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International Forum

Pelvic Inflammatory Disease and the Intrauterine Device: A Causal Relationship?

DAVID A. EDELMAN, PhD, *the Associate Director for Research for the International Fertility Research Program (IFRP), Research Triangle Park, NC, USA, provides an overview of the relationship between the occurrence of pelvic inflammatory disease (PID) and the use of intrauterine devices and identifies some pertinent points for discussion by an International Forum of experts.*

Over the past five years, there has been a gradual decline in the number of intrauterine device (IUD) users, at least in the USA. This decline may be attributed to the adverse publicity given to IUDs during recent years, particularly that about the increased risk to the IUD user of acquiring pelvic inflammatory disease (PID).

In 1977 the Conception Control Subcommittee of the Panel on Review of Obstetrical-Gynecological Devices of the US Food and Drug Administration (FDA) recommended that IUD labeling include the statement that "IUD use is associated with a three- to fivefold increase in infection rate" (8). This recommendation was primarily based on the results of epidemiologic studies, in particular, case-control studies designed to assess the association between IUD use and PID.

Table I summarizes the major results and some of the features of these epidemiologic studies in which the contraceptive practices of a group of women with PID (cases) were compared to those of a group of women without PID (controls). The study data are used to compute an odds ratio, which is the ratio of the odds that an IUD user will have PID to the odds that a nonuser will have PID. When applicable, odds ratios and their approximate 95% confidence limits have been computed for the studies listed in Table I.

An odds ratio that is significantly greater than 1 implies an increased risk of PID among IUD users compared to nonusers. The significance of the odds ratio is that it is the statistic that is usually quoted in reference to the "increased risk" of PID among IUD users compared to nonusers.

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The studies in Table I point to an increased risk of PID among IUD users; even in the studies in which the odds ratio is not significantly different from 1, there is nevertheless an elevated risk.

Except for the study of Vessey et al (15), the studies listed in Table I do *not* provide any estimate of the magnitude of the increased risk of PID to the IUD user; they indicate only an association between IUD use and PID and do *not* provide evidence to ascertain whether there is a cause-and-effect relationship between IUD use and PID.

Weström et al (16) reported a threefold increased risk of PID among IUD users compared to nonusers. In a reanalysis of these data, Gray (5) found that the risk was increased only for nulliparous women under 26 years of age.

In a prospective study of 750 women who had Cu-T IUDs inserted and who were followed up for one year, Osser et al (9) found similar rates of laparoscopically verified PID for women of different ages and parities (16–25 years, 26+ years; nulliparas, multiparas).

Vessey et al (15) estimated the magnitude of the increased risk of PID for IUD users compared to nonusers (see Table I): the increased incidence of PID among IUD users was only 1.65/1000 woman-years, and when compared with the nonusers, the IUD user was at a 3.5-fold increased risk of PID.

There is as yet no evidence that any one type of IUD is associated with a higher rate of PID. Data from the Cooperative Statistical Program (14) did not indicate any significant difference in the PID rates for different nonmedicated IUDs (Lippes Loop, Margulies Spiral, Birnberg Bow, steel ring and Saf-T-Coil). The rates for these IUDs are similar to those for the Dalkon Shield and Progestasert (Table II). Similar data for copper-bearing IUDs, such as the Cu-T or Cu-7, are not available.

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Table I. Summary of studies to assess the association of PID and IUD use. Source: Edelman et al (2).

