

Oxford Translational Gastroenterology Unit

# Pregnancy and Inflammatory Bowel Disease (IBD)



Most women with inflammatory bowel disease (IBD) have a normal pregnancy and deliver a healthy baby.

Active disease is more of a risk to a normal pregnancy than most medication. If you are planning for pregnancy, you should discuss the potential risks of IBD and pregnancy with your gastroenterologist. They will be able to help you make changes to improve outcomes, such as taking high-dose folic acid before you become pregnant.

If you are already pregnant, you will need to have regular medical visits and follow a set treatment plan. This will be organised by the IBD and pregnancy specialist staff. It is important that you are also regularly monitored by an obstetrician, to monitor your baby's growth, as well as a gastroenterologist to check for signs of an IBD flare.

If your pregnancy is unplanned, you should continue to take all medication (except methotrexate) until you have talked with your gastroenterologist. Please make an appointment with them as soon as possible. Some GPs and even some obstetricians may be unfamiliar with managing IBD in pregnancy. Please check with your gastroenterologist, who can then discuss your care with the team of doctors involved in your pregnancy.

There can be lots of confusing advice on the internet about pregnancy when you have IBD, so we have written this leaflet to offer our specialist advice.

Most importantly, dozens of healthy babies are born every year to mothers with IBD at the John Radcliffe Hospital!

## How can I prepare myself for pregnancy?

**Keeping your disease under control before conception and throughout your pregnancy will help ensure the best outcome for yourself and your baby.**

If you are thinking about starting a family, now is the time to invest in your own health as much as possible. This would be a good opportunity to discuss your current lifestyle with your specialist and IBD nursing team, to see how you might be able to further reduce your chances of having a flare. For example, it is extremely important to take your medicine on time and to avoid triggers, such as stress or foods that you know will make you unwell.

It is very important that you take the best possible care of yourself to maximise your chances of a healthy pregnancy.

There is no evidence that ulcerative colitis or inactive Crohn's disease affects fertility. If you have inactive IBD you are likely to be just as fertile as someone who does not. However, active Crohn's disease, previous surgery involving the pelvis (e.g. pouch surgery), or a past complication such as a pelvic abscess, may reduce your fertility.

It is important that your IBD is under control. We will help you monitor this by assessing your symptoms, carrying out blood tests and possibly performing an endoscopy, to maximise your chance of becoming pregnant.

Any woman planning a pregnancy should try to eat as healthily as possible. This also applies if you have IBD. You may also need to have blood tests to check that your vitamin B12, vitamin D, folate, and iron levels are normal. These nutrients should then be replaced, if necessary. Your GP should be able to prescribe you supplements, if needed. When planning a pregnancy, it is generally recommended to take a higher dose of folic acid (5mg once a day).

It is also important to stop smoking and avoid alcohol before and during your pregnancy.

Before becoming pregnant, you may also wish to discuss a plan for the medications you will take during your pregnancy with your specialist. This will help you to feel comfortable that you know what any changes will be and will give you time to assess your options, together with your specialist.

Most drugs used in IBD appear to be safe in pregnancy. The benefits of continuing with medication in pregnancy outweigh the potential risk to the baby.

The exception to this is methotrexate, which should be stopped for about 6 months before you try to conceive, as it can cause birth defects.

If you discover that you are pregnant before speaking to a healthcare professional, you should continue taking your medications (apart from methotrexate) and get in touch with your GP or gastroenterologist as soon as possible.

All prescription, non-prescription or herbal medications should be reviewed by a doctor if you discover you are pregnant, to check whether they are safe. If you have any specific questions about drugs for IBD (mesalazine, azathioprine, mercaptopurine, methotrexate, steroids, adalimumab, infliximab, golimumab, or vedolizumab) you should discuss these with your gastroenterologist.

## What are the effects of IBD medication on fertility?

**There is no evidence that medication for IBD affects fertility in women.**

In men, sperm quality may be affected by sulfasalazine or methotrexate. The effect of sulfasalazine is reversed once the drug is stopped. Methotrexate can also cause a low sperm count, which improves within a few months once the drug is stopped. Azathioprine does not appear to effect sperm count or quality.

## What is the risk of my child developing IBD in the future?

The risk of your child developing IBD because you have IBD is low. It would be approximately 5% over the child's lifetime if you have Crohn's and approximately 2% if you have ulcerative colitis.

