

CLINICAL PRACTICE

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Long-Acting Reversible Contraception

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This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.

A 17-year-old high school student who has never been pregnant presents for advice regarding contraception. She has an unremarkable medical history and is planning to become sexually active with her boyfriend in the near future. Her primary concern is an unintended pregnancy, and she inquires about methods of contraception that are highly effective. How would you counsel her about options for contraception?

THE CLINICAL PROBLEM

UNINTENDED PREGNANCIES ARE A DIFFICULT PUBLIC HEALTH PROBLEM for clinicians and policy makers. After three decades of minimal change in the rate of unintended pregnancy in the United States among adolescents and women, the rate has decreased in recent years — from 54 unintended pregnancies per 1000 adolescents and women 15 to 44 years of age in 2008 to 45 cases per 1000 adolescents and women in 2011.¹ However, the most recent U.S. data still indicate that 45% of all pregnancies in the United States are unintended, as compared with 34% in Western Europe.^{1,2} Unintended pregnancies are associated with an increased risk of adverse reproductive outcomes and sociodemographic challenges; contraception is a primary means of prevention. Overall, between 2011 and 2013, a total of 62% of all women 15 to 44 years of age reported current use of contraception.^{3,4} However, the most highly effective, reversible methods — intrauterine devices (IUDs) and hormonal implants — were being used by only a small proportion of the women who reported using contraceptives between 2011 and 2013. A comparison of the use of IUDs and hormonal implants between 2002 and 2011–2013 showed that the use of IUDs increased from 2% to 10% and the use of implants increased from 0.4% to 1% (Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org).^{3,4} Increasing access to these most effective, reversible methods of contraception is a key strategy to further decrease the rate of unintended pregnancy in the United States.

STRATEGIES AND EVIDENCE

Long-acting reversible contraception, or LARC, methods provide reliable, long-term, highly effective prevention of pregnancy after one-time placement of a device. LARC methods include IUDs (hormonal IUDs and nonhormonal copper-containing IUDs) and the subdermal hormonal implant (Fig. 1). These methods are sometimes termed “forgettable”⁵; they do not depend on user adherence such as taking a pill

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KEY CLINICAL POINTS

LONG-ACTING REVERSIBLE CONTRACEPTION

- Intrauterine devices (IUDs) and hormonal implants are the most effective reversible methods of contraception — approximately 20 times as effective as pills, patches, and rings; couples should be counseled and informed about the superior effectiveness of long-acting reversible contraception (LARC) methods.
- IUDs and hormonal implants are safe for almost all women, including adolescents, as well as women in the postpartum or postabortion period.
- The main side effect of IUDs and hormonal implants is a change in bleeding patterns; anticipatory counseling about expected changes in bleeding may increase rates of continuation.
- Barriers to access to IUDs and hormonal implants remain, including those related to education, provider training, cost, and logistics; successful interventions have been shown to minimize these barriers.
- Adolescents and adult women should be counseled about contraception and should have access to the full range of contraceptive methods, including LARC methods.