Reference	Study Description	Odds Ratio (95% Confidence Limits)	Results/Comments
12	Case-control. 50 emergency room patients with a putative diagnosis of PID. 50 controls #1: women attending general medical clinic. 50 controls #2: women appearing with sick children in pediatric emergency room. Cases matched to controls by age, marital status and time since last pregnancy.	9.3 (4.2–20.9)	PID diagnostic criteria: temperature 99.8 F and above and two of the following: lower abdominal pain and tenderness, cervical motion tenderness, adnexal tenderness. The control groups were similar with respect to their contraceptive practice distributions. Types of IUDs not stated.
6	Case-control. 91 cases with a hospital discharge diagnosis of PID, salpingitis, endometritis. 38 controls discharged from same hospital with admitting diagnosis of acute appendicitis.	1.9 (0.5–7.2)	Types of IUDs not stated.
4	Case-control. 50 febrile cases (temperature ≥38 C), 100 afebrile cases, 100 controls. Cases: uterine or adnexal tenderness on pelvic examination, no diagnosis other than PID to explain "illness" at initial emergency room visit or within 1 month. Controls: emergency room patients without complaint of abdominal pain or discomfort and without diagnosis of any gynecologic problem.	5.1 (2.5–10.5) for febrile cases. 2.7 (1.4–5.0) for afebrile cases.	Past diagnosis of PID: febrile cases, 58%; afebrile cases, 75%; controls, 43.5%. IUDs: Lippes Loop, Saf-T-Coil, Dalkon Shield, Cu-7.
16	Case control. 515 cases of laparoscopically verified acute salpingitis. 1545 controls: women matched for age and date of birth selected from a regional population register, contacted by a postal questionnaire (response rate, 78.8%). 156 controls excluded for a number of reasons (eg, current pregnancy). Excluded women using no contraception. Only 741 controls included in analysis.	3.0 (2.2–4.1)	IUDs: Lippes Loop, Saf-T-Coil, Cu-T, Cu-7.
5	Reanalysis of Weström et al data (16).	Age / Multips / Nullips 16–20 / 1.1 / 8.1[a] 21–25 / 1.1 / 7.5[a] 26–30 / 1.6 / 2.6 31–35 / 3.1 / – [a] *Significantly different from 1 ($p < 0.10$).*	Only nulliparous women ≤25 years of age at an increased risk of PID.
3	Case-control. 173 cases; 173 controls matched for age, race, marital status, parity, number of sex partners, presence of gonorrhea.	4.4 (1.9–5.7)	Odds ratio = 2.8 for gonococcal PID, 6.5 for nongonococcal PID. IUDs: Dalkon Shield, Lippes Loop, Saf-T-Coil, Cu-7.
13	Case-control. 101 cases; women with recurrent PID were excluded. 101 controls matched for age, current marital status, interval since last pregnancy termination.	3.3 (0.9–5.9)	Types of IUDs not stated.
17	Incidence of acute PID documented in a poor urban population in a 1-year period. 902 acute first episodes of PID; 478 termed definite.		PID diagnostic criteria: temperature over 99.8 F, lower abdominal cervical motion tenderness, visualization of acute supracervical pelvic inflammation at laparotomy. Attack rates/1000 woman-years of first definite episode of PID among women within 1 year of pregnancy termination, by contraceptive: IUD, 66.2; oral, 13.4; vaginal foam, 25.2. Attack rate for overall female population (15–44 years of age) 9.6/1000 women per year.
7	Gonorrhea screening program. 1706 women screened over a 9-month period. Symptoms of PID: complaints of pelvic pain or abdominal cramping other than during menstruation or pelvic tenderness on physical examination.	2.2 (1.8–2.7) for women with symptoms of PID.	Method / % with Symptoms Oral / 20.6 IUD / 33.3 Other / 16.2 Method / % with Gonococcal PID Oral / 0.7 IUD / 3.1 Other / 0.2

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Reference	Study Description	Odds Ratio (95% Confidence Limits)	Results/Comments
1	1583 consecutive cases of sterilization at four hospitals. Evidence of PID noted by surgeons.		Evidence of PID: tubal adhesions, hydrosalpinx, adnexitis, uterine adhesions, enlarged ovary. Contraceptive Method — % Cases with Tubal Adhesions Never used (N = 213) — 8.9 IUD only (N = 162) — 12.3 Pill only (N = 612) — 4.9 Rates for never used and IUD-only groups not different ($p > 0.10$). Pill-only group rates lower than rates for never used and IUD-only groups ($p < 0.05$).
10	Observations of PID in 200 women undergoing transvaginal tubal sterilization. Retrospective study based on operative notes.	12.3 (4.4–34.0)	Criteria for diagnosing PID included one or more of the following: adhesions, congestion, tubal occlusion with clubbing, oozing of pus from fimbria. Contraceptive Method — PID No. — PID % IUD (N = 101) — 28 — 27.7 Hormonal (N = 73) — 3 — 4.1 None (N = 26) — 0 — 0.0 Risk of PID increased with duration of IUD use. Time from IUD Insertion (years) — % Cases with PID <1 — 13 1–3 — 24 4–6 — 28 7+ — 50
11	Histologic examination of tubal specimens from 49 IUD users and from 1500 nonusers. All patients underwent voluntary laparoscopic sterilization.		Nonbacterial chronic salpingitis noted in 46.9% of IUD users versus 0.7% of nonusers. Among the IUD users, those with normal oviducts or salpingitis were similar in terms of age, race, marital status, parity, type of IUD, duration of IUD use and symptoms. IUD types: Dalkon Shield, Lippes Loop, Saf-T-Coil, Majzlin Spring; 44.9% were Dalkon Shield users and reflected use of the Shield in the community.
15	Long-term follow-up study of 17 032 white women aged 25–39 using different methods of contraception in 17 family planning clinics. Prospective study.		First event rates/1000 woman-years of salpingitis, PID, endometritis, standardized for age, parity, social class, smoking.[a] IUD User — Nonuser Inpatient only — 2.02 — 0.57 Inpatient and outpatient — 2.59 — 0.94 [a] *IUD user rates significantly higher than nonuser rates ($p < 0.001$).*

