

Intrahepatic cholestasis in pregnancy



BRITISH
LIVER
TRUST

Pioneering Liver Health

Intrahepatic cholestasis in pregnancy

This publication is for people diagnosed with intrahepatic cholestasis in pregnancy and for those who would like to better understand the condition.

The British Liver Trust works to:

- support people with, and affected by, liver disease
- improve knowledge and understanding of the liver and related health issues
- encourage and fund research into new treatments
- campaign for better services and improved patient care
- increase awareness of the risk factors of liver disease and promote earlier diagnosis

All our publications are reviewed by medical specialists and people living with liver disease. Our website provides information and our Helpline gives advice and support on enquiries about liver health. Call the Helpline on **0800 652 7330**, general enquires on **01425 481320**, or visit **britishlivertrust.org.uk**

For the latest updates to this information, please refer to our website **britishlivertrust.org.uk**

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The liver

Your liver is your body's 'factory' carrying out hundreds of jobs that are vital to life. It is able to repair itself (even renewing large sections). **However, the liver's ability to repair itself is limited and continuous harm can lead to permanent scarring.** Your liver is very tough and able to function even when some of it is damaged, which means you may not notice any symptoms until your disease is quite advanced and noticeably affecting your health.

Your liver performs hundreds of functions. Importantly it:

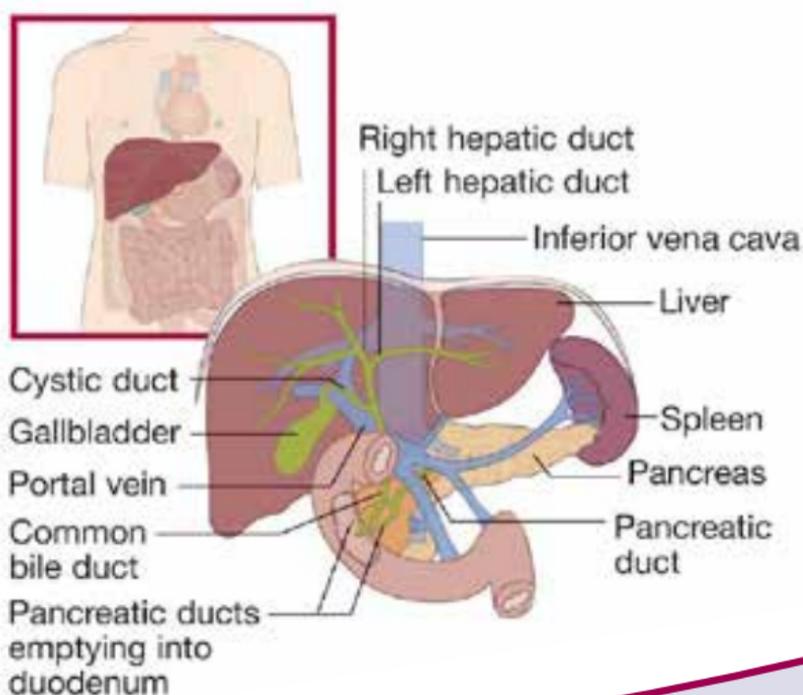
- filters and cleans the blood
- fights infections and disease
- deals with and destroys poisons and drugs
- makes vital proteins which make your blood clot when you cut yourself
- produces bile to help break down food in the gut
- processes food once it has been digested
- stores energy that can be used rapidly when the body needs it most
- regulates fat breakdown and distribution in the bloodstream
- stores sugars, vitamins and minerals, including iron
- gets rid of waste substances from the body
- produces and maintains the balance of some hormones
- produces chemicals – enzymes and other proteins – responsible for most of the chemical reactions in the body, for example repairing tissue
- repairs damage and renews itself (up to a point).

How liver disease develops

Your liver responds to harm by becoming inflamed. Any inflammation of the liver is known as hepatitis, whatever its cause. Sudden inflammation of the liver is known as acute hepatitis. When inflammation of the liver lasts longer than six months, it is known as chronic hepatitis.

Inflammation is part of the process of repairing damaged tissue. In a similar way to a scab forming over a skin wound, a temporary fibrous 'scaffold' forms while new liver cells regenerate. If your liver is repeatedly harmed, new liver cells cannot regenerate fast enough and the fibrous scaffold remains as a scar. This is called fibrosis, and can take a variable amount of time to develop.

