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Intrauterine Copper Contraceptive: Update and Opportunities

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- **Dr Grimes** has received research support or has served as a consultant or speaker for ALZA, Berlex Laboratories, FEI Women's Health, Gynetics, GynoPharma, Mead Johnson, Organon, Ortho-McNeil, Parke-Davis, Pharmacia Upjohn, Schering AG, Schmid, Searle, and Wyeth-Ayerst.

This supplement is based on an audio conference held on July 5, 2006, among a group of thought leaders. These experts addressed critical issues and changes to the prescribing information for the ParaGard® T380A intrauterine copper contraceptive and the effect these changes may have on clinical practice.

The intrauterine device (IUD) is the most widely used reversible form of contraception in the world.¹ However, use of IUDs remains low in the United States despite the need for long-term, non-hormonal contraception. This may be due, in part, to persistent myths and misinformation regarding the safety and efficacy of the IUD and prescriber reluctance.² Recent changes to the FDA-approved prescribing information for the copper T380A IUD were based on data generated from decades of use that support the safety of IUDs. These changes are expected to make this contraceptive an attractive option for a greater number of women.³ This roundtable was convened to provide insight into the current recommendations for use of the copper T380A IUD.

- **Dr Arias** serves as a consultant to Barr, Berlex, Novo Nordisk, Ortho, Organon, Schering AG, Synova, and Wyeth.
- **Dr Shulman** has served as a consultant or speaker for Barr-Duramed, Berlex, FEI Women's Health, GlaxoSmithKline-Roche, Organon, Ortho-McNeil, and Wyeth. Dr Shulman also receives research support from Barr-Duramed, the Bears Care Foundation, the Kaplan Family Foundation, the National Center for Complementary and Alternative Medicine (NIH), and Wyeth.
- **Ms Moore** has served as a consultant or speaker for Berlex, Duramed, Organon, Ortho, and Wyeth.

TABLE 1

Attractive Features of Copper Intrauterine Contraception

Highly effective (equivalent to sterilization)
Offers long-term contraception
Safe
Immediately effective
High patient satisfaction
Reversible
Rapid return to fertility
Nonhormonal contraception
Cost effective
Offers broad options for timing of insertion

■ Counseling Patients With the Evidence: Features of the IUD

Counseling about contraception should include a discussion of IUDs. The copper T380A IUD possesses a number of characteristics that make it a very attractive contraceptive option (TABLE 1). The manufacturer’s patient product information brochure and checklist can facilitate discussion and should be given to patients who are interested in the copper T380A IUD.

Explaining Contraceptive Efficacy

Efficacy of the copper T380A IUD is among the highest of all contraceptives available (hormonal or nonhormonal methods).^{4,6} In 2 long-term studies, the annual pregnancy rate for years 0 to 8 was less than 0.4 per 100 women.⁶ This analysis, by the United Nations Population Fund/World Health Organization (UN/WHO), showed a 12-year cumulative pregnancy rate of 1.9 per 100 women for the copper T380A IUD based on experience in 7159 woman-years; no pregnancies were reported beyond year 8. In sharp contrast, the first-year pregnancy rate reported with typical use of combined hormone (estrogen/progestin) pills is 8%.⁷

Women report that the most important criterion for choosing a contraceptive is how well it works.⁴ However, many women do not fully understand the differences in efficacy among the various methods of contraception or the difference between “typical” and

The Copper IUD: Critical Counseling Points

- The copper intrauterine device (IUD) is an excellent alternative to sterilization for women who desire long-term contraception.
- IUDs may be offered to women who cannot or choose not to use hormonal contraceptives.
- IUDs may be inserted at any point during the menstrual cycle when pregnancy can be ruled out.
- IUDs may be inserted immediately following a first trimester pregnancy loss.
- Women at high risk of sexually transmitted infections choosing an IUD should be evaluated for such infections as indicated, including *Chlamydia trachomatis* and *Neisseria gonorrhoeae*.
- Patient counseling should include discussion of:
 - All contraceptive options
 - Small increase in the risk of pelvic infection that may occur in the 20 days after insertion
 - Reduction in overall risk of ectopic pregnancy compared with no contraception
 - Most likely cause of failure—expulsion. Risk of expulsion is highest during the first year of use, particularly within 3 months after insertion
 - Rare risk of uterine perforation (occurs about once per 1000 insertions)
 - Instruction on how to check for the IUD and its threads. Women should be advised that if they are unable to locate them, the device may have been expelled and alternate contraception should be used until they are able to see a health care professional
 - Menstrual abnormalities (spotting, light bleeding), which are common in the first 3 to 6 months after insertion
 - Possibility of dysmenorrhea, pain, cramping, and heavier or longer menstruation, which is increased with the copper IUD

