Crohn's Disease, Ulcerative Colitis and Pregnancy

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Introduction

Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, frequently occur in younger patients who are concerned about planning a family and related questions. Women and men suffering from IBD – as well as their partners – are often unsure of the effects of diagnostic and therapeutic measures on the outcome of their pregnancy. They may have questions about such issues as endoscopic examinations of the gastrointestinal tract, radiologic examinations, not to mention the possible need for surgery and/or the use of various drugs.

Patients may also have questions on how pregnancy may affect the course of their bowel disease and whether any special precautions (such as the method of delivery) have to be considered. Does pregnancy lead to a worsening of pre-existing inflammatory bowel diseases or cause an acute episode?

Patients are frequently unsure whether their fertility is reduced by inflammatory bowel diseases and whether pregnancy may be even possible. Patients and their families may also have questions relating to the probable hereditary predisposition involved in the development of inflammatory bowel diseases.

It is important for patients affected with inflammatory bowel diseases together with their spouses and families to be adequately counseled before, during and after pregnancy. This will help to reduce unreasonable fears regarding pregnancy and to recognize as soon as possible any dangers or complications for mother or baby.

The purpose of this brochure is to offer answers to commonly asked questions. Current knowledge is explained on the basis of the latest scientific studies.

At the same time, we remind our readers that this brochure does not provide the only valid answer to the many controversial questions involved in the context of pregnancy and inflammatory bowel diseases. It also cannot replace the trust you place in your personal physician and the value of personal discussions relating to your care. Finally, no brochure can address all of the many individual situations that can affect both your pregnancy and your inflammatory bowel disease.

It must also be emphasized that, as a result of advances in our understanding of these issues, our recommendations with respect to medical care and general measures may change. This applies to both diagnostic methods and especially to the use of medications, not only because of continued advances in the form of new methods and drugs, but also because increasing experience with existing methods and drugs provides improved understanding of their advantages and disadvantages. For this reason, you should always discuss these questions with your treating physicians.

Prof. Dr. Axel Dignass

Can women and men with inflammatory bowel diseases become parents?

In general, the answer to this question is "yes". There are, however, a number of fundamental issues that must be addressed when planning a pregnancy. As we will discuss in more detail below, it is particularly important to plan a pregnancy during a period when your disease is inactive. At such times, your fertility, with few exceptions, is not diminished and your pregnancy will not differ significantly from that in healthy women and men.

In some cases, inactive disease may be due to the use of drugs, which may be harmful during pregnancy. In these cases, it is very important to discuss your desire for pregnancy with the physicians involved in your care as early as possible.

How do inflammatory bowel diseases affect female and male fertility and chances for successful pregnancy?

■ Fertility in women with inflammatory bowel diseases

Women with ulcerative colitis are usually as fertile as healthy women. Exceptions are encountered more frequently after extensive surgeries. Just a few years ago, the general consensus was that reduction in fertility following extensive surgery was only temporary, more recent research has provided evidence that a total colectomy with

subsequent creation of a small bowel reservoir or pouch and attachment of the small bowel to the rectum (ileoanal pouch) may lead to a permanent reduction in fertility in a not inconsiderable number of women. Studies from Scandinavia and the United States have found that even five years after such surgeries only about 40% of women of reproductive age with a desire to start a pregnancy conceive naturally. By comparison, among women with an inflammatory bowel disease who have not undergone surgery, who are of childbearing age and desire to start a pregnancy, about 90% conceive naturally – a rate similar to that observed in healthy women. If, however, as a result of assisted reproductive techniques, a pregnancy is initiated, these women are able to sustain a normal pregnancy and give birth naturally. Hence, women who have undergone surgery and have unsuccessfully attempted to conceive should consider assisted reproductive techniques and be referred for evaluation by appropriate specialists.

In cases of less extensive surgical procedures, such as the partial removal of the bowel or creation of an artifical bowel outlet (ileostomy), reduction in fertility is more often temporary in nature. Thus, normal fertility returns within a period of weeks to months, although the overall fertility in women undergoing these types of operations is presumably reduced to some degree.

The question of female fertility is not so clear-cut in Crohn's disease. While it appears that fertility is not affected during periods of quiescent disease, a temporary reduction in fertility during acute disease phases and following extensive

surgery can be frequently observed. This may result in a missed menstrual period (amenorrhea, i.e. absence of menstruation), a symptom frequently observed following significant weight loss caused by active disease.