Table II. PID rates (per 100 woman-years) for different types of IUDs (2).

Months from Insertion	Lippes Loop, Birnberg Bow, Margulies Spiral, Steel Ring, Saf-T-Coil		Dalkon Shield		Progestasert	
	Woman-Years	PID Rate	Woman-Years	PID Rate	Woman-Years	PID Rate
≤1	1882	5.8	185	5.4	511	8.0
2–12	16 144	2.6	1468	2.5	3700	3.5
13–24	10 588	2.2	728	2.5	–	–

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Thus, the available evidence suggests that, although there is an increased risk of PID among IUD users compared to nonusers, the magnitude of the risk is small. Since the increase in risk does not appear to be similar for women of all ages and parities, it may be that other factors, such as a woman's life-style, have a greater influence on the risk of PID than the IUD per se.

These relationships between IUD use and PID have not as yet been well defined. Some investigators claim that any relationship between IUD use and PID is an incidental one, and others claim there is a cause-and-effect relationship.

To date the magnitude of the increased risk (if any) to IUD users has not been estimated. Also, questions of whether all types of IUDs are associated with similar rates of PID have not been resolved.

These controversies and uncertainties concerning the relationship between IUD use and PID were submitted to an International Forum of experts for comment. The experts were asked to consider the following questions as they prepared their comments.

1. Do the available data confirm the existence of a causal relationship between IUD use and PID? If such a relationship exists, what are the responsible factors?

2. Is such a relationship associated with all or only some IUDs?

3. Is the risk of PID associated with IUD use the same for all users, or is it greater for those women in certain age and parity groups? What other sociodemographic factors are associated with an increased risk of PID?

4. What steps can be taken to minimize the risks of PID among IUD users?

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MARTIN P. VESSEY, MD, *of the Department of Social and Community Medicine, Oxford, England,* ***discusses the Oxford-Family Planning Association prospective study of IUD-related PID and cautions that patient "background" must be considered in any study of the association between IUD use and PID.***

While some of the epidemiologic studies cited by Dr. Edelman in his review have obvious shortcomings, the general consistency of the findings is impressive, and, in my opinion, there can be no serious doubt that there is a causal relationship between IUD use and PID.

The Oxford-Family Planning Association prospective study appears to be the only investigation currently in progress that is capable of providing an estimate of the absolute size of the PID risk associated with IUD use. The data quoted by Dr. Edelman were published in 1976 and related to only 69 women with a new diagnosis of PID (1). Since that

time, the number of such cases has more than doubled and we are presently undertaking a detailed review of the clinical information for each woman prior to carrying out a comprehensive analysis of the relationship between IUDs and PID.

It is, of course, important to stress that the "background" frequency of PID varies enormously in different population groups. It should be noted that the participants in the Oxford-Family Planning Association study are all married, mostly parous and predominantly from the higher social classes. Their background risk of PID is, therefore, likely to be low, and care should be taken in extrapolating findings based on their experience to other groups of women.