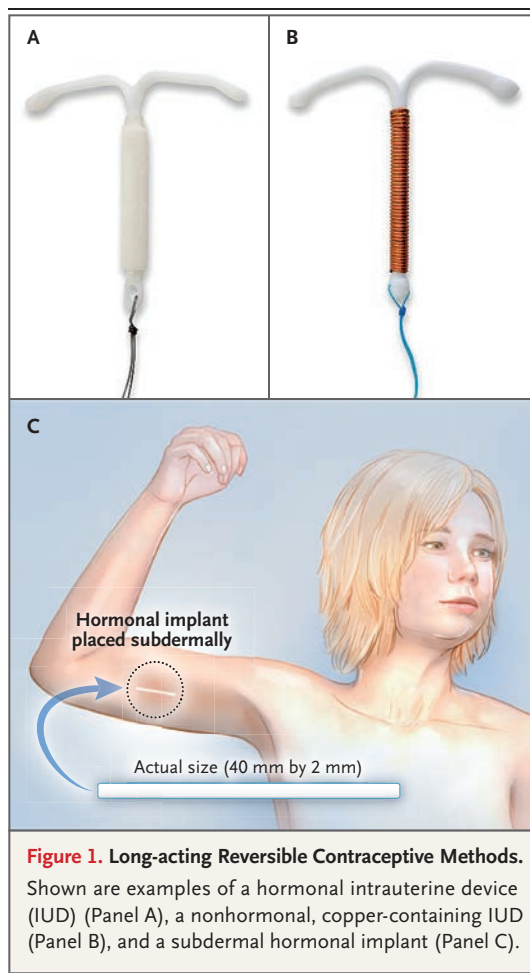
daily, receiving an injection every 3 months, or placing a ring or patch. Consequently, LARC methods are highly effective — approximately 20 times as effective as pills, patches, or rings.⁶ Among teenage girls and women enrolled in the Contraceptive CHOICE Project, a prospective cohort study involving almost 10,000 women in the St. Louis area who received tiered, comprehensive contraceptive counseling (in order of effectiveness, from LARC methods to barrier methods) and were provided contraception at no cost, pregnancy rates were 5 pregnancies per 100 participant-years among pill, patch, and ring users as compared with 0.3 pregnancies per 100 participant-years among LARC users.⁶ Young age (<21 years) doubled the failure rates among pill, patch, and ring users but had no effect on failure rates among LARC users.⁶

IUDS

As of November 2016, five IUDs were approved by the Food and Drug Administration (FDA) and were available in the United States. The copper-containing IUD, ParaGard, is a nonhormonal device and contains 380 mm² of copper around the arms and stem. The four levonorgestrel-releasing IUDs (LNG-IUDs) include two devices that contain 52 mg of levonorgestrel (Mirena and Liletta), a device that contains 19.5 mg (Kyleena), and a slightly smaller device that contains 13.5 mg (Skyla). Liletta is marketed as a lower-cost alternative for clinics eligible for 340B pricing through the Department of Health and Human Services.⁷ There has been widespread confusion regarding the mechanism of action of the IUD. IUDs do not cause the destruction of an implanted em-

bryo but rather work primarily by preventing fertilization.⁸ The copper-containing IUD releases copper ions that are toxic to sperm.⁸ The LNG-IUD inhibits ovulation and thickens cervical mucus, which obstructs the penetration of sperm.⁹ Less than 1% of women become pregnant during the first year of IUD use, with pregnancy rates with the LNG-IUD (0.1 to 0.2%) generally reported as lower than the rates with the copper-containing IUD (0.5 to 0.8%).¹⁰⁻¹² ParaGard is approved by the FDA for 10 years of use, Mirena and Kyleena for 5 years, and Skyla for 3 years. As of November 2016, Liletta is approved for 3 years of use, but data are being collected to assess 5-year use. In the Contraceptive CHOICE Project, continuation rates with the LNG-IUD and the copper-containing IUD were 88% and 85%, respectively, at 1 year, 79% and 77% at 2 years, and 52% and 56% at 5 years.^{13,14} In other studies involving various populations in the United States, 12-month IUD continuation rates of 87 to 89% have been reported.^{15,16}

Almost all women can safely use IUDs. Exceptions include women who have hypersensitivity to copper, which would preclude the use of the copper-containing IUD, or hypersensitivity to other components of either type of IUD; women with a current pelvic infection or a sexually transmitted disease (STD); women with gynecologic cancers; and women with certain other serious medical conditions (Table 1).¹⁷ Women who have current purulent cervicitis or known chlamydial infection or gonococcal infection should not undergo insertion of an IUD. Women generally do not require screening for STDs at the time of IUD insertion if they have already



been screened according to the STD Treatment Guidelines of the Centers for Disease Control and Prevention (CDC) (e.g., annual screening for chlamydial infection for women younger than 25 years of age or for older women at increased risk for STDs).¹⁸ If a woman with risk factors for STDs has not been screened according to the guidelines, screening can be performed at the time of insertion of the IUD, and insertion should not be delayed (Table 2).¹⁹ Women who have cervical or endometrial cancers should not undergo IUD insertion but may continue to use an IUD while awaiting cancer treatment.¹⁷ Given theoretical concerns about the adverse effects of progestin on breast cancer, the use of the LNG-IUD is considered to be contraindicated in women with current breast cancer and is generally not recommended in women who had recent breast cancer; however, evidence to assess this concern is limited.¹⁷