Reduced fertility during phases of increased inflammatory activity would also seem to make sense biologically: Pregnancy is postponed until the best possible conditions for its successful outcome can be assured, while, at the same time, additional stresses are avoided for the patient.

Following complete surgical wound healing and stabilization of disease activity, female fertility does not appear to be significantly affected, though studies do suggest a slight reduction in

fertility in surgically treated patients. It should be remembered that the failure of pregnancy to occur cannot always be blamed on inflammatory bowel diseases: Even in healthy women experiencing regular, unprotected intercourse, only about 90% become pregnant.

■ Fertility in men with inflammatory bowel diseases

Male fertility is usually not affected in inflammatory bowel diseases. Abscesses and fistulas in the pelvis and anal region may, however, cause disturbances in erection and ejaculation. Similar disturbances can also occur in patients who have undergone extensive surgery, particularly following ileo-anal pouch operation. They are, however, very rare.

A particular situation may arise in connection with the use of salazosulfapyridine or sulfasalazine. These drugs can cause temporary infertility in men, which normalizes about two months after discontinuing the drugs or switching to pure mesalazine or 5-aminosalicylic acid (5-ASA) preparations.

The reasons for this temporary infertility include a decreased sperm count, a reduced amount of seminal fluid and abnormalities in the structure and motility of the sperm cells. These changes occur in about 80% of men treated with these drugs.

How do inflammatory bowel diseases affect the course of pregnancy and the baby's health?

Numerous studies have investigated the effect of the inflammatory bowel diseases Crohn's disease and ulcerative colitis on the outcome of pregnancy and the health of the child. Results of these studies have generally shown that about 85% of women with Crohn's disease or ulcerative colitis experience normal, uncomplicated pregnancies. Congenital malformations in infants born to women with Crohn's disease or ulcerative colitis occur in only about 1%. The risk of miscarriage also does not, in general, appear to be increased. These rates correspond to those observed in healthy women. Here again, one should not forget that pregnancies, even in healthy women, do not progress normally in all cases: In fact, problems or complications relating to the pregnancy or affecting the baby's health occur in about 15% of cases.

Although pregnancies in women with inflammatory bowel diseases usually progress in a manner comparable to healthy women, various studies have shown that, in both Crohn's disease and ulcerative colitis, increased inflammatory activity at the time of conception may unfavorably affect the pregnancy and is associated with a significantly higher rate of complications (table 1).

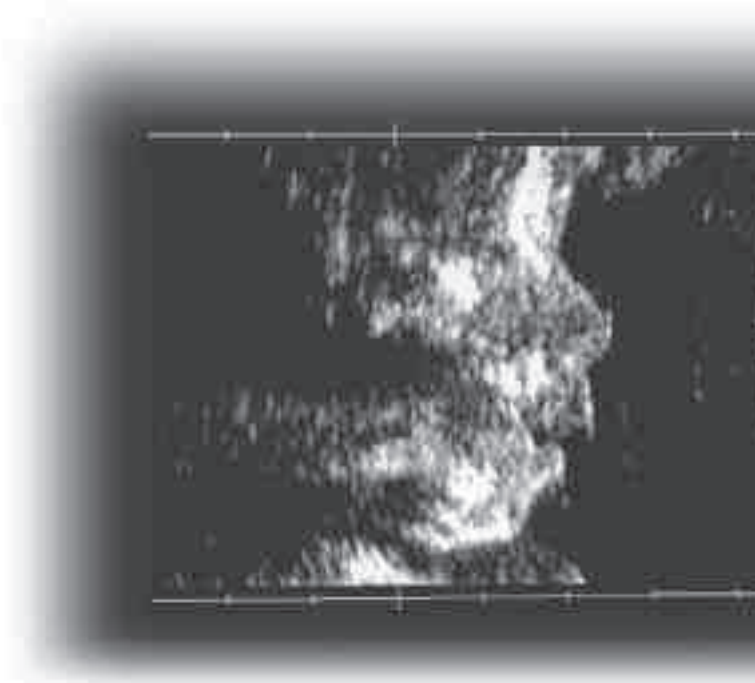
Table 1

Course of pregnancy in healthy women and in patients with inflammatory bowel diseases in relation to disease activity (%).
(Mean percentages from European and American studies)