It is extremely uncommon for both parents to have IBD, so exact estimates in these circumstances are hard to come by. However, in this situation, the chance of a child developing IBD at some stage in their life is higher than if only one parent has the condition.

The way in which your child is born (vaginally or by Caesarean section) does not affect their risk of developing IBD in the future.

## What might be the effect of pregnancy on my IBD activity?

If your IBD is inactive, the risk of relapse is the same as for non-pregnant women; this is approximately a 30% chance of a flare over a year.

Studies show that if IBD is inactive at the time of conception and during the pregnancy, this will allow for the best outcomes for both you and your baby.

Becoming pregnant when your IBD is active can increase the risk of having active disease during your pregnancy.

If you do develop a flare during your pregnancy, the management of it will be very similar to when you were not pregnant.

Pregnancy increases the chances of blood clots in the legs (deep vein thrombosis, also known as DVT) or the lungs. Active IBD is also a risk factor for DVT, so if you are having a flare of your IBD you may be asked to take a medication to thin your blood and reduce the risk of clots. This medication does not carry a risk to the baby.

After pregnancy, you may find that your IBD is more manageable than before.

## What is the effect of IBD on the baby?

**Most babies born to mothers with IBD are normal and healthy.**

Although most babies born to women with IBD are healthy, if you have Crohn's disease you may have a higher risk of delivering early (prematurely), and having a baby with a low birth weight. The most important reason for problems developing is having active disease during your pregnancy.

For babies born at term, there does not seem to be an increased likelihood of complications, such as infections.

## How safe is IBD medication in pregnancy?

**Most IBD medications, except methotrexate, are considered to be of low risk during pregnancy. The most important priority is to maintain your health.**

As you can imagine, the safety of medications during pregnancy has been vigorously discussed over the years, but reported studies have had conflicting results.

Controlled trials of treatment are unethical during pregnancy, so most of the available data are taken from reviews of medical records. Nevertheless, these reviews still provide important information for medical practitioners and patients.

Product information leaflets that come with medication will always caution against use during pregnancy or breastfeeding without medical advice. This is the default position of pharmaceutical companies. Most specialists agree that mothers-to-be should continue with their maintenance medication, to keep disease under control.

The table below is based on information from the second European Evidence-Based Consensus on Reproduction and Pregnancy in IBD, carried out by ECCO (European Crohn's and Colitis Organisation). It shows the risk of taking certain medications during pregnancy and breastfeeding.

<b>Medication:</b>	<b>During pregnancy:</b>	<b>During breastfeeding:</b>
Mesalazine	Low risk	Low risk
Sulfasalazine	Low risk	Low risk
Corticosteroids ( <i>prednisolone and budesonide</i> )	Low risk	Low risk, but a 4 hour delay before breastfeeding is advised
Thiopurines ( <i>azathioprine (AZA) and mercaptopurine (MP)</i> )	Low risk, limited data on 6-TG (6-thioguanine or 'metabolites')	Low risk
Anti-TNF agents ( <i>infliximab and adalimumab</i> )	Low risk, consider stopping around week 24 if in long-term remission. See text on page 10.	Probably low risk, limited data
Methotrexate	Do not take during pregnancy	Do not take when breastfeeding
Metronidazole	Avoid in the first trimester	Do not take when breastfeeding
Ciprofloxacin	Avoid in the first trimester	Do not take when breastfeeding

**Mesalazine** is almost universally considered safe (by the European Crohn's and Colitis Organisation and the Food and Drug Administration in the United States) for use during conception, pregnancy and breastfeeding. However, there have been reports of lower birth weight babies born to mothers taking mesalazine, although this could have been because of the active disease itself.

A particular brand of mesalazine, Asacol®, comes with dibutyl phthalate coating. This has been associated with urinary tract abnormalities in animal studies, but these have not been seen in humans. If you take this brand of mesalazine, it may be best for you to switch to another type. Please speak to your specialist about this.

If you are taking **sulfasalazine**, then you should also take a higher dose of folic acid (5mg/day. This is because sulfasalazine treatment affects how well your body absorbs folate.

**Prednisolone** and **budesonide (corticosteroids)** are also considered safe. Corticosteroids used in IBD can cross the placenta to the fetus but are rapidly inactivated by enzymes in the placenta. This means that the baby would only be exposed to very low levels of these drugs.

High doses of corticosteroids in the last few weeks of pregnancy should be avoided, if possible, because the baby can become dependent. However, high doses should be used if you require it, as uncontrolled inflammation could be more harmful.