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MAX ELSTEIN, MD, MRCOG, *Professor of Obstetrics and Gynaecology at the University Hospital of South Manchester, University of Manchester, West Didsbury, Manchester, England, states that the risk that an IUD user might develop PID "must be related to the background prevalence of sexually transmitted diseases in the population . . . ." He also suggests that the cervical appendage of the IUD facilitates the ascent of organisms up the genital tract.*

The risk that the IUD user might develop PID must be related to the background prevalence of sexually transmitted diseases in the population under review. The evidence does suggest that in the clinic populations of the USA the incidence of gonorrhea is higher than that found in Western Europe, for example. Keith et al (4) looked specifically at gonorrhea rates in a North American family planning clinic and found a high incidence of cervical gonorrhea (9.5%) in 168 IUD users. A similar high rate of 10.6% in 802 oral contraceptive users was far higher than the 1.7% found in the 60 barrier method users. In studies conducted at a family planning clinic in the United Kingdom, the incidence of gonorrhea was found to be extremely low (0.4%), even though 70% of the women surveyed were single girls (5). Indeed, in pregnancy there is a similar high incidence of gonorrhea ranging from 4.0% to 7.3% in an American series, compared with 0.2%–0.6% in Britain (8).

Thus, in British reports, PID in IUD users has not been found to be a major problem, as compared to those emanating from the USA (7). Nevertheless, in a detailed prospective cohort study conducted in a relatively upper economic class population in Oxfordshire in the United Kingdom, Vessey et al (11) reported convincing evidence of an increased risk of PID in IUD users, as compared to nonusers, even though the absolute PID incidence was lower than most US studies. In the studies of PID reported from Lund in Sweden, Weström et al (13) also report the higher incidence of PID in IUD users, stating that the relative risk of acute salpingitis for any woman using an IUD was threefold, as compared to that of nonusers. Indeed, for nulliparous women using the IUD, the corresponding risk was found to be sevenfold. Gray (3) analyzed the data of Weström et al (13) further and reiterated the significantly increased rate of PID in the young nulliparous IUD user. He rightly pointed out that this group would contain a higher percentage of single women; this is suggested in the original report. These women were thus likely to have more sexual contacts than the older women. The increased salpingitis rate may then be explained as resulting from a combination of the presence of an IUD and subclinical sexually transmissible organisms leading to invasion of the upper genital tract.

Thus, the IUD probably acts as a means of facilitating the ascent of organisms up the genital tract in a woman prone to develop PID because of her sexual behavior pattern. Weiner et al (12) recommended that the IUD was relatively contraindicated in all nulliparae, especially those with a history of previous pelvic infection or a life-style predisposing to it.

The next question posed is whether or not all IUDs are associated with this risk. In 1967, Elstein (1) drew attention to the greater incidence of signs and symptoms suggestive of pelvic inflammation in women using an IUD with a cervical appendage. The view that tubal damage resulted was supported by his findings in a salpingographic study published in 1969 (2). From these findings he recommended that the IUD should be reserved for parous women for whom the retention of fertility potential was not vital.

The role of the cervical appendage in facilitating the ascent of organisms has been studied in detail in subjects undergoing hysterectomy by Sparks et al (9, 10). The non-IUD-containing uterus is sterile from a level above the lower half of the cervical canal. In the uterus containing an IUD with a cervical appendage, be it monofilamentous or mul-

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tifilamentous, bacteria are present throughout the cervical canal and into the uterine cavity, thus demonstrating the ascent of bacteria in relationship to the IUD tails. In women wearing IUDs with no tails, similar findings were obtained to those obtained in women not wearing IUDs.

The role of the cervical appendage in facilitating the ascent of organisms was clearly demonstrated in a further study using an in vitro model comprising a cervical mucus column containing a cervical appendage (6). Potentially pathogenic organisms were shown to colonize the cervical mucus adhering to the threads above the cervical mucus column, irrespective of their physical nature. These findings support the suggestion that in vivo vaginal and cervical bacteria migrate along the mucus-covered tails of IUDs. As a result of these studies, it was proposed that an IUD with no cervical appendage be fabricated. This IUD would thus require some other means of localization and, perhaps, of removal. In the meantime, young women who wish to retain their fertility potential and yet find the existing IUDs the most acceptable method of contraception should be advised to be meticulous about their personal hygiene, choose faithful partners and be so likewise. The physician fitting a currently available IUD might consider cutting the thread so short that it remains high up within the cervical canal.