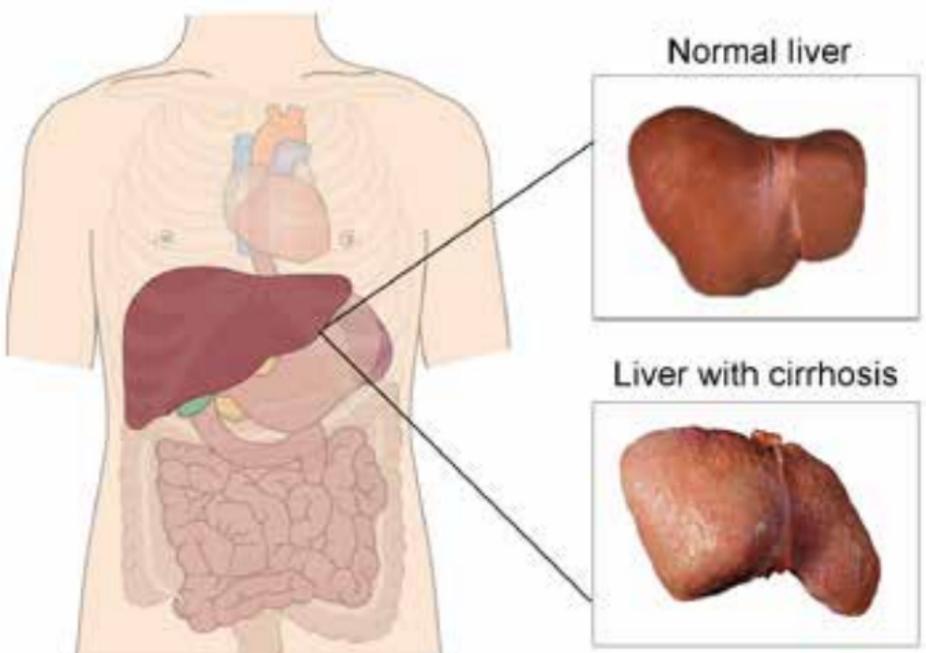
When fibrosis is present, your liver may be able to keep functioning quite well. Removing or treating the cause of the inflammation may reverse some, or all, of the fibrosis and prevent further liver damage.



If the harm to your liver continues, the inflammation and fibrosis can spread throughout your liver, changing its shape and affecting how well your liver cells work. This is known as **compensated** cirrhosis. Even at this stage, people can have no obvious signs or symptoms.

The scar tissue in cirrhosis interrupts the blood flow through the liver. As a result, the blood pressure in the veins in your abdomen is increased and may result in bleeding. Scar tissue in cirrhosis is difficult to remove and may be permanent. However, further progression can be halted and your cirrhosis stabilised, if the cause of the liver damage is removed.

Cirrhosis increases your risk of liver cancer and can lead to liver failure. If damage to your liver continues, it will become unable to function sufficiently (**decompensated** cirrhosis) and start to fail; this is sometimes referred to as 'end stage liver disease'. At this stage chemicals and waste products can build up in the body, commonly causing jaundice, ascites (a build-up of fluid in the abdomen) and hepatic encephalopathy (confusion and memory loss). In the final stages of liver disease the build-up of waste products may lead to multiple organ failure and loss of life.



What is Intrahepatic cholestasis in pregnancy?

Intrahepatic cholestasis of pregnancy (ICP), also known as obstetric cholestasis (OC), is a relatively common pregnancy-specific liver disorder that occurs in around one in 140 pregnancies in the UK. It is a condition in which the normal flow of bile out of the liver is reduced. Chemicals in the bile called bile acids (also often referred to as bile salts) can then build up and 'leak' into the bloodstream. This causes affected women to have increased levels of bile acids in their blood.

ICP is also characterised by itching, known as pruritus. The itching generally appears in the last three months of pregnancy but can appear sooner (as early as 6 weeks of pregnancy). It may be mild or severe and can be extremely distressing for the mother. Both the raised bile acids and pruritus completely disappear soon after the birth.

Several fetal complications have been reported in ICP pregnancies. There is an increased risk of preterm delivery (both spontaneous and induced) and fetal distress. Some case studies have also reported stillbirth occurring near the end of pregnancy in women with ICP. Therefore it is essential that the condition is recognised and treated in time.

At present, most obstetricians in the UK managing ICP pregnancies aim to induce the pregnancies early, at around 37 or 38 weeks. This is done because it is thought that it may help prevent the possibility of stillbirth. A clinical trial is being performed in the UK with the aim of finding out whether this is the case.

There have been no reports of any harmful effects to babies from ICP pregnancies once they have been delivered.

What is bile?

Bile is a yellow-green fluid produced by your liver which contains:

- chemicals to aid digestion, including bile acids
- waste products for excretion via the bowel.