Some studies have found the possibility of a small risk of cleft lip or palate in babies whose mothers have been receiving treatment with steroids in the first trimester of pregnancy, though this has not been found in larger studies.

**Azathioprine (AZA)** and **mercaptopurine (MP)** are generally thought to be low risk, as the benefits of controlling disease outweigh any theoretical or potential risk.

AZA is converted to MP in the body, so both drugs have the same effects on pregnancy or breastfeeding, even if the product information that comes with each drug is different.

Exposure of babies during pregnancy to AZA or MP has been reported in many hundreds of cases. Most studies have shown the safety of these drugs when being taken by mothers (or the baby's father), with no increased risk to the baby.

In cord blood, the breakdown products of AZA or MP ('metabolites' called 6-thioguanine) were found at a level of about half that which was measured in the mother. Although some of the 30 babies in this study had a low haemoglobin level (anaemia), which may have been caused by 6-thioguanine metabolites, this soon got better and caused no ill effects.

Low birth weight, miscarriage, and premature delivery have all been reported, but these are almost certainly related to the severity or activity of the IBD, which was why the women were taking AZA or MP in the first place.

A summary of all studies (a 'meta-analysis') reported no increased risk for adverse pregnancy outcomes in women with IBD who were treated during pregnancy with thiopurines (the class of drugs which includes azathioprine and mercaptopurine). This was compared to the pregnancy outcomes of IBD patients who did not take this treatment.

The use of AZA or MP in pregnancy does not appear to affect the immune system of babies, although there are reports of abnormalities in animals that were given much higher doses of the drug than are used for humans. Overall, the large majority of specialists agree that either AZA or MP are considered to be safe to take during pregnancy and when breastfeeding.

**Infliximab** and **adalimumab (anti-TNF agents)** are also generally considered low risk during conception, pregnancy and breastfeeding. There are several hundred reports of successful pregnancies in mothers treated with these drugs, with the

number of miscarriages and birth defects not significantly different from national statistics of women not taking infliximab and adalimumab, even when they are taken in combination with AZA or MP.

However, both drugs can cross the placenta and stay in the circulation of the baby for up to 12 months. For this reason, a decision to stop these drugs at around 30 weeks of pregnancy should be considered, as this helps to lower the levels of these medicines in the baby's bloodstream after birth. This will depend on whether your disease is in stable remission and unlikely to flare in the near future. If your disease is particularly active, it is best to continue treatment throughout pregnancy.

When all published studies were collected, no differences in adverse pregnancy outcomes, congenital abnormalities, prematurity or low birth weight were detected in mothers with IBD who had adalimumab or infliximab in pregnancy. Reassuringly, anti-TNF use also does not appear to delay the development of the baby after birth.

We would recommend that you have a discussion with your gastroenterologist to weigh up the potential benefits or risks to both yourself and your baby of continuing the use of these medications during your pregnancy. The decision should be decided on an individual basis, and it is important to consider that protecting your health is the most vital aim to help you have a safe pregnancy.

The most important point to think about when using adalimumab or infliximab in pregnancy, is the fact that these drugs will remain in your baby's circulation for some months after they are born (up to 12 months). This can affect live vaccines (such as the MMR vaccine, BCG against tuberculosis or rotavirus vaccines), which means your baby may not be able to have some of the scheduled vaccinations in their first year.

**Vedolizumab** is an antibody that has recently become available for use in IBD. As it is so new, there is relatively little information available about its safety in pregnancy.

It is expected that some amount of the drug will be transferred across the placenta to the baby, but we do not yet know about its effects.

All the available information from 46 conceptions (24 pregnancies in women with IBD, 19 fathers and 3 pregnancies in mothers who had a placebo during the trials) that occurred during 6 clinical studies has been collected. There were 11 live births with no problems reported, of which there were 2 premature births at 30 and 36 weeks. One premature birth was in a mother with a history of premature births. One infant who was born at full term (40 weeks) subsequently had a brain abnormality discovered after birth. There is also a case reported to the manufacturers of growth restriction of a baby in a woman who received vedolizumab, with a decision to proceed to an induced abortion.

As such, there is currently insufficient information to draw meaningful conclusions, since major congenital abnormalities affect up to 3% of births in the normal population and miscarriages are common.

To help doctors understand as much about the drug as possible over the next few years, a registry has been set up to record all pregnancies and outcomes in women receiving vedolizumab.

