

Editorial

Reproductive health risks in perspective

Dramatic headlines about women's health — deaths of women using the OrthoEvra patch, for example, or after medication abortion — can quickly lead patients and healthcare practitioners into a state of panic and uncertainty over the appropriate course of action to take. Should therapy be continued or not? What is the real risk of death?

Alarmist, misleading, inaccurate or incomplete media coverage is certainly a source of confusion, but such stylized reporting is not likely to be eliminated from most large media outlets in the near future. That fact, coupled with the lack of courses in biostatistics and risk-assessment analysis in most medical training programs and the reality that health professionals have little time to counsel patients about the risks of various treatments, can lead patients to make poor health-related choices.

This danger is particularly worrisome when patients are dealing with contraceptive issues and the threat of an unplanned pregnancy. Doctors, nurses and other providers have little time to investigate and consolidate risk-related information for their patients, and patients have few resources available to help them ascertain the risks from using various contraceptive methods. The brief summary provided here is intended to help inform clinicians and their patients of the risk of death from pregnancy, abortion and the use of various forms of hormonal contraception, as well as from other voluntary activities.

In general, contraceptives pose few serious health risks to users. Moreover, the use of contraceptive methods is generally far safer than pregnancy. Unintended pregnancies unnecessarily place women at risk. Women in many developing countries will experience an even greater advantage in using contraceptive methods than those in the developed world in comparison with pregnancy-related mortality. Nonetheless, use of some contraceptive methods may entail potential risks.

- Use of the method may lead to serious outcomes such as death, hospitalization, surgery, medical side effects, infections, loss of reproductive capacity or pain.
- Contraceptive failure (pregnancy) is associated with risk: a woman must assess the likelihood of contraceptive failure and the dangers that a pregnancy would pose.

- Future fertility may be influenced by choice of a contraceptive method.

When it comes to the most serious outcome of all — death — the absolute level of risk is extraordinarily low for most women. [Table 1](#) puts into perspective some of the risks of everyday life in the United States [1–9]. Other major health risks from contraceptive use are not only uncommon, but they are also most likely to occur in women who have underlying medical conditions.

1. Pregnancy

The risk of death from pregnancy and delivery is about 1 in 8700, lower than the annual risk of death from an automobile accident but higher than the annual risk of death from use of combined oral contraceptives (OCs) for all women except those aged 35–44 years who smoke and higher than the risk of death from abortion, even at gestational ages ≥ 21 weeks.

2. Combined OCs

Combined OCs have been associated with an increased risk of myocardial infarction (MI) and stroke. Smoking definitely increases the risk of MI, especially in women older than 35 years. However, nonsmoking, normotensive, nondiabetic women of any age who use combined OCs are not at increased risk for MI. The risk of stroke in nonsmoking women younger than 35 years is not increased by use of OCs with less than 50 μg of estrogen [10]. The risk of venous thromboembolism is increased by combined OC use, but the absolute risk of this increase is quite low among women who use OCs with less than 50 μg of estrogen, ranging from 9 events per 100,000 women-years of exposure among those aged 20–24 years to 18 events per 100,000 women-years of exposure among those aged 40–44 years [10].

Use of combined OCs is associated with a decreased risk of cancers of the endometrium and ovary and an increased risk of cancer of the cervix and liver, a small increased risk of breast cancer in young women and a decreased risk of colorectal cancer [10]. However, there is great uncertainty

Table 1
Everyday risks in perspective

Activity	Risk of death	Source
Risk per year		
While skydiving	1 in 1000	Laudan [1]
From an accident	1 in 2900	
From an automobile accident	1 in 5000	
From a fall	1 in 20,000	
From a fire	1 in 50,000	
From riding your bicycle	1 in 130,000	
In an airplane crash	1 in 250,000	
From being struck by lightning	1 in 2,000,000	
Risk per year for women preventing pregnancy		
Using OCs		Schwingl et al. [2]
Nonsmoker		
Aged 15–34 years	1 in 1,667,000	
Aged 35–44 years	1 in 33,300	
Smoker		
Aged 15–34 years	1 in 57,800	
Aged 35–44 years	1 in 5200	
Undergoing tubal sterilization	1 in 66,700	Escobedo et al. [3]
Risk per year from using tampons	1 in 5,734,000	Hajjeh et al. [4]; U.S. Census Bureau [5]
Risk from pregnancy	1 in 8700	Berg et al. [6]
Risk from spontaneous abortion	1 in 142,900	Saraiya et al. [7]
Risk from legal induced abortion		
Mifepristone/misoprostol	1 in 110,000	Summers [8]
Surgical		
≤ 8 weeks	1 in 1,000,000	Bartlett et al. [9]
9–10 weeks	1 in 500,000	
11–12 weeks	1 in 250,000	
13–15 weeks	1 in 58,800	
16–20 weeks	1 in 29,400	
≥ 21 weeks	1 in 11,200	

regarding the causal link, if any, between combined OC use and liver and colorectal cancer [10], and recent evidence suggests no association between current or former combined OC use and breast cancer [11]. Regardless, the net effect of pill use on cancer is negligible [10].

Persistent infection with certain types of human papillomavirus (HPV) is the most frequent cause of cervical cancer. However, the incidence of cervical cancer is increased in women using OCs, particularly long-term users, even among women infected with HPV; this risk increases as duration of use increases [12]. Results from limited data also suggest a slight increase in the risk of cervical cancer among women who use injectable contraceptives for 5 years or longer [12].

