

Correspondence



Copper Intrauterine Devices and Tubal Infertility among Nulligravid Women

To the Editor: Hubacher and colleagues (Aug. 23 issue)¹ report that the use of copper intrauterine devices (IUDs) is not associated with an increased risk of tubal occlusion among nulligravid women. However, only 6 percent of the women in the study had used an IUD. Accordingly, the numbers used to test for an effect of the duration of IUD use, an extremely important aspect of the study, were even smaller. Only 44 women had used a copper IUD for more than one year, of whom only 8 had tubal occlusion. Nevertheless, the odds ratios for tubal occlusion show a moderate, nonsignificant trend of increasing risk with increasing duration of IUD use (up to 6 months, 0.8 [95 percent confidence interval, 0.4 to 1.8]; 7 to 12 months, 1.1 [95 percent confidence interval, 0.4 to 2.8]; and 13 months or more, 1.3 [95 percent confidence interval, 0.6 to 3.2]). The upper limits of these confidence intervals are consistent with a marked effect of longer duration of IUD use on tubal infertility.

We believe that the authors' conclusion that contemporary copper IUDs are safe is unwarranted. In a study of women using IUDs, mostly devices containing copper, we reported no deleterious effect on fertility of short-term use (up to 42 months) but strong evidence of such an effect after long-term use (78 months or more).² The study by Hubacher et al. cannot rule out an adverse effect of these devices and should be interpreted with caution.

MARTIN P. VESSEY, M.D.

HELEN A. DOLL, M.Sc.

University of Oxford
Oxford OX3 7LF, United Kingdom

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2. Doll H, Vessey M, Painter R. Return of fertility in nulliparous women after discontinuation of the intrauterine device: comparison with women discontinuing other methods of contraception. *BJOG* 2001;108:304-14.

To the Editor: Hubacher and colleagues conclude that the previous use of a copper IUD is not associated with tubal occlusion, whereas chlamydia infection is. However, inserting a "safe" IUD into a woman with an active chlamydial infection can spread the infection to the upper genital tract, resulting in pelvic inflammatory disease. Hubacher et al. argue that an IUD is suitable for women who are not likely to be at risk for sexually transmitted diseases, but chlamydia is common and is often unrecognized. The problem is greater when an IUD is used for postcoital contraception and there is no opportunity for screening. In our opinion, there is no reason to pardon the IUD.

VERONIQUE VERHOEVEN, M.D.

DIRK AVONTS, M.D., PH.D.

LIEVE PEREMANS, M.D.

University of Antwerp
2610 Wilrijk, Belgium
verover@uia.ua.ac.be

The authors reply:

To the Editor: Vessey and Doll state that long-term use of copper IUDs may impair fertility. We disagree that our case-control study did not include enough long-term use of the IUD to show this putative effect. Vessey and Doll cite odds ratios based on data from the control group of infertile women; however, if their reasoning were applied to our second control group of primigravid women, they might have concluded that the longer a woman uses a copper IUD, the less likely she is to become infertile. With these women serving as controls, the odds ratios for tubal occlusion associated with IUD use of 6 months or less, 7 to 12 months, and 13 or more months were 1.4 (95 percent confidence interval, 0.6 to 3.6), 1.0 (95 percent confidence interval, 0.3 to 3.0), and 0.6 (95 percent confidence interval, 0.3 to

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1.4), respectively. On the basis of the interpretation of our data and the research of others,^{1,2} we stand by our conclusion that copper IUDs do not impair fertility.

Chlamydia is common and often goes unrecognized, as Verhoeven and colleagues state, but withholding the IUD is not the answer if a woman says she is in a mutually monogamous relationship and has no clinical signs or symptoms of genital tract infection. In Belgium,³ the rates of cervical chlamydial infections in women who opted for an IUD were far lower than the rates in women who used oral contraceptives (presumably as a result of a combination of self-selection and careful screening). Perhaps, then, the fear with regard to chlamydia is misdirected. At the time of insertion of the IUD, bacteria can be pushed into the upper genital tract; though they require validation, clinical studies indicate that the rates of pelvic inflammatory disease, even in the presence of cervical infection, are within or below the reported ranges without IUD insertion.⁴ Even when sexually transmitted diseases are more prevalent, the increased risk of pelvic inflammatory disease attributable to IUD insertion is estimated to be very low (about 1 in 667).⁵ Blaming the IUD for problems that require a bacterial pathogen is misleading. We believe that decisions about contraception should be based on the best available evidence, rather than on clinical opinion. A growing body of literature indicates that IUD use is far safer than previously thought.

DAVID HUBACHER, PH.D.

Family Health International
Research Triangle Park, NC 27709
dhubacher@fhi.org

ROGER LARA-RICALDE, M.D.

Instituto Nacional de Perinatología
Mexico City 11000, Mexico

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GB Virus C and Mortality from HIV Infection

To the Editor: The reports of Xiang et al.¹ and Tillmann et al.² (Sept. 6 issue) further document that coinfection with the apparently nonpathogenic flavivirus GB virus C (GBV-C, or hepatitis G virus) prolongs survival in patients infected with the human immunodeficiency virus (HIV). As the accompanying editorial³ emphasizes, there are no causal inferences to be drawn from these observations, and the suggestion that therapy with GBV-C might improve survival among HIV-infected patients is correctly labeled as "premature." Although viral cross-talk of this sort has been described in

a number of other experimental systems,⁴ there are other possible explanations for the "protective" effect. For example, a potent cytotoxic-T-lymphocyte response to one viral infection may reduce the level of cytotoxic-T-lymphocyte activity directed to infection by a second virus.⁵ Persons who have a strong cytotoxic-T-lymphocyte response to HIV may have more difficulty mounting such a response to GBV-C and may thus be less likely to clear GBV-C infection. Tillmann et al. demonstrate no clear protective effect of exposure to GBV-C (as determined by a test for anti-E2 antibodies) but do demonstrate an obvious "protective" effect in those in whom GBV-C RNA was detected. Failure to clear active GBV-C infection may thus be an indirect marker of a particularly potent cytotoxic-T-lymphocyte response to HIV. This hypothesis, which can be readily tested, predicts that "therapeutic" coinfection with GBV-C would have no benefit for HIV-infected patients.

DONALD E. MOSIER, PH.D., M.D.

FRANCIS V. CHISARI, M.D.

Scripps Research Institute
La Jolla, CA 92037
dmosier@scripps.edu

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To the Editor: We are concerned that the analysis of Xiang et al. may not have taken into account the changes that occurred in the management of HIV between 1988 and 2000. These changes have dramatically decreased mortality from HIV. On the basis of the data presented in the article by Xiang et al., we calculate that 27 of the 144 patients with GBV-C viremia (19 percent) enrolled in the study before 1990, as compared with 67 of the 218 patients without GBV-C viremia (31 percent, $P=0.005$). It is unclear how the investigators adjusted for this difference. The conclusion regarding improved survival may be confounded by the era of HIV therapy.

ALEXANDER R. MACALALAD, M.D.

DAVID R. SNYDMAN, M.D.

New England Medical Center
Boston, MA 02111
amacalalad@lifespain.org

To the Editor: In cases of coinfection with hepatitis C virus (HCV) and HIV, differences in the progression of HIV infection according to the HCV genotype have been reported.¹ Three studies of GBV-C and HIV — those of Yeo et al.,²