History of Long-Acting Reversible Contraception (LARC) in the United States

In June 2016, the Jacobs Institute of Women's Health published a white paper summarizing the scientific evidence related to LARC methods. The full white paper summarizes research on the safety, efficacy, and use of LARC methods; explores the factors that influence women's access to these methods; and highlights the importance of prioritizing women's needs and preferences in contraceptive decision-making and is available at http://ow.ly/l4WH301I9yn. This document summarizes the history of LARC methods in the US, adapted from that white paper.

The IUDs and implant available today were preceded by earlier versions that left a problematic legacy for both patients and providers. Although many of the problems associated with earlier methods have since been addressed, the history of these two categories of methods continues to have an impact on LARC provision and use today.

IUD History

First Generation IUDs: Initial Uptake, Challenges, and Rapid Decline

The first generation of IUDs, available in the United States starting in 1968, were made out of a variety of different materials, including plastic and copper, and were manufactured in a variety of different shapes. Some of the more common types of IUDs in the first generation were the Lippes Loop, the Copper-7, and the Copper-T. Within a few years, more than 10% of US women who used contraception were using an IUD (Sonfield, 2007).

The Dalkon Shield came on the market in the United States in 1971, and during the four years that it was available, more than two million women used this IUD. It was a distinctively shaped plastic IUD, and it was the only IUD with a tail made out of a multifilament thread rather than monofilament tail. Ultimately, this tail string was identified as a significant design flaw. Although initial clinical trials reported a pregnancy rate of only 1.1% and an expulsion rate of 2.3%, a study conducted soon after introduction raised questions about the developer's claims, finding a pregnancy rate for the device of 4.7 per 100 woman-years (Davis, 1970; Jones, Parker, & Elstein, 1973). The pregnancy rate would develop particular importance because risks associated with continuing pregnancy in Dalkon Shield users were later identified as another significant problem with this product.

Despite IUDs' initial popularity, use of the method began to decline rapidly as serious health problems associated with their use came to light. These problems included high rates of pelvic

inflammatory disease (PID) – which, when not treated effectively, can lead to infertility and even death – and high rates of septic miscarriages in cases when the IUD failed to prevent pregnancy. By 1973, there was enough concern about IUD-associated infections that Congress held hearings where two physicians testified about the hazards the devices posed to women's health (Boonstra, Duran, Gamble, et al., 2000; Sonfield, 2007). Simultaneously, the CDC began conducting a survey about IUD-related complications that physicians had observed among their patients, which identified more than 3,500 unduplicated case reports of hospitalizations associated with an IUD in the first six months of 1973. Applying these estimates to national data yielded estimates of 7,900 IUD-associated hospitalizations, and five IUD-associated fatalities (Centers for Disease Control and Prevention, 1997). However, these numbers represent estimates from only a single, limited time period, and the total number of infections and deaths associated with IUD use during the 1960s and 1970s has not been definitively established.

The survey also found a relative excess of Dalkon Shield users among those suffering from IUD-associated complications, including complicated pregnancies among these users. The original report concluded that the association might be explained "by an elevated rate of pregnancy with this device, by an increased rate of complications once a pregnancy is established, or by a combination of these postulated factors" (Centers for Disease Control and Prevention, 1997). After publication of the survey, the CDC continued to monitor the problem, publishing an analysis that concluded death from miscarriage was three times more likely among Dalkon Shield than other IUD users (Cates, Ory, Rochat, & Tyler, 1976) and later reporting that Dalkon Shield users were at greater risk for PID than users of other IUDs or people not using IUDs at all (Centers for Disease Control and Prevention, 1983).

The manufacturer (the A.H. Robins Company) suspended US sales of the Dalkon Shield in 1974, although it continued to distribute the device globally (Mintz, 1986). In the United States, women brought hundreds of thousands of lawsuits against the company, resulting in $24 million in jury awards, more than $375 million in payments to dispose of cases, and more than $100 million in legal expenses. In 1985, the company declared bankruptcy, and the Dalkon Shield has not been offered since (Mintz, 1986).

NEW REGULATION OF MEDICAL DEVICES

The scale of the damage done by the Dalkon Shield and the enormous public attention it drew led to major changes in US regulation of medical devices (Rados, 2006). Up until 1976, FDA had very little authority over medical devices – device manufacturers were not required to provide evidence of safety or efficacy for their products before marketing them, and the agency had only limited authority to address problems that emerged afterward. Then, in 1976, the Medical Device Amendments were enacted, requiring device makers to register with the agency and follow quality control procedures. The law gives FDA the ability to subject some devices to pre-market review and approval, and authorizes the agency to ban a device that presents a substantial deception or substantial unreasonable risk of injury or illness (Food and Drug Administration, 2014). The standards for device approval are still, however, significantly less stringent than for drugs; for

example, manufacturers are not always required to provide FDA with data from clinical trials for devices before selling them in the United States.

