The Norplant System: Where Are We in 1995?

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The Norplant System, the only long-acting subdermal contraceptive implant currently available in the United States, is the topic of three papers in this issue of *The Journal of Family Practice*. These papers are particularly timely and relevant in light of growing concern over unplanned and teenage pregnancy, as well as media attention directed at the Norplant System itself.

In the United States, 56.5% of the 6.3 million pregnancies that occurred during 1987 in women aged 15 to 44 were unplanned.[1] The United States also has the dubious distinction of leading five other developed nations in the number of unintentional pregnancies among its teenagers,[2–4] despite the similarity in rate of teenage sexual activity among industrialized countries.[3] Only 40% of US teenagers are reported to use contraception during the first year of sexual activity.[1,5] Since the late 1970s, one in eight women aged 15 to 19 have become pregnant each year.[6,7]

At the same time, data suggest that it is possible to improve these statistics by introducing new contraceptive methods and continuing to encourage appropriate use of existing methods, supported by intensive patient counseling.[8–10] It follows, therefore, that correct contraception education must be incorporated into an individual's lifestyle as early as possible. If this could be accomplished before adolescence, then perhaps these good contraceptive habits would have a positive impact on the unacceptably high unintentional pregnancy rate in both adults and teenagers.

Teaching couples about the appropriate use of contraceptives does little good without the availability of several contraceptive choices to meet a range of lifestyle needs. The paucity of options in the mid-1980s was capped off when the Cu-7 (G. D. Searle, Chicago, Ill), a copper intrauterine device (IUD), was withdrawn from the market without a new method on the horizon to replace it.[11] The copper IUD, which had been used extensively and successfully by several industrialized nations to reduce unintended pregnancy, did not become an option again until ParaGard, an intrauterine copper contraceptive now approved for 10 years of use, became available for the US market in 1990. As a result of the limited availability of long-term contraceptive options for so many years, however, surgical sterilization increasingly became the primary contraceptive choice of US couples.

The need for reversible, effective contraception for all couples led to the development of several new options in the 1990s. Because 66% of sexually active US couples wish to defer childbearing temporarily, the 5-year levonorgestrel implant (Norplant System), the 3-month injectable (Depo-Provera), two new progestins (norgestimate and desogestrel) in oral contraception, and new condoms (including the polyurethane female condom) have been welcome additions to the array of contraceptive options, allowing the best fit between patient needs and contraceptive efficacy.[1]

When the Norplant System came on the market in 1991, it was the first new contraceptive system approved for use in the United States in 30 years. It is also the most extensively tested contraceptive implant, with nearly 60,000 women participating in clinical trials to date.[12] Today, the Norplant System is used by nearly 1 million US women and 2.5 million women worldwide (1995 data on file at Wyeth-Ayerst Laboratories, Philadelphia, Pa).

Norplant consists of six subdermal Silastic capsules that are placed in the inner aspect of the upper nondominant arm in a minor surgical procedure, requiring a local anesthetic. Removal of the Norplant System, which can take place at any time up to 5 years after insertion, also requires local anesthesia but a slightly longer incision.[13] Its 5-year efficacy approaches that of surgical sterilization, yet it is completely reversible.[14] This high efficacy can be attributed to the long-term release of low blood levels of the progestin levonorgestrel, which inhibits ovulation and thickens cervical mucus, blocking sperm penetration. The

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method is not coitally dependent, which also contributes to its efficacy rate, as poor user compliance is an important reason why other contraceptive methods may frequently fail.

International Experience

One 5-year study of Norplant use in 10,718 Chinese women is particularly instructive in understanding the risks and benefits of Norplant use.[15] The 5-year average annual pregnancy rate was 0.3 per 100 women, with an ectopic pregnancy rate of 0.09 per 1000 women. Five-year continuation rates were extremely high: 72 per 100 original acceptors. Bleeding disturbances were by far the most common reason leading to discontinuation during the 5 years (20 per 100 women). This bleeding usually took the form of continuous spotting, rather than hemorrhage, as most patients experienced hemoglobin increases with time. These bleeding episodes result from the acyclic endometrial shedding typical of all progestin-only methods. Approximately 10% of US users request removal of the capsules because of irregular bleeding.[13,16] Medical reasons for terminations (excluding pregnancy) in the Chinese study, which occurred at a rate of 5.7 per 100 users, included headache, dizziness, and weight gain, all of which are common side effects of all hormonal methods.

US Experience

Although the international experience of Norplant System users has been extensively looked at[17] and is similar to that of the Chinese investigators, it is possible that the efficacy findings may not be directly applicable to US women, as constitutional factors, such as weight, may differ.[18–24] In addition, findings of high continuation rates despite high reported rates of prolonged nuisance bleeding do not necessarily reflect acceptance by the patient. Some patients, for example, may find it difficult to have their implant removed, often because of limited access to those with the skill to remove it.[25]

One of the first US studies to examine acceptability rates was published by Darney et al[25] in 1990. Their findings characterized the 5-year experience of 205 Norplant users attending an urban family planning clinic in San Francisco. The majority (70%) of these women were using the two-rod system (Norplant-2), which is not yet commercially available. In general, they were multiparous and married, with a wide range of ethnicity, education, and family income. Many women chose to enroll in this clinical trial because of dissatisfaction with other available methods of contraception (89% were using contraception) and because they planned to have children in the future.