“perfect” use data. Perfect use data should not be used in counseling patients because they are not reflective of real-life practices. Steiner et al have proposed a simplified approach that communicates contraceptive effectiveness better than traditional tables with numeric estimates of pregnancy risk (TABLE 2).⁴ This table categorizes sterilization, implants, hormone shots, and IUDs with and without hormones as “more effective”; oral contraceptive pills as “effective”; and barrier methods, spermicide, and behavioral methods as “less effective.”

TABLE 2

Categories of Contraceptive Efficacy

Effectiveness Group	Typical Success Rate
Sterilization (male and female) Implants (etonorgestrel subdermal implant) Intrauterine Device (copper T IUD, LNG IUS) Hormone Shot (depot medroxyprogesterone acetate, 3-month injection)	More Effective (effective for all users)
Oral Contraceptive Pills (combined pill and minipill) Vaginal Ring Transdermal Patch	Effective (effective for most users; however, more effective if used consistently and correctly)
Barrier Methods (male latex condoms, diaphragm, vaginal sponge, cervical cap, female condom) Spermicide Behavioral Methods (fertility awareness-based methods, withdrawal)	Less Effective (less effective for most users; however, effective if used consistently and correctly)

IUD, intrauterine device; LNG IUS, levonorgestrel intrauterine system.

Adapted from Steiner MJ, et al. *Obstet Gynecol.* 2003;102:709-717. Available at: <http://www.com>.

Regret After Sterilization and Reversible Alternatives

In the United States, more than 10 million women have undergone tubal sterilization.⁸ In 2002, 27% of women aged 15 to 44 years using contraception relied on sterilization. A systematic review of the published literature showed that women 30 years or younger at the time of sterilization were twice as likely to report regretting their decision as women older than 30.⁹ Women who undergo sterilization and later regret their decision may seek to reverse the procedure or use assisted reproductive technologies, which are expensive and often unsuccessful.

Like sterilization, IUDs provide long-term contraception. However, the contraceptive effect of the IUD is rapidly reversible. Underscoring this point, the WHO recommendations regarding sterilization state that “young women, like all women, should be counseled about the permanency of sterilization and the availability of alternative, long-term, highly effective methods.”¹⁰

Long-Term Cost Effectiveness of IUDs

Cost is an important variable that women must consider when choosing a contraceptive method. According to a model that examined effectiveness and cost, the copper IUD and the levonorgestrel intrauterine system are the least costly among 9

“I no longer even counsel numbers, I just talk about high, middle, and low tiers of effectiveness. The top tier can really be thought of as ‘forgettable contraceptives.’”

► DAVID GRIMES, MD

contraceptive methods compared.¹¹ Women may perceive tubal sterilization as free because it generally is covered by insurance. Although the acquisition cost of an IUD may be daunting to women whose insurance plans do not provide coverage, the manufacturer does offer a payment plan which can ease the financial burden. The price of the IUD pales in comparison with costs associated with surgical reversal of tubal sterilization or in vitro fertilization, procedures that also are often not covered by insurance policies.

■ Mechanism of Action

Most likely, the copper IUD protects against pregnancy by reducing motility and viability of sperm, inhibiting ova development, and thereby preventing fertilization. This appears to be the primary mechanism of action.

The copper T380A IUD is not an abortifacient; it acts as a contraceptive before the union of the gametes.

