

Fertility and Contraception in Women With Inflammatory Bowel Disease

Jason Martin, MD, Sunanda V. Kane, MD, and Linda A. Feagins, MD

Dr Martin is a third-year gastroenterology fellow and Dr Feagins is an associate professor of medicine in the Division of Gastroenterology and Hepatology at the University of Texas Southwestern Medical Center and the VA North Texas Healthcare System in Dallas, Texas. Dr Kane is a professor of medicine in the Department of Gastroenterology and Hepatology at the Mayo Clinic College of Medicine in Rochester, Minnesota.

Address correspondence to:

Dr Linda A. Feagins

Division of Gastroenterology and Hepatology

UT Southwestern Medical Center

VA North Texas Healthcare System

4500 S. Lancaster Rd, 111B1

Dallas, TX 75216

Tel: 214-857-1603

Fax: 214-857-1571

E-mail: Linda.Feagins@UTSouthwestern.edu

Abstract: Inflammatory bowel disease (IBD) carries a high burden in women during their reproductive years, and family planning issues are often a significant cause of concern. Fertility is normal in women with nonsurgically treated ulcerative colitis and similar or slightly reduced in women with Crohn's disease. Women who undergo ileal pouch anastomosis have reduced fertility. Fertility is likely worsened by disease activity but unaffected by medications used to treat IBD. Infertile patients with IBD respond as well as non-IBD patients to in vitro fertilization (IVF). Despite normal fertility, patients with IBD have fewer children due to concerns regarding infertility, disease inheritance, congenital abnormalities, and disease-related sexual dysfunction. Patients rarely discuss these issues with a physician. When discussion does occur, it may lead to changes in decision-making. Contraceptives are an important part of family planning, particularly during times of high disease activity. All forms of contraceptives are acceptable in patients with IBD, although there are specific considerations. The risks of combined oral contraceptives outweigh the benefits in patients with active disease and patients with prior or high risk for thromboembolism. Oral contraceptives and IBD are independently associated with an increased risk for thromboembolism, although it is not known whether this effect is compounding. Depot medroxyprogesterone acetate injection should be avoided in patients with or at risk for osteopenia. Intrauterine devices and implants are the most effective form of contraception and should be a first-line recommendation. The use of oral contraceptives is associated with the development of IBD, although there is no increased risk of disease relapse with the use of any form of contraceptive.

Keywords

Fertility, contraception, contraceptive, inflammatory bowel disease, Crohn's disease, ulcerative colitis

Inflammatory bowel disease (IBD) is estimated to affect over 1 million people in the United States, with a significant burden of disease during reproductive years.¹ Approximately 50% of patients are less than 35 years of age at the time of diagnosis, and 25% conceive for the first time after their diagnosis of

IBD.² Young women who are affected face unique challenges and often have significant concerns regarding family planning. Evidence suggests that patients with IBD typically have low levels of knowledge in regard to their reproductive health, and a deeper understanding could have a significant impact on decision-making.³ This article summarizes the current data regarding female fertility and contraception in IBD to assist in patient counseling.

Overview of Fertility in Ulcerative Colitis and Crohn's Disease

An operational definition of *infertility* is the inability to conceive within 1 year of having unprotected sexual intercourse. Excluding those who have undergone intestinal resection, women with Crohn's disease (CD) have normal or only slightly reduced fertility, whereas those with ulcerative colitis (UC) have normal fertility. However, despite a similar physiologic ability for childbearing, women with IBD have fewer children than those who are unaffected.⁴

In an early study of CD, nearly 300 women were interviewed in regard to the number of children conceived before and after their diagnosis. The researchers found an almost 60% reduction in birth rate among women with CD compared with that of controls, while controls were found to use contraception more often. The conclusion was that CD affected fertility, although the desire for pregnancy was not addressed.⁵ Later studies have surveyed patients' desire for children. A Scottish survey showed the rate of involuntary infertility in CD to be the same as that of controls, while 36% of patients were voluntarily childless compared with 7% of controls.⁶ This notion was confirmed in a systematic review that found a 17% to 44% reduction in birth rate for women with IBD compared with controls; the reduction was linked to voluntary childlessness, as there was no evidence of physiologic infertility.⁷ A large cohort study was recently performed reviewing the cases of over 4000 women with CD in the United Kingdom. The researchers found an age-specific adjusted fertility rate ratio (AFRR) of 0.88 compared with that of the general population; significantly lower rates were found in women with CD both before (0.88) and after (0.87) diagnosis. After excluding time periods during which women used contraceptives, the researchers found similar overall fertility rates in women with CD and those without the disease (AFRR, 0.95).⁸