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LARS WESTRÖM, MD, *of the Department of Obstetrics and Gynecology at the University Hospital, Lund, Sweden, discusses the relationship of PID and contraceptive use and suggests that PID rates in IUD users may be similar to those found in noncontracepting sexually active women, but cites a trend of increased risk of PID in young, never-pregnant IUD users.*

A prerequisite for PID is, in the vast majority of cases, an often sexually transmitted lower genital tract infection (LGTI) in a sexually active woman. This statement is based on the following observations: (a) Nontuberculous infections of the fallopian tubes are in 99% of the cases caused by ascending (canalicular) spread of an LGTI (4, 15); (b) PID in women who are not sexually active is a rarity (9, 12);(c) The annual incidence of PID per 1000 sexually active women decreases with increasing age of of the women (9); (d) In women under the age of 26 years, the majority of tubal infections are caused by microbial agents that are transmittable during sexual intercourse (10); and (e) Iatrogenic factors account for 10%–12% of the PID cases (15). Thus, two major risk factors for PID are (a) a sexually transmitted disease (STD) in the sexual partner(s), and, accordingly, a risk increase proportional to the number of sexual partners, and (b) a doctor performing diagnostic or therapeutic gynecologic procedures, unaware that the woman has an LGTI.

Does the use of a specific contraceptive method affect the establishment of an LGTI? On this topic, the available information is diverse and complex. The important problem of whether or not there is a correlation between a woman's risk of acquiring an STD and her choice of a specific contraceptive method has not been properly analyzed. Reports on contraceptive usage by women attending venereal disease clinics indicate that the distribution of dif-

ferent contraceptive methods among such women is roughly the same as that among sexually active women in corresponding age groups in the general population (J. Wallin, personal communication; Mårdh et al, unpublished data, 1979). On the other hand, proper use of barrier methods has been reported to have a protective effect against infections caused by *Trichomonas vaginalis* and *Neisseria gonorrhoeae* (2, 6). Users of oral contraceptives (OCs) have been reported to have higher rates of uncomplicated gonococcal and chlamydial infections than women not using OCs (3, 11).

Does the use of a specific contraceptive method affect the mechanism(s) of ascent to the fallopian tubes of an LGTI? Many investigators have observed an increased rate of IUD-using women among PID cases, as compared with non-PID controls. Through the use of calculations of the odds ratios, this has been interpreted as an increased risk of PID among IUD users as compared to "nonusers," indicating that IUDs play a role in the mechanism(s) of the spread of a cervical infection. However, "nonusers" do not constitute a homogeneous group of women. If other contraceptive methods used by women included among the "nonusers" of IUDs have a protective effect against infections, then the difference between the IUD users and the correct reference group, ie, noncontracepting sexually active women, might disappear.

In an attempt to define this, we extended the analysis of earlier-used control material (14) and studied the monthly prevalence per 1000 women of contraceptive usage, pregnancies and "sexual inactivity" in women 20–29 years of age registered in the city of Lund during 1970 through 1974 (Weström et al, unpublished data, 1979). The results are summarized in Table I.

Table I shows that the rate of PID per 1000 woman-years of IUD usage was 1.5-fold that of the sexually active noncontraceptors, whereas the use of OCs and barrier methods seems to protect the women from PID when compared with the noncontraceptors. If the material was divided into never-pregnant and ever-pregnant women, the figures for the OC users and users of barrier methods were the same as in the total material. Among the never-pregnant IUD users, the risk was calculated to be 11.8 per 100 woman-years, and for the ever-pregnant IUD users to be 3.4 per 100 woman-years, ie, the same as in noncontraceptors. The risk in never-pregnant noncontraceptors was 4.2 per 100 woman-years. The IUDs used were Lippes Loops C and D, Saf-T-Coils, Cu-T 200 and Cu-7 200. There were no differences among the various types of IUDs in relation to PID risk. It should be pointed out, however, that IUDs were rather uncritically used in never-pregnant women in the early 1970s.

