

# Pregnancy, Fertility and Inflammatory Bowel Disease

- Inflammatory bowel disease (IBD) affects people in their peak reproductive years
- Active IBD increases the risk of adverse pregnancy outcomes, including spontaneous abortion, intrauterine growth restriction and preterm birth
- It is important to get your disease under control ('in remission') before conception and to keep it controlled during pregnancy
- Most IBD medications are safe during pregnancy and while breastfeeding and should not be stopped without consulting your specialist
- Getting advice and establishing a pregnancy plan before pregnancy have been shown to improve outcomes for babies and mothers
- Careful monitoring by your specialist in each trimester of pregnancy can detect active disease early and allow treatment adjustment to reduce the impact on your baby

Crohn's disease and ulcerative colitis are the two most common forms of inflammatory bowel disease (IBD), frequently affecting people who are contemplating having children. If you or your partner has IBD, you may be wondering how this will affect your ability to have children, and how pregnancy will affect your IBD.

It is important to discuss these issues with your treating team early, well before planning a pregnancy.

The good news is that most women and men with IBD have normal fertility, and women can expect a normal pregnancy and birth and development of a healthy baby.

Remember that a healthy mother is required for a healthy baby.

## What are my chances of conceiving with IBD?

### For women

#### **Ulcerative colitis (UC)**

If you have UC, your chances of conceiving are unaffected by the disease.

Even if you need to have a colectomy, fertility only appears to be reduced if you undergo pouch surgery. Laparoscopic (keyhole) surgery, now used for most pouch

surgery, appears to reduce scarring and has less impact on fertility than traditional 'open' operations. Reduced fertility is much less of a problem when colectomy with an ileostomy (stoma) is done. This is an alternative to pouch surgery. Women who may need colectomy should discuss these issues early with their IBD specialist and surgeon, as good fertility and obstetric results can be achieved with planning.



## Crohn's disease (CD)

If you have well-controlled CD, your chances of conceiving are the same as the general population's.

When you are having a flare of CD, your chances of conceiving are reduced. This is thought to be due to several possible mechanisms:

- Severe inflammation in the small intestine can sometimes affect the normal functioning of the ovaries and fallopian tubes.
- Previous abdominal operations may result in adhesions (internal scars), which can block the passage of the egg from the ovary to the fallopian tube and uterus.
- Reduced levels of general health, including low weight or poor nutrition, may impair release of eggs (ovulation) and the likelihood of successful implantation.
- Reduced libido: complications such as abscesses and fistulas in the pelvic and anal areas, and general difficulties associated with living with IBD, such as fatigue, abdominal pain, diarrhoea and a poor body image, can all contribute to poor libido.

The good news is that if these issues are addressed and your CD is brought into remission, your fertility and chance of conceiving a healthy baby are generally restored to normal.

### For men

There is no evidence that IBD affects male fertility. However, for men as well as women, problems such as fatigue and poor body image can affect libido and sexual relationships and make it more difficult to conceive a child. Abscesses and fistulas in the pelvic and anal regions may also cause difficulties with erection and ejaculation.

Very rarely, men with IBD who have had a pouch operation, or who have had both their colon and their rectum surgically removed, may have difficulty having an erection. However, this problem is usually temporary or can be successfully treated with medication.

## What is the risk of my child getting IBD?

The risk that your child will develop IBD is about 5–8% when there is one affected parent and about 35% when there are two affected parents.

## General risks in pregnancy

Even in the general population, pregnancy does not always progress normally. Problems or complications affecting the baby's health occur in about 15% of pregnancies. All pregnancies have a risk of birth defects (3–4%) and miscarriage (12–15%). Some medical conditions in mothers may increase these risks, especially when they are not well controlled.

### Before pregnancy

It is important to see your GP to update your immunisations to chickenpox, measles, mumps and rubella, whooping cough and flu. Your GP will check if you are anaemic or iron-deficient and screen you for hepatitis B, hepatitis C and HIV.