Of the women participating in the trial, 95% experienced at least one side effect. Over 80% experienced menstrual changes, 32% weight changes, 24% headaches, 16% mood changes, and 15% acne. Nevertheless, because of dissatisfaction with previous methods, the majority of women were willing to tolerate these side effects, as evidenced by a 53% 5-year continuation rate. Interestingly, 61% of women who *discontinued* Norplant said they would use this method again. The authors concluded that Norplant appeared to be a highly acceptable method of contraception, despite the frequent occurrence of bothersome side effects in a group of fairly diversified women in an urban setting. Despite frequent side effects, experiences of high acceptability are similar among many different groups of women, including adolescents,[26,27] inhabitants of scattered inner city areas within Dallas,[28] Houston,[29] and Baltimore,[30] and finally, within a predominantly middle-class private practice setting.[31] All programs can attribute their apparent success to the tendency of Norplant users to be a highly self-selected, intensely counseled group of women who desire long-term reversible contraception.

Current Issues

Although most Norplant users appear highly satisfied with their method, recent media coverage of the method has been less than flattering because of class-action lawsuits filed in Texas, Illinois, and Florida against the manufacturer, Wyeth-Ayerst Laboratories in Philadelphia.[32–35] The number of newspaper solicitations by lawyers willing to file claims on behalf of plaintiffs also is rising.[36] Because the majority of suits are based on claims of postinsertional pain, prolonged or difficult removals, and inadequate warning of potential side effects, an examination seems in order. Moreover, clinicians should be aware that publicity surrounding this litigation may increase apprehension among current users and lead some women who are considering using Norplant to select other, perhaps less effective or less appropriate methods of contraception.

In the majority of cases, insertion and removal of the Norplant System are 15- to 30-minute surgical procedures that are not difficult. Placement-related complications have been reported in 4.5% to 7.5% of medically prompted terminations.[21] Additional reported reactions at the insertion site include infection (0.8%), expulsion (0.4%), and other local reactions (4.7%), including itching, pain, rash, and hematoma.[37–39] Zuber et al[38,40] de-

scribed skin blistering at the insertion site, which apparently was the result of inappropriate capsule placement in the dermis (rather than subdermal insertion). In 1993, Chang and co-workers[41] reported the occurrence of peripheral neuropathy, which also is described by Hueston and Locke[42] in this issue of the *Journal.* Although neither case was serious or life-threatening, each was believed to be related to improper capsule placement, resulting in acute nerve compression.

Difficult Norplant removal cases are primarily those in which the capsules were improperly inserted or in which the clinician was still gaining proficiency in the procedures.[43–45] For example, capsules that are inserted too deeply under the skin or are positioned too widely apart cannot always be located for removal. Such cases may require a larger incision, more extensive use of instruments, or more than one removal attempt.

Although the insertion and removal procedures are not difficult, they do require specialized training. Both the manufacturer and various independent groups provide training programs and videotapes for educating health professionals about insertion and removal procedures. The manufacturer also maintains a referral network of trained providers.

In addition, a number of alternative techniques are now available for use in case of difficult-to-remove capsules. These include the "pop-out" technique of Darney and colleagues,[46] which involves manual manipulation of the capsules through a transverse incision; the Emory method of Sarma and Hatcher,[44] which employs a longer incision and a larger amount of anesthetic; and the "U" method developed by Indonesian physician Untung Praptohardjo,[45] which uses a vertical incision and a special oval ring-tipped forceps. The papers in this issue by Reynolds[47] and Cecil and Holtz[48] offer two additional approaches. Reynolds reports a "Modified U" technique, and Cecil and Holtz describe the successful use of ultrasonography to visualize difficult-to-locate capsules. Ultrasonography, fluoroscopy, radiography, and needle localization all have been previously described as useful for the location of Norplant System implants.[49–52] Physicians facing a difficult removal procedure also have the option of referring patients to a physician with greater experience in this area.

Removal can be difficult even if a well-trained clinician has exercised meticulous care to ensure appropriate capsule placement. Difficult removals have been reported in 13.2% of patients participating in clinical trials.[53] We have had opportunities at the Mount Sinai Family Planning Clinic to remove implants in women who had Norplant inserted by a variety of clinicians in a range of geographic locations, including Colombia, South America, and Kenya. All had been properly inserted.

Careful patient screening and counseling also are essential for lowering the risk of problems related to insertion and removal of the Norplant System, as well as for managing expectations regarding side effects. Women differ in their sensitivity to nuisance side effects and in their ability to tolerate even simple types of outpatient surgery. Before selection of Norplant, women should be carefully questioned about their willingness to undergo these procedures and their expectations regarding the method. Counseling of Norplant System candidates with respect to side effects, specifically the high incidence of irregular bleeding, has already been found to have a favorable impact on continuation rates.[28,30,54] Women who are aware of the likelihood of menstrual cycle changes may be more willing to accept these changes.

If prolonged bleeding is a problem for a patient, clinicians also should be aware that treatments are available to help control irregular bleeding during the first year of use of the method, after which time menstrual patterns will become more regular. These treatments include use of ethinyl estradiol, nonsteroidal anti-inflammatory drugs (such as ibuprofen), and the progestin levonorgestrel.[55]

Rather than litigation, perhaps a better response to Norplant removal difficulties is identifying additional alternative techniques for capsule removal and developing contraceptive implants that minimize or even avoid removal problems. Toward this end, Norplant-2 and a biodegradable contraceptive implant are currently undergoing clinical trials.[12,43] Clearly, continuing the practice of deciding medical issues in the courtroom rather than in the clinical setting can only result in the discouragement of future scientific research and development. In addition to costly legal issues, reduced availability of liability insurance coverage, regulatory barriers, and, sadly, the reality of widespread public misperception regarding contraception continue to jeopardize the availability of new contraceptive options.[56,57] In the case of contraceptives such as the Norplant System, these barriers could mean that women may be denied access to safe and effective means of birth control that is not dependent on user compliance.

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