	Normal	Malformations	Premature births	Abortions
General population	83	2	6	9
Crohn's disease in remission	82	1	7	10
Crohn's disease in active phase	54	1	25	20
Ulcerative colitis in remission	84	1	6	9
Ulcerative colitis in active phase	65	2	12	21

These findings indicate that pregnancies conceived during inactive disease or during a phase of mild inflammatory activity progress normally and without an increased risk of complications. Therefore, pregnancies should, if possible, be planned during phases of inactive disease or mild inflammatory activity. If conception occurs in a period of increased disease activity, the rate of abortions, premature births and other pregnancy complications increases significantly. If possible, active disease should be treated and the necessity of therapeutic intervention should be clarified prior to beginning a pregnancy. For example, if it is known that surgery will be necessary in the near future (for example, to treat stenoses caused by scarring), the operation should occur prior to a planned pregnancy.

Ultrasound profile of the face of a healthy female fetus in the 25th week of pregnancy.



Which medical examinations are important prior to a planned pregnancy?

No general plan can be offered here. This is a matter to be discussed individually with your doctor. Invasive procedures such as endoscopies or radiologic examinations are not required in all cases.

A detailed discussion with your doctor regarding your medical history and actual condition and laboratory tests to determine the activity of the disease and to exclude any dietary deficiencies seem advisable prior to a planned pregnancy. An ultrasound examination of the abdomen and the intestine performed by an experienced examiner can also provide valuable information.

Individual patients may require more extensive examinations including endoscopic and radiologic studies of the bowel. Results of these tests may indicate the need for anti-inflammatory therapy or additional supplementation of certain vitamins and minerals (e.g., vitamin B_{12}, folic acid, iron). In particular, dietary supplementation with folic acid is recommended in the period leading up to a planned pregnancy, since it helps to prevent the occurrence of rare neural tube defects in the developing fetus. It is possible that the absorption and metabolism of folic acid is further reduced during treatment with sulfasalazine or sulfapyridine. Thus, these women should either receive prophylactic administration of folic acid or consider switching from this group of medications to other 5-ASA-containing agents.

How does bowel surgery for treatment of inflammatory bowel disease affect a pregnancy?

Past abdominal operations for treatment of inflammatory bowel diseases do not in general appear to have a negative impact on the course of pregnancy. Pregnancies without complications are seen even after extensive intestinal surgery including colectomy or creation of an ileostomy. Here, it is important that a sufficient interval passes between the operation and the time of conception, so that surgical wounds have healed and there is no significant disease activity.

As described above on pages 8 and 9, the total removal of the bowel (proctocolectomy) with subsequent creation of a small bowel reservoir and connection of the small bowel to the rectum (ileoanal pouch) is more frequently associated with permanent reduction in fertility. Women in this situation desiring to start a pregnancy should be referred promptly for consultation with a fertility specialist to discuss the option of assisted reproductive techniques.

Following a surgical procedure, it is usually advisable to wait 6–12 months before becoming pregnant. This is true regardless of whether an artificial intestinal orifice has been created or the patient has undergone continence-preserving surgery. Occasionally, complications relating to the ileostomy (e.g., prolapse, occlusion) may occur during pregnancy. It has been suggested that the rate of premature births may also increase following total colectomy and ileostomy. In certain cases, surgical intervention may become necessary during an existing pregnancy. This may in a few, generally rare cases result in premature birth or in spontaneous abortion (miscarriage). On the other hand, normal pregnancies free of complications are possible even in cases in which extensive surgery, such as total colectomy, was required during the pregnancy due to severe ulcerative colitis flares that did not respond to pharmaceutical treatment.

Does pregnancy have an impact on the natural course of inflammatory bowel disease?

In the large majority of cases pregnancy has no effect on the activity or maintenance of remission of inflammatory bowel diseases. In individual cases, however, a dramatic improvement or worsening of symptoms of inflammatory bowel diseases can be observed (tables 2 and 3).