It is important to not smoke or drink alcohol during conception and pregnancy and to achieve a normal weight range (body mass index [BMI] of 18.5–25 kg/m<sup>2</sup>). Low weight may be associated with irregular ovulation and difficulty conceiving. A BMI > 25 is associated with the development of diabetes in pregnancy and worse outcomes for the baby.

Start folate (0.5–0.8 mg) supplements before conception and keep taking them throughout pregnancy to prevent spina bifida. Women taking sulfasalazine (Salazopyrin) need a higher dose of folate (2 mg). Folate-containing foods include vegetables (such as asparagus, spinach and broccoli) and fruits (such as oranges, bananas and strawberries), as well as legumes (such as chickpeas, dried beans and lentils), cereals, nuts and yeast extracts, such as Vegemite. Choose foods that have been fortified with folic acid – this includes some breakfast cereals and fruit juices and most breads.

Ideally 3 to 6 months before conception, you should see your gastroenterologist for preconception counselling to confirm disease remission, discuss your concerns and fears and establish a pregnancy treatment plan, which will be sent to your GP and pregnancy care team. You may need extra tests to confirm your disease is well controlled, such as blood tests to look at inflammatory markers and drug levels, measurement of faecal calprotectin level, a colonoscopy, x-rays, magnetic resonance imaging (MRI) and/or intestinal ultrasound.

If either symptoms or test results show evidence of significant disease activity, your specialist may recommend delaying conception until your disease is well controlled, depending on your age and situation.

## How does IBD affect pregnancy?

The chances of a successful pregnancy and a healthy baby are excellent when IBD is well controlled ('in remission') at the time of conception and during pregnancy. Therefore, it is recommended that women achieve sustained remission (confirmed by faecal calprotectin level or endoscopy) for at least 3 to 6 months before conception, to improve the chances of a successful pregnancy.

For women with active IBD, rates of adverse pregnancy outcomes are slightly higher than in the general population, including higher rates of miscarriage, poor baby growth, prematurity and low birth weight.

### How does pregnancy affect my IBD?

In the past it was thought that IBD became less active during pregnancy, but we now know this is not true.

Active disease at conception is strongly associated with ongoing disease activity and symptoms during pregnancy.

If you have CD affecting the small bowel and your disease is in remission, the risk of a flare is the same as that for patients who are not pregnant. There is a slight increase in the risk of flare for women with UC or Crohn's colitis.

### Use of IBD drugs during pregnancy and breastfeeding

Many people are afraid to take medication while pregnant, and this is understandable.

This fear may be increased by the Therapeutic Goods Administration (TGA) classification of medication safety in pregnancy, which is often based on animal studies or theoretical concerns. Electronic prescribing programs used by GPs may show warnings when IBD medications such as mesalazine are prescribed. However, these pop-up warnings are based on outdated data that do not take into consideration the negative effect of disease activity during pregnancy. In recognition of this problem, the Food and Drug Administration (FDA) in the United States has changed its pregnancy category system so that categories A, B, C, D and X are now not used in product labelling. The TGA in Australia is also reconsidering its approach.

The guidelines that IBD doctors use to care for pregnant patients are those from expert agencies, such as ECCO (European Crohn's and Colitis Organisation), which classifies medications as 'safe', 'probably safe'

or 'harmful' based on postmarketing studies with real patients, and expert experience with these drugs. It has been found that many IBD drugs are safer in real-world experience than their 'official' ratings.

Therefore, it is usually not necessary to change the medicines you take for IBD before you try to conceive.

The only exceptions to this are:

#### 1. Sulfasalazine (Salazopyrin)

Sulfasalazine leads to reversible male infertility. This effect is temporary, and fertility should return to normal levels within 2 to 3 months of stopping the medication. There are several good alternatives to sulfasalazine, such as mesalazine, olsalazine or balsalazide, which may be used instead. These have the same beneficial effects on IBD control but usually do not affect fertility.