In women with UC who have not undergone colectomy, studies have shown that fertility is normal, although similar to CD, there is an increase in voluntary childlessness. Two large European studies found birth rates to be similar among women with UC and controls in a total of 700 patients,^{9,10} whereas 2 smaller American

studies showed a 30% to 50% reduction in birth rates.^{4,11} However, the American studies showed a significant increase in the rate of voluntary childlessness with no difference in involuntary infertility between the groups. As noted above for CD, a recent large cohort study of over 4000 women with UC confirmed these results. This study showed an AFRR of 0.99 for women with UC when compared with controls. For women with UC, the AFRR was slightly higher before diagnosis (1.07) but lower after diagnosis (0.92). However, when considering only times when contraception was not used, AFRR returned toward normal (1.05), suggesting that increased contraceptive use after diagnosis may play a role.⁸

Fertility After Surgery

Although fertility is usually normal in IBD patients who have not undergone surgery, those who have done so experience significantly reduced fertility. Large population studies have indicated that approximately 10% of patients with UC and 25% with CD will need surgery despite the advancements in treatment that have occurred with the introduction of biologic agents.^{12,13} The current gold standard for surgical therapy is total proctocolectomy with ileal pouch–anal anastomosis (IPAA), although ileal rectal anastomosis (IRA) or ileostomy is performed in select cases.¹⁴ IPAA has the advantage of completely removing all diseased mucosa and lowering the risk of cancer. However, there have been numerous studies demonstrating the significant impact of these surgeries on fertility. A meta-analysis found that the relative risk of infertility was 3-fold greater after IPAA. Across 7 studies, the average rate of infertility for medically treated patients was 14%, and the rate of infertility after IPAA was 48%. Nearly half of patients who attempt to conceive after IPAA will be unable to do so within 12 months.¹⁵ These findings are likely due to anatomic changes and fallopian tube scarring after extensive pelvic dissection. Postoperative hysterosalpingography of 21 patients showed that 52% had at least unilateral tubal occlusion and 48% had fallopian tubes that adhered to the pelvic floor.¹⁶ These anatomic changes are likely dependent on deep pelvic dissection, and similar issues with fertility have been documented with total proctocolectomy with end ileostomy.¹⁷ Recent evidence suggests that some of these issues may be ameliorated by a laparoscopic approach. In a recent small survey, 70% of patients who underwent laparoscopic IPAA were able to obtain spontaneous pregnancy vs 39% who underwent an open procedure, although this finding has not yet been validated with additional data.¹⁸ In some situations, an approach that spares deep pelvic dissection, such as IRA, may be justified. IRA does not involve extensive pelvic dissection, therefore theoretically reducing the risk of

infertility. However, this operation should be performed only in UC patients who have normal anal sphincter tone, lack severe perineal or rectal disease, and have no evidence of dysplasia or cancer at the time of the intervention.¹⁹ After IRA, there is continued risk for inflammation and dysplasia in the rectal stump, and continued surveillance is necessary. Studies providing evidence for better fertility rates after IRA in UC patients are lacking, so any benefit is purely theoretical and its role is limited. Lastly, an additional consideration is performing subtotal colectomy with rectal stump and temporary ileostomy (to avoid pelvic dissection) during the childbearing years with reversal to IPAA after childbearing is complete. However, the benefit of this approach is also unproven.