Until more information is available, if you are thinking of starting to take vedolizumab you would also need to think about your plans to have a baby. You may want to look into other treatment options, if they are available. It is best to discuss the options and any more recent information about vedolizumab with your IBD specialist.

If you are on vedolizumab and become pregnant, then you and your baby will need careful monitoring. You will also need to talk about continuing treatment with your IBD specialist and obstetric physician.

**Methotrexate (MTX)** causes fetal birth defects and should not be used during pregnancy. Normal pregnancy outcomes have been reported, but exposure to MTX, particularly during the first trimester, may result in miscarriage, slow growth, and major congenital malformations.

If you are planning on becoming pregnant, or find that you are already pregnant, and are taking methotrexate, you will need to stop immediately and start high-dose folic acid replacement.

If you have become pregnant without planning it, we may discuss the option of termination with you. However, this may not necessarily be something that needs to happen.

To avoid exposure to methotrexate, it should be stopped in both women and men who are thinking of starting a family. Current guidance suggests that it is best to wait 3 to 6 months after stopping methotrexate, whilst using effective contraception, before trying to conceive.

If you are taking methotrexate and are planning a pregnancy, please discuss this with your IBD specialist.

**Metronidazole** and **ciprofloxacin** are antibiotics commonly used in IBD. Some studies have shown an increased risk of cleft lip or palate with the use of metronidazole, but not others.

Animal studies have shown a link between musculoskeletal abnormalities and ciprofloxacin, but this has not been seen in humans. As a result, they are both best avoided in the first trimester of pregnancy.

## Is endoscopy safe in pregnancy?

**Both colonoscopy and sigmoidoscopy are considered to be safe in pregnancy.**

However, colonoscopy (which involves a laxative bowel preparation and a look around the whole colon) is generally avoided in pregnancy, despite reports that it can be safely performed.

Flexible sigmoidoscopy (which simply requires an enema and look at the rectum and lower part of the colon) is considered safe, with or without sedation, and does not increase the risk of miscarriage.

## Are imaging tests safe in pregnancy?

Occasionally, imaging tests (such as scans and X-rays) may be arranged to help assess your IBD activity. Ultrasound and MRI scans are considered to be safe, whereas tests which involve radiation (X-rays), such as CT scans and barium studies, should generally be avoided where possible.

## What is the effect of pregnancy on ileostomy or pouch function?

If you have had surgery, you may have an ileostomy/stoma ('bag') or ileo-anal pouch.

Pregnancies in women with a stoma or pouch generally proceed without problems, but we would need to plan with you the best way of delivering your baby. You will also need to make sure you stay well hydrated and your bowel movements are regular.

Approximately 30% of mothers with a stoma (30 in 100) experience increased bowel frequency when pregnant. If you have a pouch, you may find that your pregnancy temporarily affects your continence (ability to 'hold in' faeces or urine). These are simply the physical effects of the stoma or pouch being squashed by the growing baby – they usually get better after delivery. Make sure you keep up a good fluid intake throughout your pregnancy, especially if you are sick at any point.

## What is the effect of smoking and alcohol on pregnancy and on IBD?

**Smoking and alcohol are harmful to the baby. They may cause low birth weight and increase the risk of deformity and miscarriage.**

Smoking can increase the risk of a flare in Crohn's disease, as well as the risk of blood clots (deep vein thrombosis, commonly known as DVT). If you smoke then you should stop, for your own health and that of your baby.

## What is the follow-up during pregnancy?

It is important that your pregnancy is managed by a team of specialist practitioners, including obstetricians, obstetric physicians, midwives, gastroenterologists, clinical nurse specialists, your GP and, if relevant, a colorectal surgeon. This team of specialist practitioners will be able to discuss with you the effect of IBD on pregnancy, delivery and care after delivery. This will help you to achieve the best possible outcome for your pregnancy.

You should have an outpatient review by a gastroenterologist within 3 months of becoming pregnant, a few weeks before delivery and shortly after delivery.

You will be able to discuss any decisions that may affect you or your baby with your gastroenterologist and obstetrician. You may need extra visits if you have symptoms of a flare of IBD (diarrhoea, abdominal pain or rectal bleeding).

Regular review by the obstetric team is important, to monitor your baby's growth. In Oxfordshire this is usually carried out by the Silver Star Unit, in the Women's Centre at the John Radcliffe Hospital. They specialise in the obstetric care of mothers with current medical conditions. You will be referred to the Silver Star Unit, either by your GP, midwife or your consultant.