Again, the difference might be explained by unknown psychological factors causing women at high risk of STD to choose IUDs. In an attempt to circumvent this, a group of Swedish investigators from Linköping (5) studied contraceptive usage and PID in 744 women treated for cervical gonorrhea. After exclusion of pregnant and sterilized women, as well as some from whom the information was judged as unreliable, 672 women remained. These were divided into groups of IUD users, OC users and "others." There were no differences in parity, socioeconomic status, number of sexual contacts and previous episodes of gonorrhea among the three groups of women. Eighty-seven instances of laparoscopically verified PID were diagnosed. Among the IUD users, 23.5% developed PID. The corresponding figures for OC users and the "others" were 8.8% and 12.9%, respectively. The authors concluded that use of OCs seems to protect the women from the

Table I. PID in women 10–29 years of age using different methods of contraception (Lund 1970–1974).[a, b]

					Noncontraceptors		
	Total	IUD users	OC users	Barrier users	Sexually active	Not sexually active	Pregnant
Mean prevalence/1000 women	1000	70	389	168	120	120	133
Sum of woman-years	41 798	2940	16 222	7007	5038	5038	5553
Number of PID cases	571	153	148	98	172	0	0
Index PID/100 woman-years	1.3	5.2	0.9	1.4	3.4	0	0

[a] *Mean female population in age group = 8386.*
[b] *Information for table from Weström et al, unpublished data, 1979.*

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ascent of a cervical infection. This is supported by our study mentioned above and by observations of others (3, 16).

The whole panorama of the interactions between sexual behavior, epidemiology of genital infections and contraceptive usage is at the moment too complex and insufficiently analyzed to allow definite conclusions. From the epidemiologic observations, we can, however, outline two trends: (a) an increased risk of PID in young never-pregnant IUD users and (b) a protective effect of OC usage.

We know that the myometrial muscular activity pattern is different in uteri with and without IUDs (8) and in uteri under and not under the influence of OC hormones (1). Furthermore, orgasmic contractions in the uterus have been reported (7), as well as pregnancy-induced irreversible functional damage to the adrenergic nerve plexus of the myometrium (13). These observations fit with the epidemiologic findings of differences in PID rate between IUD users and OC users, between never-pregnant and ever-pregnant women, and the correlation between PID and sexual activity. If true, this indicates that myometrial activity is a key factor in the ascending spread of a cervical infection. Further research is necessary.

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STELLAN OSSER, MD, PERCY LIEDHOLM, MD, and NILS-OTTO SJÖBERG, MD, *of the Department of Obstetrics and Gynecology, University of Lund, Malmö, Sweden, report findings of a 2.1-fold increased risk of PID in IUD users. They attribute this to (a) bleeding irregularities with the IUD that change the vaginal milieu, facilitating ascending infections, and to (b) diminished natural resistance to bacteria as a result of the inflammatory response of the endometrium and the oviduct to IUD insertion.*

Most published papers indicate a correlation between IUD use and PID. In some publications, however, this risk seems to be overestimated. One cause of this may be the misinterpretation of the clinical symptoms, as the only way to confirm a diagnosis of salpingitis is through laparoscopy. Another cause for the overestimation of PID could be bias in a study's control group, as when a large number of women in the lower age groups drop out of a study.

We have recently completed a study where we compared a group of laparoscopically verified PID patients to a sexually active age-match control group from the same sociodemographic region in Sweden. This study showed a 2.1-fold increased risk of developing PID for women using the IUD.

We think that the bleeding irregularities associated with IUD use change the vaginal milieu, which

facilitates ascending infections. It is also possible that the inflammatory response of the endometrium and the oviduct may diminish the natural resistance to bacteria that now and then enter the uterine cavity and the fallopian tubes.

We were able to confirm our earlier observation that parity does not affect the risk of PID associated with IUD use. We found the risk for parous women to be 2.6 and for nulliparous women, 1.6. We also could not demonstrate any correlation between age and increased PID risk with IUD use. We found, however, an age-dependent correlation between the time of IUD insertion and the onset of the PID: women under 25 years of age were more prone to develop PID within one month after insertion, possibly because of a too short period of sexual abstinence after the IUD insertion.

Our experience is mainly confined to Cu-T and Cu-7 IUDs. We have not registered any difference in PID incidence between use of these two devices. In our latest investigation, a small number of patients with inert plastic IUDs were analyzed separately. No difference in the occurrence of salpingitis was seen between the users of plastic and copper-medicated IUDs. We have, however, observed that women using the copper IUDs have a lower incidence of gonorrhea. This clinical finding confirms the in vitro studies that show that copper may offer protection against gonorrhea.