Table 2

Effect of pregnancy on disease activity in Crohn's disease following conception during remission

Remission maintained	~85%
Beginning of an acute episode:	~15%
• during the first trimester	~13%
• during the second trimester	<1%
• during the third trimester	<1%
• during puerperium (childbed)	~2%

Table 3

Effect of pregnancy on disease activity in Crohn's disease following conception in a phase of acute disease

Achieving remission	15%
Improved	20%
No change in disease activity	30%
Worsening during pregnancy	25%
Worsening during puerperium (childbed)	10%

Only about 15% of women with Crohn's disease who conceived during a remission phase experience an acute disease episode during their pregnancy. This rate approximates the normal clinical course of Crohn's disease. If an increased disease activity is already present at the beginning of pregnancy, this increased activity remains more or less constant throughout pregnancy in about one-third of patients (table 3). Episodes of acute disease occur more frequently during patients' first trimester of pregnancy and during the puerperium (childbed).

Pregnancy also does not seem to exert a major effect on disease activity in patients with ulcerative colitis. About one-third of women with ulcerative colitis who conceived during a phase of remission experience an episode of acute disease during pregnancy (table 4). This corresponds to the normal course of the disease in women who are not pregnant.

Table 4

Effect of pregnancy on disease activity of ulcerative colitis following conception during remission

Remission maintained	~70%
Beginning of an acute episode:	~30%
• during the first trimester	~20%
• during the second trimester	~7%
• during the third trimester	<1%
• during puerperium (childbed)	~3%

Episodes of acute disease occur more frequently during the first six months of pregnancy and during the puerperium (childbed). As in Crohn's disease, the majority of women who conceive during an active disease phase usually continue to have active disease throughout pregnancy (table 5).

Table 5

Effect of pregnancy on disease activity in ulcerative colitis following conception in a phase of acute disease

Achieving remission	19%
Improved	18%
No change in disease activity	32%
Worsening of disease activity	31%

Generally, the natural course of inflammatory bowel diseases can be improved by drug therapy even during pregnancy. Drugs may induce remission or decreased disease activity, which can then be maintained for the remainder of the pregnancy. In addition, worsening of symptoms in inflammatory bowel diseases during one pregnancy does not automatically implicate that this may occur in subsequent pregnancies.

Can inflammatory bowel disease first appear during pregnancy?

Both Crohn's disease and ulcerative colitis can show their first symptoms during pregnancy. In general, the course of inflammatory bowel diseases in these patients is not more unfavourable than in patients who are not pregnant.

A significant problem that may delay the definite diagnosis is the understandable fear of undergoing diagnostic procedures, such as endoscopy or radiologic examinations, at this time (see also page 48).

Can drugs for the treatment of inflammatory bowel diseases be taken during pregnancy?

Everyone knows the importance of avoiding medications during and even prior to a planned pregnancy in order to protect the unborn child from unnecessary risks. The use of drugs in treating inflammatory bowel diseases represents a special problem. It is only natural that patients and their families may be unsure and have many questions relating to this issue. These concerns are reinforced by the package inserts of a great majority of medications, which advise patients to use them during pregnancy only on the advice of a doctor and for a strictly defined indication. The decision to treat a pregnant woman with any drug

must be made for each patient individually, if necessary after consultation of the proper specialists. This advice is based on the requirement for the highest possible degree of safety. Even in the case of drugs for which no adverse effects have been reported to date for either mother or baby, there is always a remaining risk, which, though it may be ever so slight, cannot be totally excluded.

Therefore, the general rule during pregnancy is to take only those medications that are absolutely necessary. However, we should not forget that many diseases, if inadequately treated, also pose a serious threat to the well-being of the mother and her child.

In this context, it is important to repeat, what we said above: Even in healthy women, only about 85% of pregnancies develop without any complications.

Overall, the treatment of inflammatory bowel diseases in pregnant women is, in most of its components, based on the same general principles as are applied to patients who are not pregnant. Optimal care, however, depends on close and regular interaction between the gastroenterologist and the gynecologist and should consider some important differences and exceptions with regard to determining the individual medical treatment of a single patient.

Does the standard drug treatment of inflammatory bowel diseases harm the baby?

Unfortunately, it is impossible to give a generally valid answer to this question. The care of each individual patient should be one of cooperation between the gynecologist and the specialist in internal medicine or gastroenterology. The various cortisone (prednisone, prednisolone, hydrocortisone) and mesalazine or 5-ASA preparations in the customary doses generally prescribed for the treatment of inflammatory bowel diseases do not appear to represent an increased risk to the unborn fetus based on current evidence. Nevertheless, the package inserts for all of these drugs do urge caution and strict determination of indication during the first trimester of pregnancy. Patients who depend on 5-ASA- or corticosteroid- (cortisone) preparations for maintaining remission, should continue this therapy even after pregnancy is confirmed: An increase in the inflammatory activity of the disease is a much greater risk for the fetus. If an acute episode of an inflammatory bowel disease should occur during pregnancy, these drugs should be taken in adequate dosages in order to control disease activity as quickly as possible. Inadequately treated, inflammatory bowel diseases harm both the baby and its mother more than the drug therapy.