You may be offered additional appointments, scans or other care to help monitor and support you and your baby during pregnancy.

## What is the best way to give birth?

Your gastroenterologist, obstetrician and/or colorectal surgeon will discuss with you whether you should aim for a natural delivery (vaginally) or Caesarean section.

The different options for delivery need to be discussed, as the pelvic floor muscles used to help deliver naturally are also important for stool continence. This is particularly important if you might need surgery (such as a pouch) in the future.

Caesarean sections should only be carried out when there is a medical reason to do so. You are likely to be recommended to have a Caesarean section if you have active Crohn's disease in your rectum or anus, an ileo-anal pouch, or ileo-rectal anastomosis.

This is done to minimise the risk of damage to your anal sphincter and perianal area, as these affect your continence.

We will also recommend a Caesarean section if you are likely to need surgery in the future. This might be because you have had a troublesome course of colitis. Your IBD specialist, obstetric physician and colorectal surgeon (if necessary) will discuss this with you.

The decision of how to give birth appears to be more important for the first baby than subsequent pregnancies. If you have had a successful vaginal delivery before, you are likely to be able to have another vaginal delivery, if there are no medical reasons not to.

During a natural delivery, we may need to carry out an episiotomy (a cut made to the perineum to help with delivery). However, we will try to avoid doing this, as the perianal area may be affected, although this is likely to be a better option than an uncontrolled tear.

The decision of whether to carry out an episiotomy will be made based on the circumstances of your delivery.

## What will happen after delivery?

**It is important to continue with your medication after you have given birth, as this will reduce the possibility of relapse.**

This will allow you the time to enjoy the new experience of motherhood without the distraction of active disease. You will have an appointment in the IBD clinic 6 weeks after your delivery, to check how your IBD symptoms are.

## Is breastfeeding safe while taking medications for IBD?

The benefits of breastfeeding far outweigh the risks for most medications. However, it is best to discuss the safety of taking IBD medications when breastfeeding with a gastroenterologist.

**Mesalazine** medication can be taken during breastfeeding.

**Prednisolone** appears in low concentrations in human breast milk. To minimise exposure, you should wait for 4 hours after taking this medication, before breastfeeding, but this may not always be practical.

**Azathioprine** and **mercaptopurine** appear in tiny amounts in breast milk in their metabolised form, but haven't been found in the circulation of breast-fed babies. Consequently (and despite the advice on the product information leaflet for mercaptopurine), the benefits of breastfeeding can generally be considered to outweigh the risks of exposing the baby to such tiny amounts.

**Infliximab** and **adalimumab** can pass through into breast milk in very small amounts, but they are proteins and will normally be digested. To date, there is no information to suggest any ill-effects to the baby.

**Vedolizumab** is likely to be passed through into breast milk in very small amounts, but currently there is no information to make recommendations about its safety.

If you have taken vedolizumab during your pregnancy, it is likely that the benefits of breastfeeding will outweigh any risks of ingestion of vedolizumab by your baby. This is because vedolizumab, like adalimumab or infliximab, is a protein that will be digested.

However, you should discuss this with your IBD specialist and obstetric physician, as it may affect whether your baby can have their scheduled vaccinations.

**Metronidazole** and **ciprofloxacin** are passed over into breast milk and should be avoided where possible.

## Further information

### **UpToDate, Patient information: Inflammatory bowel disease and pregnancy (Beyond the Basics)**

[www.uptodate.com/contents/inflammatory-bowel-disease-and-pregnancy-beyond-the-basics](http://www.uptodate.com/contents/inflammatory-bowel-disease-and-pregnancy-beyond-the-basics)

### **Crohn's and Colitis UK, Pregnancy and IBD**

[www.crohnsandcolitis.org.uk/about-inflammatory-bowel-disease/publications/pregnancy-ibd](http://www.crohnsandcolitis.org.uk/about-inflammatory-bowel-disease/publications/pregnancy-ibd)

*The Oxford IBD team hopes that you find this information useful. We will be very happy to discuss any further questions or concerns you may have in clinic.*

If you have a specific requirement, need an interpreter, a document in Easy Read, another language, large print, Braille or audio version, please call **01865 221 473** or email **[PALS@ouh.nhs.uk](mailto:PALS@ouh.nhs.uk)**

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