#### 2. Methotrexate and thalidomide

Methotrexate and thalidomide both increase the risk of birth defects when taken by either men or women. These drugs should therefore be stopped 6 months before conceiving, after discussion with your IBD treatment team, and a safer alternative should be prescribed. All women taking methotrexate or thalidomide should use a reliable form of contraception. If you are taking either of these drugs and experience an unplanned pregnancy, you should stop using the drug and see an obstetrician and your IBD specialist for immediate counselling.

#### 3. Allopurinol

Some people need to take this medication with azathioprine or 6-mercaptopurine. There is not yet enough information from studies to recommend continuing use of allopurinol during pregnancy, and it may be unsafe to continue taking it, so it is best to discuss this with your doctor before conception. Your doctor may stop the allopurinol and either find another medication to treat your IBD during pregnancy or continue use of azathioprine without allopurinol.

#### 4. Vedolizumab (Entyvio) and ustekinumab (Stelara)

These are newer medications and there are limited data about their safety in pregnancy. If you are using either of these medications, please discuss them with your gastroenterologist before conceiving. Women who conceive while using these drugs may elect to continue, after discussion with their gastroenterologist about alternative options, but should have close monitoring of the baby.

Short courses (1–2 weeks) of antibiotics, such as metronidazole or ciprofloxacin, may be required for women with perianal fistulas. They appear safe to use in this way during pregnancy if needed.

The most important way to improve your chances of having a healthy baby is to keep the disease under control before and during pregnancy. So, if your current medication is working well (and is NOT methotrexate, thalidomide or allopurinol), it is usually better not to change your medication.

## Monitoring during pregnancy

You should undergo regular review of your IBD with your treating team, at least once per trimester during pregnancy and 6 weeks after birth, in addition to your usual obstetric care.

Blood test results and symptoms can be affected by pregnancy, so alternative tests, such as measurement of faecal calprotectin and an intestinal ultrasound, may be recommended to check for disease activity. CT scans and x-rays can't be used during pregnancy. MRI (without use of a contrast agent) can be considered after Week 20. Endoscopy can be used during pregnancy if the disease is severe, with light sedation and close monitoring, and is safe for the baby.

## Management of a flare during pregnancy

If your disease flares, it is important to get treatment without delay to prevent any impact on the baby. Medication choices are similar to those available for non-pregnant patients. The 5-aminosalicylic acid (5-ASA) medications (sulfasalazine [Salazapyrin], mesalazine [Asacol, Pentasa or Mezavant], olsalazine and balsalazide), steroids (prednisolone and hydrocortisone) and anti-TNF therapy (infliximab and adalimumab) can be started or recommenced in pregnancy. Thiopurines (azathioprine or 6-mercaptopurine) can be restarted in women who

have tolerated them in the past. Starting thiopurines for the first time in pregnancy can be considered for women who are very unwell and are expected to need anti-TNF therapy, but they will require careful monitoring for tolerance in the first few weeks.

## Can I have a normal vaginal delivery?

The mode of delivery of your baby is primarily guided by your obstetrician. Most women with IBD can have a vaginal delivery. The only IBD-specific reasons why you may need a caesarean section are if you have a history of perianal fistulas, narrowing at the anus (stenosis) or past damage to the anal muscles. A caesarean section is recommended for women with an ileoanal pouch.

## Breastfeeding

Breastfeeding is encouraged for women with IBD. IBD drugs, including 5-ASAs, thiopurines and anti-TNF medications, are considered safe while breastfeeding. Low levels of IBD medications may be found in breast milk, but this is not thought to affect the baby.

## After birth

There is an increased risk of disease flare in women with UC and colonic CD after giving birth. You should monitor your symptoms carefully and see your IBD team at 6 weeks after the birth or earlier if you have problems. If you have stopped taking IBD medications, you should start taking them again as soon as possible after giving birth.

## Vaccination

All standard vaccinations should be given to your baby, except if you have been taking anti-TNF therapy. Rotavirus and live travel vaccines should be avoided in babies exposed to anti-TNF therapy.

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