TABLE 3

Key Changes to ParaGard Prescribing Information and Opportunities for Use

<ul style="list-style-type: none"> • Removal of the “recommended patient profile” limiting its use to parous women in a mutually monogamous relationship with no history of PID
<ul style="list-style-type: none"> • Shortened list of contraindications <ul style="list-style-type: none"> – Pregnancy – Abnormalities of the uterus resulting in distortion of the uterine cavity – Acute PID or current behavior suggesting a high risk for PID – Postpartum endometritis or postabortal endometritis in the prior 3 months – Known or suspected uterine or cervical malignancy – Genital bleeding of unknown etiology – Mucopurulent cervicitis – Wilson’s disease – Allergy to any component of the IUD – A previously placed IUD that has not been removed
<ul style="list-style-type: none"> • Evidence-based recommendations for use in certain medical conditions <ul style="list-style-type: none"> – Depressed immune conditions, including HIV infection
<ul style="list-style-type: none"> • Flexibility with patient evaluation <ul style="list-style-type: none"> – Cervical cytology – Vaginitis and STI screening
<ul style="list-style-type: none"> • Flexibility in timing of insertion <ul style="list-style-type: none"> – With or without menses (previously menses “optimal”) – Postpartum or postabortion

HIV, human immunodeficiency virus; IUD, intrauterine device; PID, pelvic inflammatory disease; STI, sexually transmitted infection.

“The IUD is passive contraception. Women no longer need to do anything to get safe, reliable, and reversible protection against pregnancy.”

► **LEE SHULMAN, MD**

A controlled study of women with IUDs, women with tubal ligation, and women desiring pregnancy found no positive assays for human chorionic gonadotropin in the luteal sera of IUD users, which suggests that IUDs exert their contraceptive effect prior to implantation.¹² In a study of 171 women, Alvarez et al found no normally dividing ova in the fallopian tubes of IUD users undergoing sterilization after midcycle coitus, while 50% of the ova were normally dividing in women who used no contraception.¹³

■ Copper T380A IUD: Recent Labeling Changes That Expand Its Use

The FDA approved new prescribing information for the T380A copper IUD in September 2005 (TABLE 3).

The most important labeling change was the removal of any reference to a recommended patient profile, which previously had listed parity, a stable and mutually monogamous relationship, and no history of pelvic inflammatory disease (PID) as preferred characteristics for IUD users. Although the copper IUD was not necessarily contraindicated for women who did not fit the recommended patient profile, the recommendations were perceived as a limitation on use. The revised prescribing information eliminates this confusion. As a result, more women may be identified as good candidates for the copper T380A IUD.

Safe Option for Nulliparous Women

Nulliparity has never been a contraindication to IUD use. However, because the device was previously recommended for parous patients, nulliparous candidates for the copper IUD were overlooked. The removal of the patient profile was motivated by data confirming its safety in nulliparous women.¹⁴

Some clinicians have voiced concern about the use of IUDs in nulliparous women who desire future

fertility. However, use of the copper IUD in nulliparous women is not associated with increased risk of infertility. A case-control study of 1895 women, including 358 women with primary infertility and tubal occlusion, reported that the odds ratio of tubal occlusion with previous copper IUD use was 1.0 (95% CI, 0.6-1.7) compared with infertile women without tubal occlusion.¹⁵ When compared with primigravid controls, the odds ratio with the copper IUD was 0.9 (95% CI, 0.5-1.6). In contrast, this study showed that women who had serological evidence of prior *Chlamydia trachomatis* infection had a significant increase in the risk of infertility. Because IUDs do not cause sexually transmitted infections (STIs), it is clear that the focus of fertility preservation should be placed on safer sex practices.

The WHO, in its most recent publication of Medical Eligibility Criteria for contraceptive use, classifies the use of the copper IUD in nulliparous women as a Category 2 (benefits usually outweigh the risks).¹⁰

IUD Access for Immunocompromised Patients

Immunocompromised women, for whom pregnancy can be life threatening, can now have access to the most effective, reversible method of contraception available. New labeling includes copper IUD use by:

- Women with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome
- Immunocompromised women (eg, rheumatoid arthritis, inflammatory bowel disease, chronic myeloid leukemia, multiple sclerosis)
- Women receiving chemotherapy

A cohort study from Nairobi, Kenya showed that complications related to IUD use were rare among a group of women infected with HIV-1 and occurred at a rate similar to that of noninfected women.¹⁶ The authors concluded that IUDs were a safe contraceptive method for women with HIV-1 infection who had continuing access to medical services.

In its recent Medical Eligibility Criteria, the WHO has assigned the copper IUD a Category 1 designation (use of method in any circumstances) for

“The contribution of endometrial changes induced by the IUD to the device’s efficacy are questionable. Endometrial changes take months to establish, but the copper IUD is as effective the first month after insertion as it is in subsequent months.

To deny women access to the copper IUD because of theoretical concerns is not good medicine.”