The conventional therapy of inflammatory bowel diseases with pure 5-ASA- or corticosteroid-preparations in fathers does not have any adverse effects on the outcome of a pregnancy based on our current knowledge. Only the above described temporary reduction in fertility (see page 11) caused by salazosulfapyridine or sulfasalazine should lead to substitution of pure 5-ASA- or mesalazine-preparations in males who wish to start a family.

With regard to therapy with budesonide, it is not yet possible to give any general recommendations since we do not yet possess the extensive clinical experience that characterizes our knowledge of the classic cortisone preparations. Our own experience and that reported by colleagues, however, has provided no evidence of danger for either the mother or child, though a comprehensive evaluation of the pregnant patient should always be done prior to and during a contemplated treatment with budesonide. In recent years, a large number of pregnancies that were normal and free of complications have been reported in patients treated with budesonide, either orally or in the form of enemas. Based on our current experience, there is no evidence for any harmful effect of this agent during pregnancy. Because our experience with the classic cortisone preparations is much more extensive, in cases of doubt it is probably safer to choose one of these in preference to budesonide. There is no indication for pregnancy termination in cases in which conception has occurred while a patient is being treated with budesonide.

The use of other medications, such as antibiotics, or of immunomodulatory substances such as azathioprine or 6-mercaptopurine (6-MP), methotrexate (MTX), cyclosporine, tacrolimus or of TNF-α inhibitors requires critical evaluation and should only occur following comprehensive consultation with an experienced and appropriately trained specialist (see also page 32 ff. of this booklet).

The use of antibiotics, such as metronidazole or ciprofloxacin, which are used especially in patients with Crohn's disease who develop fistulae,

requires careful evaluation in pregnancy. As a rule, long-term therapy with these antibiotics is contraindicated. Because these are second-line drugs with generally lower efficacy, in cases of medical necessity, a comprehensive discussion with the treating physician should focus on other, possibly more effective therapy options.

Various other drugs used for symptomatic relief in inflammatory bowel diseases can, according to our current state of knowledge, be continued without risk to the unborn child. For example, the anti-diarrheal agent loperamide can be used safely in cases of very severe diarrhea. Patients with diarrhea may also benefit from the use of psyllium seed shells (Plantago ovata). To date, no negative effects of psyllium have been reported, as would be expected in an agent of herbal derivation. According to our current state of knowledge, probiotics, such as *E. coli Nissle* and lactobacilli, can be used without increased risk for the newborn.

Can the immunomodulating drugs azathioprine or 6-mercaptopurine be taken before or during pregnancy?

There have been, in recent years, significant changes in the risk assessment for use of the immunomodulatory drugs azathioprine and 6-mercaptopurine (6-MP). While it was believed only a few years ago that use of these drugs before a planned pregnancy or during the pregnancy itself was associated with a relatively high risk of side effects (miscarriage, premature birth, birth defects), current data and the increased use of azathioprine and 6-MP in other disorders (e.g. organ transplantation, rheumatoid arthritis) have shown that use of these drugs before or during pregnancy is not associated with an increased risk of complications during pregnancy or with birth defects in the child. There have also been a number of case reports that suggest that patients with inflammatory bowel diseases do not experience an increased risk due to use of azathioprine or 6-MP. Naturally, there can be no 100% guarantee that a given drug will not adversely affect the course of pregnancy. A careful review of the literature also reveals case reports which show a slightly increased rate of pregnancy complications and miscarriages in association with the use of azathioprine or 6-MP. Upon closer examination, however, it becomes rapidly clear that, because of the small number of cases, no statistical conclusions can be made; in addition, other factors, such as an increased disease activity, may be responsible for the negative effects in these patients. Thus, a consensus has formed in Europe and the United States that azathioprine and 6-MP can be used during pregnancy if medically necessary and, in fact, should be used if other measures fail to control inflammatory activity. The decision on whether azathioprine should be stopped in women planning a pregnancy or whether con-

ception should be planned during ongoing azathioprine therapy requires careful consideration of the advantages and disadvantages and comprehensive counseling of the parents. This decision requires a high degree of responsibility and should include a joint interview between the parents, the treating gynecologist and/or family physician, as well as a gastroenterologist with the corresponding experience. There is no indication for pregnancy termination in women who become pregnant while being treated with azathioprine or 6-MP.