First Generation IUDs: Legacy/Impact on Current Uptake

Although the Dalkon Shield has not been sold in the United States since 1974, the high level of public awareness of the problems associated with it created enormous doubt about the safety of all IUDs. Additionally, a 1976 CDC study identified a health risk associated with IUDs that was not limited to Dalkon shield users. That analysis concluded that when an IUD user became pregnant, the risk of death from miscarriage was more than 50 times greater for women with an IUD in place who continued their pregnancies than for those without an IUD. The authors of that study wrote that while "the Dalkon Shield carried an increased risk of death, as compared to other devices, […] pregnant women with either a loop or a coil [IUD] in place also had a higher risk of dying from spontaneous abortion than those without any device" (Cates et al., 1976).

Despite the accumulation of data showing the association between early IUDs and infection, almost 2.2 million US women continued using IUDs through the early 1980s, making up more than 7% of contraceptive users in the country (Forrest, 1986). The rate of IUD use dropped again when the manufacturers of the Lippes Loop (with 31% of the US IUD market) and of the Copper-7 and Copper-T (with a combined 66% of the US market) stopped providing devices in this country (Forrest, 1986). Starting in 1986, there was just one IUD available to US women – Progestasert, a hormone-releasing device that had to be replaced annually – and it was not widely used. By 1995, fewer than 1% of US contraceptive users were using an IUD (Piccinino & Mosher, 1998).

This history of IUDs, while unknown to many contraceptive users and even healthcare providers today (Sonfield, 2007), appears to have had a lasting effect on IUD use in the United States. When redesigned IUDs were later brought back to the US market, they faced an unreceptive climate. A new copper IUD (ParaGard) was introduced in 1988, and a new hormone-releasing IUD (Mirena) was approved in 2000, but uptake of both devices was negligible for many years. Contraceptive experts attribute this in great part to the facts that both contraceptive users and healthcare providers in this country had little or no direct experience with IUDs, and what they knew about them was mostly negative (Sonfield, 2007).

By contrast, IUD use was significantly greater in Europe, where sale and use of copper IUDs continued uninterrupted throughout the 1980s and 1990s, and where the Dalkon Shield was rarely used. The level of IUD use varies in Europe from country to country but for many years has dwarfed use in the United States. A study conducted in 2006 by the manufacturer of one IUD found that 27% of contraceptive users in Norway were using IUDs; 21% in Sweden; and about 10% in the Czech Republic, Germany, and the United Kingdom (Sonfield, 2007).

In the United States, perceptions about the risks of the method continue to be shaped by its history in this country, even while knowledge of the historical facts has begun to fade. The association with serious infection and consequent infertility, in particular, may have suppressed use by young

women and women who had not had children (Whitaker, Dude, Neustadt, & Gilliam, 2010). The FDA labels for both ParaGard and Mirena at the time of approval stated that users should have had at least one child and should be in a mutually monogamous relationship (Teal & Romer, 2013). ParaGard's manufacturer publicly stated that the company was taking a "conservative approach" when it introduced the product in the United States, believing that this would reduce the likelihood that a woman using an IUD would be harmed and sue the company (Roan, 1993). The restrictions were taken off the label for the copper IUD in 2005, but many contraceptive users and healthcare providers still had significant doubt that the method was safe for young women.

Unlike in Europe where IUDs had continuity of use over the same time period, re-uptake of IUDs in the US has proceeded slowly. Recent surveys of reproductive age women have shown that many women do not know about the method or whether it would be safe and appropriate for them (Kaye, Suellentrop, & Sloup, 2009; Stanwood & Bradley, 2006). Until recently, high upfront costs have also compounded these barriers, making it difficult for some women who want an IUD to get one (Sonfield, 2007). Furthermore, studies among healthcare providers suggest that many providers still believe that IUDs are not appropriate for adolescents or for women without children (Harper, Blum, Thiel de Bocanegra, et al., 2008; Tyler, Whiteman, Zapata, et al., 2012).

Implant History

The history of implanted contraceptives in the United States is quite different from that of IUDs, but it also created a backdrop that affects how current methods are viewed and approached by both healthcare providers and contraceptive users today. Unlike Dalkon Shield users, the health problems women experienced with the first implant marketed in the United States were not typically life-threatening, but there was significant negative public attention to the method as a result of both clinical problems and policy controversies.