To avoid potential cases of PID associated with IUD use, we recommend the following: (a) The IUD should be inserted immediately after cessation of menstruation to avoid cervical trauma. (b) The IUD should never be inserted when vaginal infection is suspected. (c) Sexual abstinence should be observed for some days following insertion. (d) The IUD thread should be cut short to avoid a knot developing in the thread on which vaginal debris could accumulate and become a matrix for bacteria. (e) If gonorrhea or chlamydia is suspected, a culture should be done before insertion.

NICHOLAS H. WRIGHT, MD, MPH, *of the Department of Community Medicine, Rutgers Medical School, College of Medicine and Dentistry of New Jersey, Piscataway, NJ, USA, discusses the clinical importance of the relationship between IUD use and PID.*

A variety of epidemiologic evidence suggests persuasively that the chance of having upper pelvic infection (PID) is increased significantly among IUD wearers, and, further, that the relationship is a causal one. The finding of higher risk emerges from a range of studies, including those documenting evidence of asymptomatic pelvic infection among formerly IUD-wearing fertile women seeking tubal ligation and both case-control and cohort studies of women with acute symptomatic PID defined laparoscopically or clinically. The relationship is not only consistent but also biologically plausible. Based on the evidence reviewed by Dr. Edelman, there seems little need to argue this point further. Other questions, however, remain.

How important is the increased risk to IUD wearers clinically? If, *at minimum*, the increased risk to IUD wearers is about a fourfold one, it is not at all clear what the underlying incidence of PID is among nonwearers. One study estimated the incidence of PID in a population of lower socioeconomic class women as one acute event per 100 women per year (10). Although there seem to be no other studies of PID incidence using a standard definition in a closed or otherwise defined population, it is generally agreed that for most nonwearers the risk of acute PID is less, and probably very much less, than 1% per year (5). Among IUD wearers, most attacks of acute PID are rather mild and can be treated without removing the device. While the amount of risk of later involuntary infertility among former IUD wearers is unsettled, initial evidence is reassuring (9). Although PID has long been associated with later ectopic pregnancy, it does not appear that IUD use increases the risk of ectopic gestation after the IUD is removed for the woman to become pregnant (6).

While most women will find the elevated PID risk with IUD use acceptable, some will not. It has been suggested that some younger women may be at much higher risk from IUD use (1), and it seems likely that the incidence of acute PID is generally higher among younger women, especially those who are unmarried or formerly married (10). While sexual behavior variables may explain these differentials, they do not satisfactorily explain case-control differences in IUD use in at least one study (7).

Among nonpregnant women, there is no reliable evidence that different intrauterine devices carry different risks of PID. Unfortunately, the largest body of data bearing on this issue failed to use a uniform clinical definition of PID (8). Although a well-controlled study remains to be done, it does seem reasonable to hypothesize that copper-bearing IUDs may carry a lower risk of PID. The support for this notion lies in the epidemiology of PID. It has long been observed that the onset of upper

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pelvic infection is strongly correlated with the immediate postmenstrual phase of the cycle (3). It seems likely that, by increasing both menstrual flow and its duration in many wearers, the IUD facilitates PID by any of a number of resident microorganisms (4). Since it has been shown that the copper-bearing IUDs are associated with a smaller increase in menstrual flow than noncopper IUDs (2), it is plausible to ask whether or not they may also minimize the risk of acute PID. Because the underlying incidence of acute PID is low, this question might best be answered by a case-control design in a population using a variety of IUD types, including copper-bearing ones.

The clinician can justify minimizing the risk of PID to women interested in IUDs based in part on documentation, but he must also necessarily rely on clinical judgment. In a population of women of lower socioeconomic background with a higher baseline incidence of PID and less access to medical care, one might treat the PID vigorously and remove the IUD. At the other end of the socioeconomic ladder, it might seem reasonable to treat the PID, but remove the IUD only if the infection was unresponsive. Other clinicians may prefer to avoid the IUD altogether in younger women whose sexual mores might be expected to expose them to a higher risk of PID. Since there is evidence that some barrier contraceptives may actually protect against the PID that is associated with venereal disease, such methods may be preferable in these subgroups.