A common side effect of using a copper-containing IUD is increased menstrual bleeding; in contrast, the LNG-IUD generally reduces heavy menstrual bleeding.¹⁹ Anticipatory counseling regarding expected changes in bleeding may increase rates of IUD continuation. For women with copper-containing IUDs who request treatment for their heavy bleeding, a short course (5 to 7 days) of a nonsteroidal anti-inflammatory drug may decrease bleeding.¹⁹

The copper-containing IUD can also be used as emergency contraception (inserted after sexual intercourse to prevent pregnancy). For women who meet eligibility requirements for IUD insertion and who have had unprotected sex within the previous 5 days, the copper-containing IUD is the most effective form of emergency contraception and has the benefit of becoming a long-term contraceptive method.^{19,20}

SUBDERMAL HORMONAL IMPLANT

Currently, Nexplanon is the only hormonal implant available in the United States. Nexplanon, which slowly releases the progestin etonogestrel, differs from a similar previous implant, Implanon, in that it has an improved inserter and contains barium to facilitate the radiologic detection of implants that cannot be palpated. The contraceptive mechanism of action of the hormonal implant is twofold: inhibition of ovulation and thickening of the cervical mucus. The contraceptive effectiveness of the implant is high, with an estimated 0.1% of users becoming pregnant in the first year of use,^{10,21} and does not seem to vary with body-mass index.^{21,22} The etonogestrel-releasing implant is approved by the FDA for 3 years of use. Data from the Contraceptive CHOICE Project showed that young women 14 to 19 years of age reported high continuation rates (82% at 12 months).²³ In other studies involving various populations in the United States, implant continuation rates of 75 to 83% at 12 months have been reported,^{15,24} and a large, multicountry study showed continuation rates of 88% at 1 year and 70% at 2.5 years.²¹

Almost all women can safely use implants; exceptions are women who have hypersensitivity to barium or to the components of the implant. Given theoretical concerns about the adverse effects of progestin on breast cancer, the use of the hormonal implant is considered to be contraindicated in women with current breast

Table 1. Medical Eligibility Criteria (MEC) for Initiation of LARC Methods — Conditions for which at Least One LARC Method Should Not Be Used (MEC 4) or Should Not Generally Be Used (MEC 3).*

| Condition | Category of Medical Eligibility Criteria | | | Comments |
|---|--|---------|---------|--|
| | Copper-Containing IUD | LNG-IUD | Implant | |
| Pregnancy | 4 | 4 | NA | The use of an implant is not needed; no known harm to the woman, to the course of her pregnancy, or to the fetus occurs if an implant is inadvertently used during pregnancy. |
| Distorted uterine cavity incompatible with IUD placement | 4 | 4 | NA | An anatomical abnormality that distorts the uterine cavity might preclude proper IUD placement. |
| Current pelvic inflammatory disease, gonococcal or chlamydial infection, or purulent cervicitis | 4 | 4 | 1 | Insertion of an IUD might worsen the condition. |
| Postpartum or postabortion sepsis | 4 | 4 | NA | Insertion of an IUD might worsen the condition. |
| Persistent intrauterine gestational trophoblastic disease | 4 | 4 | 1 | An IUD should not be inserted because of the theoretical risk of perforation, infection, and hemorrhage. |
| Cervical cancer | 4 | 4 | 2 | Concern exists about the increased risk of infection and bleeding at insertion. The IUD will probably need to be removed at the time of cancer treatment. |
| Endometrial cancer | 4 | 4 | 1 | Concern exists about the increased risk of infection, perforation, and bleeding at insertion. The IUD will probably need to be removed at the time of cancer treatment. |
| Unexplained vaginal bleeding (raising suspicion of serious condition) | 4 | 4 | 3 | If pregnancy or an underlying pathologic condition (e.g., pelvic cancer) is suspected, it must be evaluated and the category adjusted after evaluation. Irregular bleeding patterns associated with the method used might mask symptoms of underlying pathologic conditions. |
| Current breast cancer | 1 | 4 | 4 | Hormonal stimulation may worsen the condition. |
| History of breast cancer with no evidence of disease for 5 years | 1 | 3 | 3 | — |
| Complicated solid-organ transplantation | 3 | 3 | 2 | Data on risks and benefits are limited in this population. |
| Systemic lupus erythematosus (with severe thrombocytopenia) | 3 | 2 | 2 | Concern exists about an increased risk of bleeding. |
| Systemic lupus erythematosus (with positive or unknown antiphospholipid antibodies) | 1 | 3 | 3 | Concern exists about an increased risk of both arterial and venous thrombosis. |
| Severe, decompensated cirrhosis | 1 | 3 | 3 | Hormonal exposure may worsen the condition. |
| Hepatocellular adenoma or hepatic malignancy | 1 | 3 | 3 | Hormonal exposure may worsen the condition. |