First Generation Implant: Initial Uptake, Challenges, and Rapid Decline

Norplant, the first contraceptive implant available in the United States, went on the market in 1991. It consisted of six plastic capsules, which were implanted under the skin of a woman's arm. Each capsule contained 36 mg of levonorgestrel, released gradually, and the device could prevent pregnancy for up to five years. Norplant was hailed as a major advance that offered a new way to deliver contraceptive hormones, eliminating the possibility of missed doses. Studies showed that after five years of use, the cumulative pregnancy rate for Norplant users was approximately 1%. Additionally, the return to fertility was fast, with the hormones disappearing from circulation within a week after device removal (Fraser, Tiitinen, Affandi, et al., 1998). A reversible contraceptive method with such high efficacy was seen as potentially revolutionary in the field. In the headline on the front page, one major, national newspaper called it "as perfect a method as you can have" (Painter, 1990).

In Norplant's first year in the United States, the manufacturer (Wyeth Ayerst) reported that about 100,000 women received the Norplant implants; by the end of the second year there were reports that the number had risen to 500,000; and by 1994, nearly one million US women were reported to

be using Norplant. This rapid rise occurred in spite of its relatively high cost, with the device itself priced at $350 and provider insertion and removal fees of at least $150 each. Although the manufacturer did not make Norplant available at a discounted public sector price, as was done for all other contraceptive methods at the time, it did set up a foundation to distribute Norplant to low-income women who were uninsured and not eligible for publicly subsidized programs (Samuels & Smith, 1992a). Despite the cost challenges, demand grew so quickly that it outpaced the company's manufacturing capacity at the beginning. Family planning clinics put some women who wanted to get the implant on waiting lists (Boonstra et al., 2000), and state family planning programs implemented eligibility criteria to determine who would get the sought-after implants (Samuels & Smith, 1992a).

With its high public profile, Norplant also attracted significant interest from policy makers. Proposals to incorporate Norplant into social service programs proliferated; there were also cases where it was incorporated into criminal justice sentencing procedures. Both of these developments generated significant criticism and controversy.

However, the fast rise of Norplant was followed by a precipitous fall. Women began to experience unpleasant side effects, including irregular menstrual bleeding, headaches, mood changes, breast tenderness, and weight changes. Irregular bleeding was particularly problematic, as more than half of women using the method experienced bleeding lasting more than eight days per month, which continued for 20% of women after three years (Fraser et al., 1998; Samuels & Smith, 1992b; Sivin, Mishell, Darney, Wan, & Christ, 1998). After five years, about 25% of users requested removal because of bleeding and another 15% requested removal because of headache or weight gain. (Fraser et al., 1998; Sivin et al., 1998). Although some of these side effects had been observed during the clinical trials, many women did not anticipate them, potentially due to inadequate counseling from providers.

IMPLANT: REMOVAL PROBLEMS

Some women also experienced problems with incorrect placement of the Norplant capsules, infection at the site, and difficulty with removal. When an implant was not placed correctly, it could be expelled or cause an infection. Implants that were placed too deeply or capsules implanted too far apart could be difficult and painful to remove. The procedure for inserting and removing the capsules sometimes caused keloid (overgrowth) scars to form, a problem more common among African-American women (Samuels & Smith, 1992b; Scott, 1992). Problems with insertion and removal were attributed in part to lack of adequate training for providers (Samuels & Smith, 1992b; Sivin et al., 1998). Experts reviewing the US Norplant experience noted that although 26,000 physicians had been trained on insertion, training in removal was significantly less common. They recommended allocation of resources to train providers in removal, particularly those who served poor women in rural areas and medically underserved communities (Samuels & Smith, 1992a).

Tens of thousands of lawsuits were filed in the late 1990s against Norplant's manufacturer, as well as against providers inserting and/or removing the contraceptive. Although the company made

settlement payments to many women and even prevailed in some cases that went to court, it did not admit to being at fault. Views about Norplant within the reproductive health community remained sharply divided.

Norplant sales were suspended in the United States in 2002, due to manufacturing issues that raised concerns about the effectiveness of particular lots. A retrospective analysis of the US Norplant experience, published by the Institute of Medicine, attributed the downfall of this product to a combination of factors, including: women's discomfort with side effects; problems with insertion and removal of the device; lawsuits against the manufacturer; legislative and criminal justice efforts to use the implant to restrict child-bearing in ways that disproportionately affected women of color and low-income women; and negative publicity associated with all of the above (Boonstra et al., 2000; Harrison & Rosenfield, 1998). This experience made Norplant's manufacturers hesitant to sell another implant in the United States (Boonstra et al., 2000) even after second-generation implants, such as Jadelle, were developed and made available elsewhere. The single-rod implant (first branded as Implanon, now Nexplanon) made its US appearance in 2006, eight years after it was first introduced in other countries, and its slow uptake may be explained, at least in part, by lingering memories of Norplant.

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