Also controversial is the use of azathioprine or 6-MP by the male partner in couples planning a pregnancy. Here, too, extensive experience from transplantation medicine and in patients with rheumatic disorders and inflammatory bowel diseases who were treated with azathioprine or 6-MP prior to or during the period of conception does not reveal any increased risk for pregnancy complications or birth defects. As with women, however, there are also individual case reports in the scientific literature that suggest possible negative effects on pregnancy secondary to azathioprine or 6-MP. Here, too, data is based on a very small number of cases, which precludes statistical evaluation. European and American pharmaceutical regulatory agencies do not currently recommend that males being treated with azathioprine or 6-MP should discontinue therapy prior to a planned conception. Patients desiring maximum safety, however, can be advised to discontinue azathioprine three months prior to a planned conception. In the intervening period, males will produce sperm whose genetic material is not damaged by azathioprine. Over the past

years, we have followed a large number of women and men who have been treated with azathioprine before and during conception and pregnancy. There have been no reported instances of birth defects or pregnancy complications that could be associated with this therapy.

Can immunomodulatory agents such as methotrexate (MTX), tacrolimus or cyclosporine A be used during pregnancy?

The use of immunomodulatory agents other than azathioprine or 6-mercaptopurine must be carefully considered in each individual case.

Methotrexate (MTX) should never be used in patients actively planning to become pregnant. Based on data from animal experiments, there is a high risk of chromosomal damage, increased occurrence of birth defects and pregnancy complications (miscarriage, premature birth). In fact, MTX, at high doses, can be used to induce abortion. For this reason, we recommend discontinuing therapy with MTX in both men and women three to six months prior to planned conception. If therapy with MTX is absolutely necessary, patients must use a reliable method of contraception.

With respect to the use of cyclosporine A and tacrolimus, there are a series of case reports in patients undergoing organ transplantation and with inflammatory bowel diseases that describe normal pregnancies free of complications and no increased rate of birth defects during use of these drugs. The existing data, however, are by no means adequate to support a general recommendation for starting or continuing these medications during pregnancy. Use of these agents must be carefully considered in conjunction with both parents and an experienced specialist based on the patient's prior disease course and the latest scientific knowledge.

Can infliximab or the newer TNF-α inhibitors be used before or during pregnancy?

Our current state of knowledge would suggest that the administration of infliximab is not associated with an increased rate of either birth defects or pregnancy complications. Data from animal experiments do not show any negative effects of the course of pregnancy or an increase in birth defects. To date, more than 100 pregnancies have been described in patients treated with infliximab for rheumatoid disorders and inflammatory bowel diseases. Statistically, the available data do not show any increase in pregnancy complications or birth defects in cases in which prior to or during pregnancy either the male or the female parent was treated with infliximab. In a recent study in patients planning a pregnancy, therapy with infliximab was continued unchanged through the entire pregnancy without any adverse effects on either the course of the pregnancy or the rate of birth defects.

At present, corresponding statements cannot be made for the newer TNF-α inhibitors, such as adalimumab and certolizumab pegol, since significantly fewer patients have been treated with these agents and there is still inadequate experience with these agents. Experimental data, however, does not point to an increased risk. For one TNF-α inhibitor, certolizumab, there exist experimental data that show only low transfer into the child's system, which may represent a factor that enhances safety. As the use of these drugs is expected to increased in coming years, further scientific data will certainly be forthcoming. There is no indication for pregnancy termination should a patient using one of the three currently available TNF-α inhibitors experience an unplanned pregnancy.

Is the use of cortisone safe during late pregnancy and nursing?

It is generally accepted that the dosages of corticosteroid preparations (e.g. prednisone, prednisolone, hydrocortisone) usually prescribed for the treatment of inflammatory bowel diseases are not associated with an increased risk of miscarriage or fetal malformations. It is theoretically possible that very high doses of corticosteroids taken during the final phases of pregnancy might cause reduced corticosteroid production in the newborn's adrenal gland resulting in low levels of circulating cortisone after birth, together with apathy and reduced activity. Therefore, infants born to mothers taking high corticosteroid doses

in late pregnancy should be closely monitored by an experienced neonatologist. If necessary, the baby can receive cortisone substitution until the adrenal glands are able to produce sufficient cortisone.