Analysis of pooled data from 54 epidemiologic studies conducted in 25 countries found that women have a slightly increased risk (about 25% higher) for having breast cancer diagnosed while they are using OCs. Cancers diagnosed in

these women are less advanced clinically than those diagnosed in women of the same age who have never used OCs [13]. The increased risk is apparent soon after pill use begins but does not increase with duration of use, declines after use ceases and does not persist beyond 10 years after exposure ceases. These patterns are not typical for a carcinogenic agent but would be consistent with promotion of already existing tumors or with earlier diagnosis of breast cancer in women who have used the pill. A more recent study in the United States found that among women aged 35–64 years, current or former combined OC use is not associated with an increased risk of diagnosis of breast cancer [11].

3. OrthoEvra patch

The OrthoEvra patch has been recently highlighted in the press after the Food and Drug Administration (FDA) announced a label change in October 2005. The change includes a bolded “warning” indicating that use of the patch entails a 60% higher exposure to estrogen than use of a typical combined OC containing 35 µg of estrogen; however, the FDA states that the clinical relevance of this finding is unknown [14].

The actual risk of death from patch use is impossible to determine. Spontaneous reports of deaths of women using the patch have been received by the FDA. Spontaneous reports to the FDA can come from various sources, and the quality and extent of the information reported vary considerably. It is often unclear whether a death is causally related to use of a drug. Moreover, even if the intensive follow-up was to establish that a certain number of deaths were likely to have been caused by use of that drug, there remains the problem of computing an accurate mortality rate because the relevant denominator is also not known. Therefore, it is not possible to know at this time how the mortality risk from use of the patch compares with that from use of combined OCs [15].

4. Abortion

The risk of death is about the same from medication abortion and from surgical abortion; however, the risk of death from surgical abortion is greatest for higher gestational ages where medication abortion is not used. Nevertheless, induced abortion is safer than continuing pregnancy and entails about the same risk as spontaneous abortion.

5. Conclusion

As sensationalized news reporting becomes more common and thoughtful analysis becomes more difficult to find, given its perceived lack of appeal to media observers, healthcare practitioners must intensify efforts fully and

repeatedly to inform patients of their true risks of death from various contraceptive methods. This imperative is particularly important as the FDA has become extremely sensitive regarding drug safety warnings.

Women are far more likely to die from pregnancy-related complications, from automobile accidents or from a fall than they are from using hormonal contraception or having undergone either a medication or surgical abortion. Those who claim that hormonal contraception and abortion are unsafe base this assertion on ideology, not evidence-based science. The evidence in Table 1 shows otherwise.

James Trussell
Office of Population Research
Princeton University
Princeton, NJ 08544, USA
E-mail address: trussell@princeton.edu

Beth Jordan
Association of Reproductive Health Professionals
Washington, DC 20037, USA
E-mail address: bjordan@arhp.org

References

- [1] Laudan L. *The book of risks*. New York: John Wiley and Sons; 1994.
- [2] Schwingl PJ, Ory HW, Visness CM. Estimates of the risk of cardiovascular death attributable to low-dose oral contraceptives in the United States. *Am J Obstet Gynecol* 1999;180:241–9.
- [3] Escobedo LG, Peterson HB, Grubb GS, Franks AL. Case-fatality rates for tubal sterilization in U.S. hospitals, 1979–1980. *Am J Obstet Gynecol* 1989;160:147–50.
- [4] Hajjeh RA, Reingold A, Weil A, Shutt K, Schuhat A, Perkins BA. Toxic shock syndrome in the United States, 1979–1996. *Emerg Infect Dis* 1999;5:807–10.
- [5] U.S. Bureau of the Census. *Statistical abstract of the United States: 2003*. Washington (DC): Government Printing Office; 2003 [Table 11].
- [6] Berg CJ, Chang J, Callaghan WM, Whitehead SJ. Pregnancy-related mortality in the United States, 1991–1997. *Obstet Gynecol* 2003;101:289–96.
- [7] Saraiya M, Green CA, Berg CJ, Hopkins FW, Koonin LM, Atrash HK. Spontaneous abortion-related deaths among women in the United States — 1981–1991. *Obstet Gynecol* 1999;94:172–6.
- [8] Personal communication from Danco Laboratories, C Summers. 9 March 2006.
- [9] Bartlett LA, Berg CJ, Shulman HB, et al. Risk factors for legal induced abortion-related mortality in the United States. *Obstet Gynecol* 2004;103:729–37.
- [10] Burkman R, Schlesselman JJ, Ziemann M. Safety concerns and health benefits associated with oral contraception. *Am J Obstet Gynecol* 2004;190(Suppl):S5–S22.
- [11] Marchbanks PA, McDonald JA, Wilson HG, et al. Oral contraceptives and the risk of breast cancer. *N Engl J Med* 2002;346:2025–32.
- [12] Smith JS, Green J, Berrington de Gonzalez A, et al. Cervical cancer and use of hormonal contraceptives: a systematic review. *Lancet* 2003;361:1159–67.
- [13] Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,239 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;347:1713–27.
- [14] Ortho-McNeil Pharmaceutical. Ortho Evra Product labeling. Revised November 2005.
- [15] Media report on Ortho Evra patch sets off safety concerns in women. *Contracept Technol Update* 2005;26:113–5.