, young donors, 54% of transfers resulted in a live birth, regardless of the age of the recipient (6). As age increases, the risks of other disorders that may adversely affect fertility, such as fibroids, tubal disease, and endometriosis, also increase. Women with a history of prior ovarian surgery, chemotherapy, radiation therapy, severe endometriosis, smoking, pelvic infection, or a strong family history of early menopause may be at increased risk for having a premature decline in the size of their follicular pool and their fertility.

The age-related decline in fertility is accompanied by a significant increase in the rates of aneuploidy and spontaneous abortion (7). Autosomal trisomy is the most frequent finding and is related, at least in part, to changes in the meiotic spindle (8) that predispose to nondisjunction (9). Even for morphologically normal embryos selected for transfer in IVF cycles, the prevalence of aneuploidy is high in women of advanced maternal age (10). The fetal loss rate also is significantly higher, even after fetal heart rate motion is detected by transvaginal ultrasonography (11). Whereas 9.9% of women

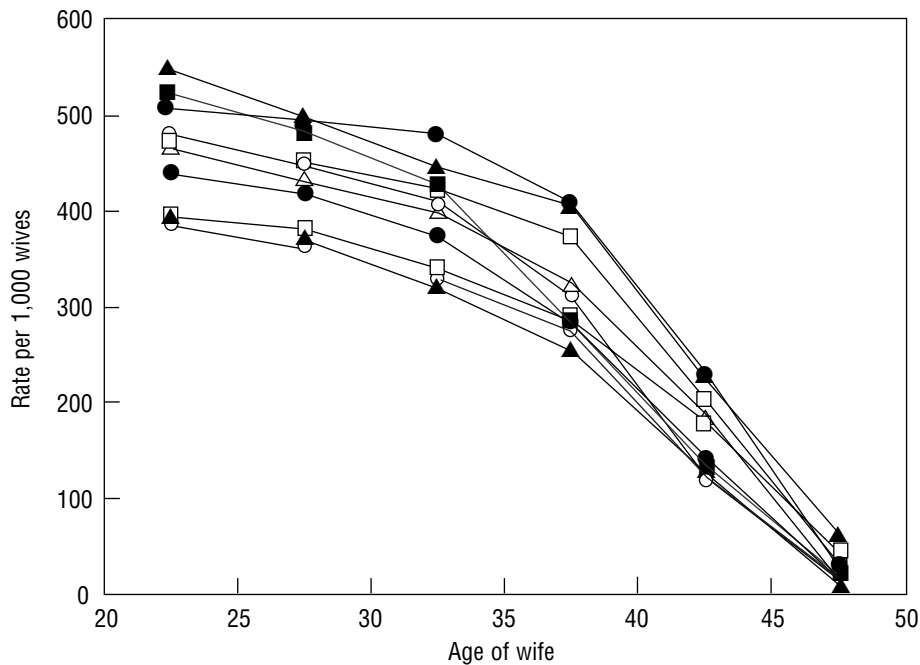


Fig.1. Marital fertility rates by 5-year age groups. The ten populations (in descending order at age 20–24 years) are Hutterites, marriages from 1921–30 (▲); Geneva bourgeoisie, husbands born in 1600–49 (■); Canada, marriages 1700–30 (●); Normandy, marriages 1760–90 (○); Hutterites, marriages before 1921 (□); Tunis, marriages of Europeans 1840–59 (△); Normandy, marriages 1674–1742 (●); Norway, marriages 1874–76 (□); Iran, village marriages, 1940–50 (▲); Geneva bourgeoisie, husbands born before 1600 (○). From Menken J, Trussel J, Larsen U. Age and infertility. *Science* 1986;233:1389–94. Reprinted with permission from AAAS.

younger than 33 years who conceive during IVF with a fresh embryo transfer experience a pregnancy loss after fetal heart activity is observed, the rate of miscarriage progressively increases to 11.4% for women aged 33–34 years, 13.7% for women aged 35–37 years, 19.8% for women aged 38–40 years, 29.9% for women aged 41–42 years, and 36.6% for women older than age 42 years (11). Therefore, given the anticipated age-related decline in fertility, the increased incidence of disorders that impair fertility, and the higher risk of pregnancy loss, women older than 35 years should receive expedited evaluation and treatment after 6 months of failed attempts to conceive, or earlier if clinically indicated.

In conclusion, fertility in women is closely related to reproductive age and becomes significantly compromised before the onset of perimenopausal menstrual irregularity. Education and enhanced awareness of the impact of age on fertility is essential in counseling the patient who desires pregnancy. Women older than 35 years should receive expedited evaluation and treatment after 6 months of failed attempts to conceive, or earlier if clinically indicated.

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