It is possible that other forms of surgery for IBD may also reduce fertility to a lesser extent, although the data are not as clear. The aforementioned large IBD cohort study by Ban and colleagues showed that patients with any intestinal resection have a reduced number of children.⁸ The researchers evaluated 1153 patients with CD and 452 with UC and found that the age-specific AFRR for these patients was lower after surgery (AFRR, 0.81) but not before surgery (AFRR, 0.97).⁸ This is corroborated by an earlier study in which unresolved infertility was more common in women with CD that was treated surgically than in women with CD that was not treated surgically (12% vs 5%).⁶ Other earlier data found no decrease in the number of live births in 78 women who had undergone surgery for CD.²⁰ Current data are insufficient; however, women with IBD who require intestinal surgery of any type may have reduced fertility compared with their counterparts, either as a marker of more severe disease or as a result of the surgery itself.

Effects of Medications on Fertility

A significant patient concern that may lead to voluntary childlessness is the belief that medications may adversely affect fertility or the fetus. However, the vast majority of medical therapy will have no effect on the ability to conceive (Table 1). Corticosteroids have not been shown to have any effect on fertility.²¹ Azathioprine has been evaluated in the transplant literature and also does not seem to affect female fertility.²¹ 5-aminosalicylic acids have not been shown to negatively impact female fertility, although there have not been adequate trials in humans. Although sulfasalazine has a well-known effect on spermatogenesis, it does not have any known effect on female fertility. In animal studies, it has been shown to have no effect on fertility in female mice and rabbits.^{22,23} The effect of anti-tumor necrosis factor therapies on fertility also has not been evaluated in humans, although there have been no issues in animal studies.²⁴ There are no data on

Table 1. Drugs Used in the Treatment of Inflammatory Bowel Disease

	Effect on Fertility	FDA Pregnancy Category
Prednisone	No effect in humans	B
5-ASAs	No effect in animals. Sulfasalazine negatively affects men.	B
Anti-TNF Agents	No effect in animals	B
Mercaptopurine/Azathioprine	No effect in humans	D
Natalizumab	Negative effect in animals at high doses	C
Vedolizumab	No effect in animals	B
Methotrexate	Contraindicated	X

5-ASA, 5-aminosalicylic acid; anti-TNF, anti-tumor necrosis factor; FDA, US Food and Drug Administration.

the effect of natalizumab (Tysabri, Biogen) in humans. However, the drug has been shown to reduce fertility in animals at doses of 30 mg/kg, which is equivalent to 36 times the dose used in humans. Natalizumab has shown no effect on fertility in animals at lower doses.²⁵ Animal studies have shown no effect on fertility for vedolizumab (Entyvio, Takeda), which is gut specific, even at supra-therapeutic doses.²⁶ Methotrexate does not affect fertility but is contraindicated (due to teratogenicity) in women trying to conceive.²⁷

Effects of Disease Activity and Severity on Fertility

Active disease can affect fertility in multiple ways. Active bowel inflammation may cause inflammation of adjacent organs, including the ovaries and the fallopian tubes. Patients may have decreased libido associated with active disease and/or experience dyspareunia from active perianal disease. Moreover, active disease has been associated with depression, malnutrition, and anemia, which may all confound the ability to conceive.²⁸ Ban and colleagues specifically assessed the effect of active disease on fertility rates in a large cohort study in which they evaluated recent corticosteroid use and pregnancy rates.⁸ The researchers found an AFRR of 0.7, which was sustained after adjusting for contraceptive use, suggesting that active disease does reduce fertility.⁸ Moreover, besides decreasing the odds of conception, active disease at the time of conception and during pregnancy has been associated with a higher likelihood for preterm birth and lower birth weight.²⁹ Therefore, experts recommend that women with IBD ideally be in remission for at least 6 months prior to trying to conceive.²⁸

Infertility Treatment in Inflammatory Bowel Disease

Women with IBD have similar rates of fertility and infertility as those of the general population. For women who are unable to conceive, new data suggest that women with IBD respond equally well to infertility treatment. Oza and colleagues evaluated 49 patients with CD and 71 patients with UC, and found similar birth rates after IVF as compared with controls.³⁰ Success rates were 57% for patients with CD, 69% for patients with UC, and 53% for controls (no statistical differences between the groups).³⁰ Additional subsequent data showed that women with UC after IPAA obtained equal success. Twenty-two patients with UC after IPAA and 49 patients with UC prior to surgery underwent IVF, with live birth rates of 64% in the postsurgical group and 71% in the no-surgery group compared with 53% in the control group (no statistical differences between the groups).³¹ Tubal infertility is the likely cause of infertility in patients after IPAA, and, not surprisingly, tubal factor infertility was more common in the CD population compared with the non-CD population (24.5% vs 14.0%).³⁰ It is logical that IVF should work well in this population given that it alleviates the need for functioning fallopian tubes. Women who experience infertility as a result of IBD can expect an IVF success rate of 50% to 60%, which is in line with the rate in women without IBD.