* This table is adapted from Curtis et al.¹⁷ and includes only the subset of conditions for which at least one of the three long-acting reversible contraception (LARC) methods was categorized as either MEC 3 or MEC 4; all other conditions, which were categorized as either MEC 1 or MEC 2 for all three LARC methods, are included in the complete MEC guidance document (Curtis et al.¹⁷). Categories of MEC for the use of LARC methods are defined as follows: MEC 4, unacceptable health risk, indicating that the LARC method should not be used; MEC 3, theoretical or proven risks usually outweigh the advantages, indicating that the LARC method should not generally be used; MEC 2, advantages outweigh theoretical or proven risks; and MEC 1, no restriction. IUD denotes intrauterine device, LNG-IUD levonorgestrel-releasing IUD, and NA not applicable.

cancer and is generally not recommended in women who have had recent breast cancer.¹⁷ The most common side effect of implants is unpredictable bleeding, and women should be counseled about this risk before implant placement.^{19,25} Although amenorrhea may occur in approximately 20% of women, irregular uterine bleeding, unpredictable uterine bleeding and spotting, or both are common and may persist over time.²⁵

Table 2. Selected Practice Recommendations for the Initiation of LARC Methods.*

| Contraceptive Method | Timing of Initiation† | Additional Contraception Needed as Back-up‡ | Examinations or Tests Needed before Initiation |
|------------------------------|-----------------------|---|--|
| Copper-containing IUD | Any time | Not needed | Bimanual examination and cervical inspection§ |
| Levonorgestrel-releasing IUD | Any time | If more than 7 days after menses started, use back-up method or abstain from sexual intercourse for 7 days. | Bimanual examination and cervical inspection§ |
| Hormonal implant | Any time | If more than 5 days after menses started, use back-up method or abstain from sexual intercourse for 7 days. | None |

* This table is adapted from Curtis et al.¹⁹

† LARC methods can be initiated if the provider is reasonably certain that the woman is not pregnant.

‡ The recommendations for the use and duration of a back-up method were determined on the basis of the mechanism of action of the contraceptive method and on the basis of data on the minimum duration of use necessary for contraceptive effectiveness.

§ Most women do not require additional screening for sexually transmitted diseases (STDs) at the time of insertion of an IUD. If a woman with risk factors for STDs has not been screened for gonococcal infection and chlamydial infection according to the STD Treatment Guidelines of the Centers for Disease Control and Prevention (CDC) (www.cdc.gov/std/treatment), screening can be performed at the time of IUD insertion, and insertion should not be delayed. Women with current purulent cervicitis or chlamydial infection or gonococcal infection should not undergo IUD insertion.