► ANITA L. NELSON, MD

women with cardiovascular disease (including history of thrombosis), headache, epilepsy, diabetes, thyroid disorders, and liver disease.¹⁰

In addition, women with other conditions in which pregnancy may produce serious or life-threatening complications or women taking medication with known teratogenic effects may benefit from use of the copper IUD. Some of these conditions include:

- Hepatitis, epilepsy, history of deep vein thrombosis or pulmonary embolism, stroke, thrombotic disorders, valvular heart disease, hyperlipidemias, migraine, or depression¹⁰
- Women on chronic medication with pregnancy category D or X (eg, methotrexate, cyclophosphamide, tamoxifen)

PID History: From a Contraindication to a Consideration

The recommendation to avoid IUD use in women with a history of PID has been replaced with the advice not to use an IUD in a woman with active cervicitis, PID, or current behavior suggesting high risk for PID. This change results from an appreciation of decades of careful epidemiologic studies. The IUD does not cause pelvic infection; most PID is caused by exposure to STIs. Increased risk of infection in the first weeks following IUD insertion is likely related to the insertion procedure and not the device itself or to the string.

Older literature regarding risk of PID in IUD users overreported the risk of device-related infection and

infertility because of methodological flaws. Use of inappropriate comparison groups (eg, women using barrier methods of contraception), overdiagnosis of salpingitis in IUDs users, and inability to control for the effects of sexual behavior led to an exaggerated apparent risk.^{17,18} After correction for these biases, however, the risk of PID declined to a level that is no longer statistically significant. The American College of Obstetricians and Gynecologists (ACOG) concurs

“The best way to assess for risk of STIs is to assess sexual behavior as part of the medical history and to reassess to find out if her relationships have changed.”

► ANNE MOORE, MSN, ANP

and states that routine use of prophylactic antibiotics before IUD insertion offers little benefit.¹⁹

Gonorrhea or chlamydial infection at the time of IUD insertion does increase a woman's risk for PID compared with uninfected women, reported a recent analysis of the literature.²⁰ The authors of this review concluded that the absolute risk of PID is low in both IUD user groups: PID was diagnosed in 0% to 5% of women with STIs and in 0% to 2% of women without STIs. WHO recommendations state that women with current purulent cervicitis, cervical chlamydial infection, or gonorrhea should not have an IUD inserted (Category 4: method not to be used).¹⁰ In some circumstances, an IUD may be inserted 3 months after treatment for cervicitis if no abnormal signs or symptoms are apparent, according to guidelines from the Royal College of Obstetricians and Gynaecologists.¹⁴ This should be done only if no other contraceptive method is acceptable, pregnancy risk is substantial, and the woman's partner has been appropriately tested and treated.

For women with an IUD already in place, diagnosis of cervical infection is not an indication for IUD removal.^{10,20} A small randomized study of women with IUDs hospitalized for acute salpingitis found

that removal of the IUD was not a useful adjunct to antibiotic therapy.²¹

To evaluate a patient's STI or PID risk, clinicians should carefully examine her medical history for information regarding high-risk behaviors—multiple partners or history of recent STI. Although medical history is an important risk factor, change in behavior should also be considered. It is reasonable to consider an IUD for women with a distant history of STIs who are no longer at high risk.

IUD Access for Women With Other Common Problems

Vaginal infection is not a contraindication to insertion of the copper IUD. Abnormalities in cervical cytology also are not contraindications to IUD insertion or continued use of an IUD; only women who have a high index of suspicion for cervical or endometrial cancer should have their IUD insertion delayed until those diagnoses are ruled out. Women with mild abnormalities on their Papanicolaou test may proceed with IUD insertion prior to colposcopic evaluation.

Reducing the Risk of Ectopic Pregnancy

The copper IUD reduces a woman's underlying risk for ectopic pregnancy by 90% and can be used by women with a history of ectopic pregnancy to reduce their risk of recurrence.²² The risk that a pregnancy is ectopic is 8% with copper IUD use; after tubal sterilization, this risk exceeds 20%. Twelve-year data from the UN/WHO study revealed an ectopic pregnancy rate with the copper T380A of 0.4 per 100 woman-years.⁶

■ Techniques for T380A Copper IUD Insertion

Timing. The copper IUD may be inserted at any time in the menstrual cycle when pregnancy can be reasonably ruled out.¹⁰ This flexibility allows clinicians to prescribe the copper T380A IUD with the same ease as hormonal contraceptives. However, unlike users of Quick Start hormonal contraception, IUD users need no back-up method after insertion. The copper IUD may be safely inserted in women who are lactating.