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ROBERT SNOWDEN, PhD, *Co-director of the University of Exeter's Institute of Population Studies, Exeter, England,* *discusses the relationship of the IUD's mechanism of action to the occurrence of PID and to subsequent fertility, especially among young nulliparous women who discontinue IUD use to achieve pregnancy.*

The available literature suggests that there is an association between PID and IUD use, but the nature of this relationship remains unclear. Data collected in the United Kingdom (UK) network of IUD clinics between 1972 and 1976 suggest that estimating the incidence of PID is difficult because of uncertainty surrounding the diagnosis and reporting of this complaint.

It is known that the incidence of PID among IUD users is higher that that among nonusers. But the diagnosis of PID is almost entirely dependent upon clinical judgment, and this makes assessments of incidence unreliable for comparative purposes.

Most reports concerning PID among IUD users indicate numbers of cases that require removal of the device, although these may account for only a portion of the total number of IUD patients experiencing this condition.

In the UK study, about one case of PID is reported for every 250 IUD insertions each year, and this rate varies according to the device inserted: from 1:104 for the Cu-7 (Gravigard, G.D. Searle and Co, Chicago, IL, USA) to 1:385 for the Lippes Loop B (Ortho Pharmaceutical Corp, Raritan, NJ, USA). In about half of the cases of PID that occurred with a device in situ reported in the UK, the device was removed, either at once or after initiation of antibiotic treatment.

Some doctors treat mild inflammatory reactions with antibiotics while the device remains in the uterus. Most doctors will remove an IUD if there is a gonococcal infection because they believe that the presence of an IUD may encourage the infection to ascend into the uterus and fallopian tubes. It has been suggested that copper-carrying devices have a bactericidal effect that provides some protection against ascending gonococcal infection, but it is

unlikely that concentratons of copper sufficient to have any therapeutic value are achieved.

My view is that the mode of action of the IUD is related to the incidence of PID in IUD users. Most reviewers and researchers concerned with ascertaining the IUD's mechanism of action accept that, regardless of the precise mechanisms involved, the IUD's presence causes an inflammatory response in the endometrium (1-3). They believe this inflammatory response also changes the biochemistry of the endometrium, which in turn reduces the likelihood of nidation. The greater the inflammatory response (in both amount and virulence), the more likely nidation will not take place. The two principal means of obtaining a strong inflammatory response are associated with the amount of surface contact between the endometrium and the IUD and the release of substances from the IUD within the uterine cavity.

The difficulty of clinically diagnosing PID may also be exacerbated by the apparent absence of an observable symptomatology. This, in itself, is cause for concern, but the relationship between a history of PID and subsequent ability to conceive should also be considered. With more young nulliparous women turning to the IUD as the preferred means of fertility regulation, the effect of its use on the ability to conceive when conception is desired becomes an important issue.

One study in the UK (4) indicates that, compared to nonusers, IUD users have a handicap in achieving a desired pregnancy after the IUD is removed for this purpose. But after a period of 3½ years, this handicap is no longer present. Despite a slow start, virtually all the IUD users in this study recovered their fertility; however, the sample was confined to women between 25 and 39 years of age.

Further studies are required to examine the effect of IUD use and different models of IUDs on subsequent fertility among younger women, so that the relationship of IUD use to PID and subsequent fertility can be adequately determined. Because of the possible intervention of other variables associated with sexual behavior and with idiopathic subfertility among young nulliparous IUD users, it will be difficult to determine whether or not a causal relationship exists between IUD use and PID.

A review of the literature on IUDs reveals that (a) IUD use increases the likelihood of PID among users and that, allegedly, PID is more prevalent among young nulliparous IUD users than among older parous IUD users; and (b) there is an increased likelihood that a normal pregnancy will prove difficult to achieve following PID. (It is not known whether such difficulties are mediated by the age of the woman concerned.) Thus, there is a prima facie case that young nulliparous women are at greater risk of having difficulty in starting and maintaining a pregnancy after IUD use, mainly because of their increased exposure to the risk of PID.

In recent years, IUD use by young nulliparous British women has increased to account for about one third of all IUD insertions. Consequently, a systematic study of the long-term effects of IUD use by young nulliparous women is needed.

If it can be shown that the IUD's mechanism of action is related to some sort of inflammatory reaction, that PID is also related to a similar reaction, that such a reaction often provides no discernible symptoms and that a history of PID is related to subsequent difficulty in achieving fertility, then IUD use by those who may desire a pregnancy some time in the future is open to question. The most obvious way to minimize the risk of PID among such women may be to advise the use of another fertility regulation method.

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