Reproductive Rates and the Effects of Disease on Reproductive Choices

Evidence suggests that women with IBD have near normal ability to conceive but choose not to have children 2- to 3-fold more often than their peers.⁴ Family planning decisions are complex, but disease may influence this decision due to sexual dysfunction, body image, impact of disease on relationships, and concern regarding the effects of the condition or medications on progeny. The term *voluntary childlessness* is disingenuous, as the psychosocial constraints of chronic disease are likely a primary driver in the reduction of birth rates.

Reduced sexual function was first documented over 35 years ago in the IBD population and has remained persistent despite improvements in therapy.³² In a European survey of over 4500 patients, 35% felt that IBD had prevented them from pursuing an intimate relationship and 17% of them felt that IBD had caused a relationship to end.³³ Up to half of women have considered both sexual desire and enjoyment worsened after diagnosis.³⁴ Across studies, women have been more affected than men, with depression being a significant predictor for sexual dysfunction.³⁵ Unfortunately, depression and anxiety are more

common in the IBD population, and in many scenarios, there is an interrelationship between the disorders in which IBD causes or worsens depression.³⁶ For those undergoing treatment of disease flares, corticosteroids can induce mood disorders, and there is an association between corticosteroids and problems with body image and sexual function.³⁵ Control of disease may have an influence in sexual dysfunction, especially in patients who have draining fistulas or whose frequent bowel movements affect their interpersonal relationships. In an older case-control study of 50 women with CD, patients with CD reported more dyspareunia (60% vs 32% in controls), less sexual activity (24% vs 4% in controls with no or infrequent intercourse), and a higher divorce rate (16% vs 6% in controls). Reasons for sexual inactivity included abdominal pain (24%), diarrhea (20%), and fear of fecal incontinence (14%).^{37,38} Despite changing therapy, persistent problems remain in sexual enjoyment, initiation, and rates of intercourse; however, fear and lack of knowledge also influence patient decisions.

Many women with IBD fear that their illness or the medications they take will prevent conception or have a negative effect on any child they conceive. A survey of women with IBD found that 36% believed that all IBD medications are harmful to unborn children, 46% were worried about infertility, 75% expressed concern about passing IBD to offspring, and 30% considered not having children as a result.³ Another study has shown that nearly two-thirds of patients had poor IBD-related reproductive knowledge.³⁹ Survey results indicate that women with IBD who are childless are more likely to have lower knowledge of their reproductive health, and discussion of these issues with a gastroenterologist led to a 72% reduction in the odds of poor knowledge and voluntary childlessness.³ Despite these fears and lack of knowledge, 68% of patients have never discussed family planning with a doctor.⁴⁰ Even in cases in which patients are taking category X medication, physician documentation of discussion has been shown to be poor.⁴¹ Concerns and lack of knowledge about infertility, IBD heritability, congenital abnormalities, and medication teratogenicity likely lead a significant proportion of patients to decide against having children.⁴² Physician discussion of these issues may have a significant effect on the decision-making of these patients.

Family Planning for Patients With Inflammatory Bowel Disease

Family planning is an important issue for any patient of reproductive age but can be even more important in the setting of IBD. Although there are some conflicting data, the majority of studies have shown that women with active disease during pregnancy have a higher risk of preterm birth, low birth weight, and small-for-gestational-age birth

Table 2. Efficacy of Contraceptive Methods and Special Considerations in Inflammatory Bowel Disease