Insertion immediately after first-trimester abortion (induced and spontaneous) is both safe and effective.^{23,24} The woman is known not to be pregnant, her motivation for contraception may be high, bleeding from the insertion will be masked by expected bleeding, and the setting may be convenient for both the woman and her provider. In addition, performing this procedure immediately postabortion may avoid insertion-related discomfort. Postabortion expulsion rates are higher after second trimester procedures than after earlier abortions. Therefore, in these cases it may be prudent to delay insertion.

In some settings, immediate IUD insertion postpartum (directly after delivery of the placenta) has been found to be beneficial; however, immediate postpartum insertion is associated with a higher rate of expulsion than with interval insertion, and the procedure requires additional training.

Insertion. Placement technique is important to reduce the risks of uterine perforation and IUD expulsion. Every effort should be made to ensure patient comfort. Use of nonsteroidal anti-inflammatory drugs, paracervical blocks, and intrauterine infusion of lidocaine have all been suggested as ways to reduce patient discomfort and may provide some individual benefit.²⁵

The insertion procedure used for the copper IUD, summarized in **TABLE 4**, differs from that recommended for other IUDs. The manufacturer's prescribing information should be consulted for a description of the insertion procedure. The instructions call for the IUD to be placed high in the uterine cavity. Often there is concern about the consequences of placing an IUD too low in the uterine cavity, thus compromising effectiveness and increasing the risk of expulsion. However, a study of 32 improperly inserted T-shaped IUDs reported that the IUDs spontaneously moved upwards a mean of 4.9 to 7.9 mm as documented by follow-up ultrasound at 2 to 3 months after insertion.²⁶ In the event of a low placement, an ultrasound can be performed at 2 to 3 months to determine whether the IUD has readjusted its position or should be replaced. Women with a lowly placed IUD should be given back-up protection until it is determined that the device is not expelling.

TABLE 4
Checklist for Placement of the Copper IUD

- Perform bimanual pelvic exam noting the size and position of uterus*
- Insert the speculum
- Cleanse the cervix and vagina with an antiseptic solution
- Place the tenaculum
- Using gentle traction on the tenaculum to stabilize the uterus and to align the cervical canal with the uterine cavity, sound the uterus to determine uterine depth. The prescribing information for the copper IUD notes that the uterus should sound to a depth of 6 to 9 cm except immediately postabortion or postpartum.
- Load the IUD into the insertion tube and set the flange to the uterine depth (*see Prescribing Information*)
- Using gentle traction on the tenaculum to stabilize the uterus and to align the cervical canal with the uterine cavity, introduce the insertion tube through the cervical canal and advance until the IUD touches the fundus of the uterus
- Release the arms of the IUD high in the uterine fundus by retracting the tubing 0.5 cm while stabilizing the IUD at the fundus with the stabilizing rod
- Withdraw the stabilizing rod and then withdraw the insertion tube
- Trim the threads so that 3 to 4 cm protrude into the vagina or tuck around the cervix

* Insertion of the IUD is contraindicated in women with abnormalities of the uterus resulting in distortion of the uterine cavity.
IUD, intrauterine device.

“Immediately effective, reversible, no regret: the IUD is something women would like to have postpartum if they realized they had options other than tubal ligation.”

► RAQUEL ARIAS, MD

Follow-up. Patients should be alerted to signs and symptoms associated with the rare complications of IUD use: expulsion/perforation, pregnancy, and infection. Minimal routine follow-up is recommended for IUD users. One visit 10 to 12 weeks after insertion is important to detect the few women who have silent partial expulsion. Otherwise, women using IUDs require only routine health-maintenance visits.

■ Impact of Labeling Changes

The changes in the prescribing information for the copper IUD may have a profound effect on use. Clinicians should familiarize themselves with the new information in order to be able to offer this reliable, reversible method of contraception to a new generation of women.

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Contraceptive Products Mentioned

Brand	Generic
Depo-Provera® Contraceptive Injection	Medroxyprogesterone acetate injectable suspension
Implanon™	Etonogestrel subdermal implant
Mirena®	Levonorgestrel-releasing intrauterine system
ParaGard®	T380A intrauterine copper contraceptive