Since cortisone can pass through breast milk into the baby, it is conceivable that an infant's cortisone intake during nursing could result in a similar depression of cortisone production in the baby's adrenal glands. Again, careful follow-up by an experienced pediatrician is important.

In both instances, however, no permanent harm to the infant is to be expected. Once cortisone therapy is discontinued, the function of the infant's adrenal gland normalizes with adequate production of cortisone.

Regarding the use of budesonide during pregnancy and lactation, it is still too early to give generally valid statements, since experience with this drug during pregnancy is quite limited. In theory, the rapid metabolism of budesonide in the mother's liver leads to relatively low circulating levels of the drug and thus only a slight transmission to the baby through the milk. Our own experience with budesonide during pregnancy and nursing has been positive and no adverse effects have been observed in the infants. The use of budesonide sprays for the treatment of asthma during pregnancy also does not seem to be associated with an increased risk of fetal malformations. Because of the limited experience with the drug, however, the use of budesonide during pregnancy and nursing should include comprehensive counseling of the mother.

Should 5-ASA therapy be interrupted prior to delivery?

Unlike acetylsalicylic acid (aspirin), 5-aminosalicylic acid (5-ASA, mesalazine) at therapeutic dosages does not affect coagulation of the blood or inhibit the aggregation of the platelets, which is important for the control of bleeding.

Therefore, interruption of 5-ASA therapy prior to delivery is not generally required, particularly since blood levels of 5-ASA are very low.

Can oral contraceptives cause or aggravate inflammatory bowel diseases?

In the past, several investigators have presented evidence suggesting that women taking oral contraceptives have a slightly higher incidence of Crohn's disease and suffer from acute episodes of the diseases more frequently. Other investigators, however, have been unable to confirm these findings. To date, no evidence has suggested an unfavorable connection between oral contraceptives and ulcerative colitis.

In general, our experience has shown that the risk of developing inflammatory bowel diseases or of a worsening of symptoms due to the use of oral contraceptives is quite low. Thus, we see no contraindication for the use of oral contraceptives in women with inflammatory bowel diseases.

It is important to remember, however, that the severe diarrhea accompanying inflammatory bowel diseases in individual cases may disturb uptake of the contraceptive hormones in the bowel and thus compromise the efficacy of the method. Patients using contraceptive medication with low amounts of hormone (such as the so-called "minipills") should be particularly aware of this possible reduction in contraceptive protection. Discussion of this issue with your gynecologist is advisable.

Are there medical reasons requiring termination of pregnancy in women with inflammatory bowel diseases?

Termination of pregnancy is very rarely or even never necessary because of inflammatory bowel diseases in the mother. Instead, there should be adequate therapy of the woman's inflammatory bowel disease together with comprehensive care by her doctors.

Which diagnostic methods are considered to be safe during pregnancy?

Ultrasound examinations of the abdomen and bowel can be performed without danger to the mother or child; these diagnostic examinations provide important evidence regarding disease activity and the extent of the inflammation. In the hands of an experienced examiner, even gastroscopy or endoscopy of the lower gastrointestinal tract (rectoscopy, sigmoidoscopy and ileocolonoscopy) are not associated with increased risk or with the increased frequency of premature birth.

These invasive methods, however, should only be used when absolutely necessary to determine the most appropriate type of therapy. Magnetic resonance imaging (MRI), which is probably also not harmful, may be useful in certain cases. Diagnostic procedures involving radiation exposure should be postponed until after delivery and reserved to emergency situations.

Capsule endoscopy or double balloon endoscopy will not, as a rule, be medically necessary during pregnancy. Especially double balloon endoscopy, because of its invasive character and increased risk of premature labor, should not be used.

What special considerations are necessary during delivery?

Vaginal delivery is generally preferred even in women with inflammatory bowel diseases. Generally, vaginal delivery is possible in women who have undergone ileostomy, although the increased intra-abdominal pressure due to contractions may cause prolapse of the intestinal orifice. In such cases, many obstetricians prefer delivery by cesarean section. The method of delivery in patients with ileostomy, therefore, should be discussed in advance with the patient's obstetrician.