	Rate of Unintended Pregnancy After 1 Year of Typical Use	Special Considerations in Inflammatory Bowel Disease
No Method	85%	Patients with active disease are likely to have worse pregnancy outcomes.
Fertility Awareness	24%	No restrictions
Barrier Methods (Condom or Diaphragm)	12%-20%	No restrictions. Condom use should be advised to protect from sexually transmitted diseases.
Oral Contraceptives	9%	Avoid in patients with prior VTE, those at high risk for VTE, or those with active inflammatory bowel disease.
Depot Medroxyprogesterone Acetate Injection	6%	Avoid in patients with osteopenia or those at risk.
Intrauterine Devices	<0.8%	No restrictions. Levonorgestrel intrauterine devices may improve menstruation-related symptoms.
Implants	0.05%	No restrictions
Female Sterilization	0.5%	No restrictions

VTE, venous thromboembolism.

compared with women in remission.⁴³ It is widely accepted that planning pregnancy while in remission is a more desired scenario. However, women with IBD are over 50% less likely to have been prescribed any form of contraception by a physician.⁴⁴ All methods, including barrier methods, hormonal methods, and intrauterine devices, are available to this population, and individual choice will determine the preferred method. However, highly effective methods that avoid complications of disease are preferred. Approximately half of all pregnancies in the United States are unintended, and half of these are the result of contraceptive failure.^{45,46} Women who use combined oral contraceptives, a contraceptive patch, or a contraceptive ring have 21 times the risk of unintended pregnancy compared with women who use long-acting reversible contraceptives, which include intrauterine devices (IUDs) and implants.⁴⁷ A recent survey of contraceptive uptake in IBD patients showed that 17% used highly effective methods (ie, implants, IUDs, or sterilization), 41% used short-term hormonal methods, and 19% chose barrier/behavioral methods.⁴⁸ Because patients with IBD do not usually have family planning discussions with physicians, this group is a target for educational initiatives that increase uptake of highly effective contraception.

Contraceptive Safety and Side Effects

When contraception is desired, there are a variety of options from which patients and physicians can choose (Table 2). Oral contraceptive pills (OCPs) are by far the most common choice among women in the United States; however, there are important notable considerations when using these drugs in patients who have IBD.⁴⁹ Combined hormonal contraceptives have been associated with an increased risk of thromboembolic events. Another con-

sideration is that oral medications may be less efficacious than expected due to malabsorption in select patients with severe disease. However, OCPs may be the preferred choice for women in certain scenarios.

The risk of venous thromboembolism (VTE) is independently increased in patients with IBD and also with the use of combined hormonal OCPs; however, it is not known whether this is a compounding effect. The estrogenic component of combination hormonal contraceptives increases hepatic production of serum globulins involved in coagulation (including factor VII, factor X, and fibrinogen) and increases the risk of VTE in all users.⁵⁰ As a result, low-dose formulations are now the standard of care, and progesterone components have also been changed to lower-risk forms. However, despite these changes, there is a continued increased risk, approximately 3-fold, for VTE with OCP use.⁵¹ Patients with IBD have a 2-fold increased risk for the development of deep vein thrombosis and pulmonary embolism. Moreover, data indicate that once a patient with IBD develops VTE, he or she is 2 times as likely to die as a result, compared with patients with VTE but without IBD.^{52,53} Thromboprophylaxis for acutely hospitalized patients is a guideline-based preventative measure.⁵⁴ However, more concerning is recent data suggesting that over half of these events occur in the outpatient setting, where there are no clear prophylactic guidelines.⁵⁵ There are currently no data available on the extent of VTE risk in patients with IBD who also take OCPs. Taken together, these data emphasize the necessity for careful consideration in selecting only appropriate patients for use of OCPs. Current guidelines from the Centers for Disease Control and Prevention (CDC) on contraceptive use state that the risks of combined oral contraceptives, as well as the contraceptive patch and the contraceptive ring, outweigh the benefits in patients who have active disease, recent

surgery, immobilization, vitamin deficiencies, and volume depletion as well as patients who are on corticosteroids.⁵⁶ However, in patients with mild or controlled disease, the benefits may outweigh the risks.