USE OF LARC METHODS IN SPECIFIC POPULATIONS

LARC methods are safe for use in almost all women, including young and nulliparous women.^{17,26} Providers may be concerned about the risks of pelvic inflammatory disease (PID) and infertility associated with the use of IUDs, particularly in young or nulliparous women.²⁷ However, evidence has shown that the risk of PID associated with the insertion and use of IUDs is minimal. Data from more than 50,000 woman-years of IUD use indicated a rate of 9.7 cases of PID per 1000 woman-years in the first 20 days after IUD insertion, which then dropped to 1.4 cases of PID per 1000 woman-years over the course of 8 years of follow-up.²⁸ More recent studies conducted in the United States have also shown low rates of PID after IUD insertion: less than 1% among 57,728 women within 90 days after IUD insertion, even in the absence of STD screening,²⁹ and 1% or less among participants in the Contraceptive CHOICE Project.³⁰ The LNG-IUD may, in fact, protect against PID; a randomized, controlled trial involving 2758 women showed that the risk of PID was lower among LNG-IUD users than among users of a copper-containing IUD (Nova-T) after 36 months of use.³¹ Observational studies have also shown that infertility was associated with a history of STDs and not a history of IUD use.^{32,33}

Both IUDs and implants are safe for use in the postpartum and postabortion periods, including

immediately post partum and post abortion^{17,26}; immediate placement has been associated with lower rates of rapid repeat pregnancy and repeat abortions than the rates with other contraceptives.^{26,34} Insertion of an IUD immediately post partum is associated with low rates of adverse events such as perforation (0 in three studies of over 3000 women in total), infection (1% in one study of 554 women), and the need for removal of the IUD as a result of bleeding and pain (5 to 11% over 12 months in three studies of approximately 7500 women in total); these rates generally did not differ from those observed with IUD insertion at times other than the postpartum period.³⁵ Uterine perforation, although rare, may be more prevalent among women who are breast-feeding (5.6 cases per 1000 IUD insertions through 36 weeks post partum in one study) than among women who are not breast-feeding, although this finding is not consistent across studies.³⁶ Among women who are breast-feeding, the use of an IUD or implant is not associated with differences in the proportions of women who initiate breast-feeding or in the duration of exclusive or partial breast-feeding, or with adverse health outcomes in the infant.^{36,37} Although the risk of thromboembolism associated with LARC use has not been well studied, these methods of contraception do not contain estrogen and therefore are not associated with the same potential for thromboembolism in the postpartum

period as are estrogen-containing contraceptives.³⁸

Although IUDs are generally safe for use in the postpartum period, the relative risk of expulsion of IUDs that are placed immediately post partum is higher than the risk with IUDs placed at 6 weeks post partum or later.³⁹ Expulsion rates vary widely by study population but are generally lower when the IUD is inserted immediately after delivery of the placenta (3 to 27%) than when it is inserted 10 minutes to 48 hours after delivery of the placenta (11 to 27%); both rates are higher than those with standard insertion at 4 to 8 weeks post partum (0 to 6%).³⁹ Trials that compared immediate versus delayed IUD insertion during either the postpartum or post-abortion period showed that even with higher expulsion rates after immediate insertion, IUD continuation rates at 6 to 12 months were generally higher among the women whose IUDs were placed immediately post partum or post abortion.^{39,40}

AREAS OF UNCERTAINTY

Although the use of IUDs and hormonal implants in the United States has been increasing, several barriers continue to limit access to these methods. The Contraceptive CHOICE Project showed that when women were counseled about all contraceptive methods in order of effectiveness and contraception was provided at no cost, high percentages of women, including teenage girls, chose LARC methods (any LARC method, 75%; IUD, 58%; and implant, 17%).^{41,42} Other barriers to accessing LARC include a lack of trained providers,^{27,43} low reimbursement for LARC supplies and services,⁴⁴ a lack of immediate LARC access at the clinical site where the method is requested,⁴³ and extra steps and visits, such as unnecessary screening tests before the initiation of contraceptive use.⁴⁵ However, several recent studies have addressed strategies for improving access to LARC methods. In a cluster-randomized trial involving 40 reproductive health clinics across the United States, intervention clinics received training on contraception counseling and on insertion of IUDs and implants, and control clinics provided standard care.⁴⁶ Higher percentages of women at the intervention clinics than at the control clinics chose LARC methods (28% vs. 17%; odds ratio, 2.2; 95% confidence interval,