Another group of patients in whom cesarean section is preferred and may be useful are those women suffering from extensive formation of fistulas in the perianal area and pelvis. This issue, however, must also be decided in consensus between the patient and her obstetrician.

Whether an episiotomy (incision in the perineum) contributes to an increased risk of perianal fistula formation remains controversial. Most data published to date do not support an increased risk of perianal fistula formation following episiotomy.

Is a special diet during pregnancy beneficial in women with inflammatory bowel diseases?

Patients with inflammatory bowel diseases generally do not require a special diet. Patients should, of course, follow the general recommendations for a balanced diet with adequate intake of calories, vitamins and minerals during pregnancy. Special dietary recommendation must, however, be considered if, due to the underlying disease or some associated disorder the patient develops lactose intolerance, bile acid loss syndrome or

stenosis (narrowing) of some segment of the gastrointestinal tract. Patients with lactose intolerance benefit from reduction or elimination of dietary lactose. Because this often means a reduction in dietary calcium intake, patients may need calcium supplementation in the form of oral tablets. Patients with existing bile acid loss syndrome often experience positive effects from foods rich in mid-chain triglycerides. Patients with confirmed stenoses in the gastrointestinal tract often benefit from a diet low in dietary fiber, which should also be continued during pregnancy.

How high is the risk of later developing an inflammatory bowel disease in children whose parent(s) suffer from Crohn's disease or ulcerative colitis?

The risk for the children of parents with inflammatory bowel diseases to develop Crohn's disease or ulcerative colitis themselves is relatively small. Inflammatory bowel diseases are not hereditary diseases in the strict sense. What is passed on to one's children is a genetic predisposition to develop these diseases under certain circumstances. In individual cases, there may be an increased prevalence of inflammatory bowel diseases in certain families.

A person's individual risk to develop an inflammatory bowel disease when another family member is affected cannot be precisely predicted and can be estimated only on the basis of empirical observations. Thus, the relative risk of developing an inflammatory bowel disease ranges from zero to 36% depending on how closely related the person is to the already affected family member (table 6).

Despite a generally increased risk that children of parents with IBD will also develop IBD, this should not be considered a reason not to have children. If diagnosed early, inflammatory bowel diseases are relatively well treated by improved medical therapy. Indeed, the life expectancy of patients with inflammatory bowel diseases does not differ significantly from that of normal, healthy subjects.

Table 6

Estimated relative risk of developing an inflammatory bowel disease

Risk for children with one affected parent	1–7%
Risk for children with both parents affected	up to 36%
Risk for other siblings, when one child is affected	2–6%
Risk for the parents, when one child is affected	1–5%

Should women with inflammatory bowel diseases nurse?

The use of cortisone or 5-ASA preparations by the mother is not a problem during nursing since only negligible amounts of these drugs enter the child's organism through the milk and no permanent harmful effects on the baby are known. The use of cortisone preparations should, however, be reduced as quickly as possible, both in pregnant and non-pregnant patients. If a high-dose cortisone therapy has been necessary, the infant should be carefully monitored by the pediatrician. If there is interruption of lactation during a period of high-dose cortisone therapy in the mother,

there is the risk of temporary adrenocortical insufficiency in the infant. The pediatrician will determine the infant's need for a possible temporary cortisone replacement therapy. The use of budesonide during lactation has been addressed in this brochure on page 41.

If the use of immunomodulatory agents such as azathioprine, 6-mercaptopurine, methotrexate (MTX), cyclosporine, tacrolimus or infliximab is necessary, the newborn should not be breast-fed since the long-term effects and possible harm to the baby cannot yet be predicted. Because the child's liver is still immature and has not developed a full detoxification capacity, it cannot be predicted to what extent the above-described medications may remain in the child's system. Thus, acute and long-term adverse effects cannot be fully excluded at this time.

Further information for patients with inflammatory bowel diseases:

– **Ulcerative colitis and Crohn's disease**
  An overview of the diseases and their treatment
  68 pages (S80e)

– **Diet and Nutrition in Crohn's Disease and Ulcerative Colitis**
  20 Questions – 20 Answers
  60 pages (S84e)

– **Crohn's disease and its associated disorders**
  40 pages (S85e)

– **Corticosteroid therapy in inflammatory bowel diseases**
  32 pages (Bu80e)

These brochures can be ordered
free of charge from Falk Foundation e.V.
or the local Falk partner.

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