Many patients considering or taking OCPs may have concern that efficacy could be effected by malabsorption. Two pharmacokinetic studies have evaluated OCPs in UC patients with and without colectomy. These studies used older, high-dose OCPs and found no difference in plasma concentrations in patients with UC compared with controls. From these data, we can conclude that women with mild UC and those with ileostomy following proctocolectomy likely have absorption similar to that of the general population.⁵⁷⁻⁵⁹ However, the majority of absorption of OCPs occurs in the small bowel, and it stands to reason that patients with CD who have significant small intestinal inflammation or resection are likely to experience malabsorption and reduced efficacy. Unfortunately, there are no studies in patients with CD. However, data from patients with jejunioileal bypass support this notion.⁶⁰ OCPs are likely equally efficacious in patients with UC and those without extensive small bowel surgery or severe active CD. Despite this, OCPs as well as the contraceptive patch and contraceptive ring cannot be considered highly effective forms of contraception because their rate of unintended pregnancy within 1 year is 9%.⁶¹ In most scenarios, more effective forms of contraception can be recommended.

The relationship of contraceptives and bone loss may be an important consideration because IBD also contributes to loss of bone density.⁶² Patients with IBD have higher rates of osteoporosis and osteopenia due to corticosteroid use, malnutrition, vitamin D and calcium malabsorption and deficiency, immobilization, and their underlying inflammatory state. The true prevalence of osteopenia is unclear, but studies have documented rates as high as 40%.⁶³ Depot medroxyprogesterone acetate (DMPA) is the most popular injectable contraceptive in the United States; however, DMPA was associated with bone density loss in a systematic review.⁶⁴ Fortunately, other hormonal contraceptives have not been shown to have any effect on bone density.⁶² On the other hand, DMPA does have other benefits, such as being an acceptable form of contraception in patients who are not good candidates for estrogen-containing contraceptives. The CDC suggests that the benefits of DMPA may outweigh the risks in women with IBD.⁵⁶ Nevertheless, avoiding the use of DMPA should be considered in IBD patients with osteopenia or those at increased risk for the condition.

Long-acting reversible contraceptives, such as copper or levonorgestrel IUDs or etonogestrel implants, are highly effective forms of contraception that, with typical use, have efficacy rates similar to those of sterilization procedures. In a 1-year period, less than 1% of women

will have an unintended pregnancy with typical use.⁶¹ The CDC recommends these forms of contraception in women with IBD without restriction. There are no known specific side effects of concern in the IBD population. However, as with all interventions, each has particular side effects of general concern. In all progesterone-only contraceptives, the most common reason for discontinuation is unpredictable bleeding.⁶⁵ For both implants and IUDs, common concerns include cost and pain associated with insertion. IUD uptake is hindered by the misconception that it is inappropriate for nulliparous women and women with a history of pelvic inflammatory disease.⁶⁶ Current guidelines suggest that the risks outweigh the benefits for both nulliparous women and populations at high risk for sexually transmitted infection.⁶⁵ IUD insertion should be avoided in patients with a high personal risk for gonorrhea or chlamydia infection.⁶⁵ There is evidence to suggest that even in a high-risk population, or with untreated sexually transmitted infection, the absolute risk of pelvic inflammatory disease is low.^{65,67} As with all of the other mentioned contraceptives, neither IUDs nor implants will protect against sexually transmitted infection. Barrier contraception as well as safe behavior should be recommended in all patients to prevent sexually transmitted infection. IUDs and etonogestrel implants are highly effective and safe, and should be considered a first-line recommendation for patients with IBD.

Benefits of Contraceptives for Symptoms of Inflammatory Bowel Disease

Several studies have shown that women with IBD can have increasing abdominal pain and diarrhea associated with menses and that this effect tends to be greater in patients with CD.^{68,69} Contraceptives are often used for menstruation-related symptoms in the general population, and recent data indicate that these agents may also be of benefit in the IBD population. In a survey of 130 women with IBD, symptomatic improvement in cyclical IBD symptoms was reported by 19% of estrogen-based contraceptive users and 47% of levonorgestrel IUD users. Only 5% of all hormonal method users reported symptomatic worsening.⁷⁰ Levonorgestrel IUDs may help with cyclic symptoms in women with IBD, but more data are necessary to confirm these findings.