1.6 to 3.1).⁴⁶ The Colorado Family Planning Initiative used private funding to procure LARC methods, to train providers and staff on provision of LARC methods, and to provide technical assistance with billing and management issues.⁴⁷ LARC use among 15-to-24-year-old persons in Colorado increased from 5% to 19% over the course of 2 years.⁴⁷ Progress has been made in several U.S. states in resolving inadequate reimbursement and other logistic and administrative barriers to LARC access, and activities such as the LARC Learning Community are addressing these issues at the national and state levels.⁴⁸

More research is needed to determine the most appropriate timing of IUD placement after a pelvic infection. Evidence is lacking to guide health care providers in determining when an infection has resolved sufficiently for IUD placement.⁴⁹ In women who test positive for gonococcal infection or chlamydial infection at the time of IUD placement, the device should be left in place and treatment should be initiated.¹⁷

For women who have human immunodeficiency virus (HIV) infection, limited evidence is available with respect to potential interactions between the use of hormonal implants and antiretroviral medications. A theoretical concern is that certain ritonavir-boosted protease inhibitors may reduce serum progesterin levels, and evidence from one retrospective trial suggested increased pregnancy rates among women who used both etonogestrel implants and efavirenz; however, confidence intervals were wide and pregnancy rates were still lower than those seen with other hormonal methods.¹⁷ For women who use certain antiretroviral medications that have the potential for interactions with hormonal implants, clinicians should counsel that an increased risk of contraceptive failure is possible, as compared with hormonal implant users who are not using those antiretroviral medications.

The duration of effectiveness of LARC methods may extend past the currently approved time periods.^{50,51} A recent multicountry study showed a 7-year cumulative pregnancy rate of less than 1 pregnancy per 100 woman-years among women who used a 52-mg LNG-IUD.¹² In a U.S. study, 1 pregnancy was reported among 263 women who used a 52-mg LNG-IUD during the sixth year of use (pregnancy rate, 0.51 per 100 woman-years), and no pregnancies were reported among 123 implant users during the fourth year of use

or among 34 implant users during the fifth year of use.⁵⁰ A multicountry study showed no pregnancies among 204 implant users during the fourth and fifth years of use.⁵² The serum etonogestrel levels remained within the thresholds of contraceptive effectiveness for the implant through 4 years of follow-up and did not vary significantly according to body-mass index.⁵⁰ A longer period of effectiveness would decrease the need for removal and reinsertion procedures. Women should also understand that the IUD or implant can be removed at any time and that these methods are appropriate choices for women who plan to use them for a shorter time than the approved life of the device.

GUIDELINES

The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics recommend that IUDs and the contraceptive implant be offered as first-line methods of contraception to all women, including adolescents.^{26,53,54} The CDC publishes recommendations for the safe use of contraception, including IUDs and implants, for women with various conditions or characteristics¹⁷; guidance regarding the initiation and use of contraception and the management of problems such as irregular bleeding that may arise with the use of LARC methods is also provided.¹⁹ Recommendations provided during contraceptive counseling encourage a patient-centered approach for choosing a contraceptive method.⁵⁵ The recommendations in this article are consistent with these guidelines.

CONCLUSIONS AND RECOMMENDATIONS

Adolescents and women of reproductive age who wish to prevent pregnancy, such as the 17-year-old described in the vignette, should be counseled about contraception and should have access to the full range of contraceptive methods.¹⁹ All adolescents and adult women should be informed about the availability of LARC methods, given their extremely high effectiveness, safety, and high rate of continuation. We would counsel the adolescent described in the vignette accordingly and would emphasize the superior effectiveness of LARC methods over other reversible contraceptive methods, given that she has requested a highly effective method. If no contraindications are present, we would provide the method of her choice during her initial visit. She should also be counseled to use a barrier method for prevention of STDs and HIV infection.¹⁸ We would advise the adolescent about expected changes in bleeding patterns with use of LARC methods¹⁹ and would suggest that she follow up as needed for questions or problems.¹⁹

The views expressed in this article are those of the authors and do not necessarily represent the official position of the U.S. Centers for Disease Control and Prevention. The use of trade names and commercial sources is for identification only and does not imply endorsement by the Department of Health and Human Services.

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