Contraceptives and the Risk of Developing Inflammatory Bowel Disease

There is no clear etiology to explain the development of IBD. Current studies indicate that the role of genetics is 20% to 25% and that the environment plays a significant role. Many studies have searched for environmental

associations, and OCPs have been shown to be a risk factor for the development of both CD and UC.⁷¹ The most recent meta-analysis of data, involving 36,000 exposed women and a similar number of controls, showed relative risks of 1.46 for CD and 1.28 for UC when adjusted for smoking.⁷² In this analysis, risk increased with the length of exposure but was no longer significant when OCPs were stopped. A more recent study analyzed 2 large prospective cohorts enrolled in the Nurses' Health Study I and II. Among the 232,000 female participants, the researchers identified approximately 700 new cases of IBD. Compared with women who never use OCPs, and adjusted for smoking and other confounders, hazard ratios for developing CD were 2.82 among current users and 1.39 among past users. Among women who either previously or currently smoked, use of OCPs was associated with a hazard ratio of 1.63 for UC. In contrast, there was no statistically significant association between OCP use and the risk of UC among women who never smoked.⁷³

The reasons that OCPs may contribute to IBD are currently unknown. Researchers have theorized that the increased risk is due to the stimulating effect of estrogen on innate immunity or that the prothrombotic effect of estrogen may cause microvasculature changes.^{74,75} There are also data suggesting that estrogen receptors may mediate colonic epithelial barrier function.⁷⁶ If estrogen was the main mediator, hormonal replacement therapy (HRT) would be a good comparator. Interestingly, in a recent analysis of data from the Nurses' Health Study, HRT was found to increase the risk of UC but not CD.⁷⁷ Yet, there is some conflicting evidence that HRT has a protective effect in postmenopausal women with IBD due to converse anti-inflammatory properties.⁷⁸ Taken together, while the exact mechanism remains unclear, sex hormones are likely an important environmental factor in the development of IBD.

Contraceptives and the Risk of Relapse of Inflammatory Bowel Disease

Given the potential effects of sex hormones on the development of IBD, there has been significant concern that contraceptive use may result in disease relapse. However, data have been conflicting. A prospective study followed 152 women for up to 48 weeks and found that current and previous OCP users were 3 times more likely to relapse than nonusers.⁷⁹ On the other hand, a prospective study of 134 women followed for 12 to 18 months showed no increase in flares with OCPs.⁸⁰ Three further cohort studies have been conducted but did not find any relationship between relapse and OCP use.⁸¹⁻⁸³ The majority of these studies were limited by small sample size and lack of reporting of the type of OCP used. In a systematic review,

the body of evidence as a whole suggested that OCP use among IBD patients did not increase the risk of relapse.⁵⁷ There are 2 case reports of 3 women who had symptoms of a flare after the placement of a levonorgestrel IUD.^{84,85} Of these events, 2 were within weeks of placement; in the other scenario, the device was removed after 2 years. At this point, there is not sufficient evidence that OCP use or IUD placement has any effect on CD or UC.

Conclusion

Patients with IBD have important issues to consider with regard to fertility and contraception that can influence their overall health and well-being. Reassurance is warranted in addressing fertility concerns. Patients with CD have similar or slightly reduced ability to conceive, while patients with UC do not differ in their ability to conceive from that of the general population. Women who have surgery, particularly those undergoing IPAA, do suffer from reduced fertility but are equally likely to respond to IVF. Active disease may affect fertility; however, medications to control disease do not. Every effort should be made to achieve disease remission prior to conception, as medications are unlikely to affect this process. Early recognition of depression is likely to benefit patients overall as well as sexual health. Discussion of fertility and sexual issues is likely to benefit patients as they make family planning decisions.

Contraceptive methods should be selected in discussions between patients and their physicians on clinical and personal concerns. Although there may be an increased risk for the development of IBD with OCP use, there is not sufficient evidence to support any specific form of contraception as a cause for relapse. Patients at risk for VTE should avoid contraceptives with an estrogen component, and patients with or at risk for osteopenia should likely avoid DMPA injections. IUDs and etonogestrel implants are safe and highly effective forms of contraception that can be recommended as a first-line intervention in patients with IBD. All patients should undergo counseling on safe behavioral choices and barrier protection to protect from sexually transmitted infection. Family planning is not commonly discussed with IBD patients, but discussion is likely to have a significant positive impact in psychosocial well-being that is sometimes overlooked in the specific quest for disease control.

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