Bile passes from the liver cells via small ducts to the common bile duct and on into the duodenum (part of your gut). It plays a central role in helping the body digest fat. It acts as a detergent, breaking the fat into very small droplets so that it can be absorbed from food in your gut. It also makes it possible for your body to take up the fat-soluble vitamins A, D, E and K from the food passing through the gut.

What are the causes of ICP?

We do not yet know what causes the restriction of the flow of bile from the liver in ICP. Evidence suggests that it is caused by a combination of hormonal, genetic and environmental factors.

Hormonal factors

All hormones are metabolised (broken down) in the liver. One theory is that the liver cannot cope with the high levels of hormones during pregnancy (oestrogen and progesterone). This affects the liver's ability to remove bile acids efficiently and causes a build up of bile acids in the blood. This is supported by observations that:

- ICP is more common in twin and triplet pregnancies, which are associated with higher levels of hormones.

- ICP has been triggered in women taking high-dose oral contraceptives (which contain forms of oestrogen and progesterone) and also in women being treated with progesterone.

Genetic factors

ICP also has a genetic cause. This means it has been linked to genetic changes making some women more susceptible to the disease and can explain cases where ICP occurs within families and also why it is more common in some ethnic groups. Although ICP affects one in 140 (0.7%) pregnancies in the UK overall, it is more common in women of Indian or Pakistani origin, affecting around one in 70 to 80 (1.2 – 1.5%) pregnancies. In other countries, such as South America and Scandinavia, the number of women affected is higher still.

However these genetic changes do not explain all the causes of the disorder and other factors such as diet and hormones may play a part. Further research is being carried out to investigate these areas.

Environmental factors

Some characteristics of ICP suggest that environmental factors may also have a role.

- ICP does not always recur in following pregnancies.
- ICP can be more common in certain seasons (in the winter months in Chile and Scandinavia).
- Cases of ICP have decreased in countries where nutrition has improved.

Other factors

Women with hepatitis C more commonly develop ICP than those who do not have the virus.

What role do bile acids play in ICP?

Although raised bile acids have previously been thought to be the cause of the itch associated with ICP, research has so far not confirmed this link. Two recent studies identified that the itch may be caused by two other chemicals in the blood – LPA (lysophosphatidic acid) and sulfated progesterone metabolites have both been found to be raised in women with ICP compared to pregnant women without complications.

What is known is that the bile acids can cross the placenta and may be linked to the reason why some babies suffer complications or are stillborn. There is evidence from human and animal studies that bile acids cause structural damage to the placenta. Further research is required to better understand this.

More recent research has also suggested that bile acids may affect some babies' hearts by causing very subtle heart 'flutters' called heart arrhythmia. This can result in the baby's heart suddenly stopping but cannot be detected using the conventional method of checking the baby's heart rate by using a machine called a cardiotocograph (CTG). However, it may be that using a machine that can perform a more in-depth reading of the baby's heart rate (called an ECG – electrocardiogram) can detect those babies that are at risk and researchers are currently investigating this.

The longer term impact of ICP is still being researched but it is now thought that women who have the condition have an increased risk of developing Type 2 diabetes or gallstones in later life, and they have a risk of recurrence of cholestasis if they take some drugs, e.g. antibiotics or the combined oral contraceptive pill. The risk may also apply to their children.

What are the symptoms of ICP?

Itching is often the only symptom of ICP. The itching typically begins on the arms, legs, hands and soles of the feet. It may also occur on other parts of the body such as the face, back and breasts and may never occur on hands and feet (although this is not common). It can be severe but may also be very mild.

It is usually worse at night, leading to sleeplessness and exhaustion and some women scratch themselves so frantically that they make themselves bleed. A few lose their appetite and feel generally unwell. A number of women (thought to be around one in ten) will develop jaundice in pregnancy. However, most women with ICP do not have jaundice.

Itching is not uncommon in normal pregnancy. However, some women may not be aware that they have ICP because they are told that itching is normal in pregnancy. This can be misleading.

It is important that if you are pregnant and itching, you should check with your doctor or midwife. A simple blood test (see below) is required to diagnose ICP. It may be helpful to take a copy of this leaflet with you.

Diagnosis

Medical and family history

Your doctor should ask about your medical and family history to aid diagnosis. If close female family members have been affected by ICP, you may be at increased risk.

It is also important to exclude all other possible causes of your itching, such as allergies or eczema (but it is possible to have a skin condition and ICP) and liver diseases such as primary biliary cholangitis (PBC) or hepatitis C. Other signs such as pale stools or dark urine may indicate a problem with your liver, including ICP.

Blood tests

Your doctor can diagnose ICP from blood tests called liver blood tests, sometimes referred to as liver function tests (LFTs) and a serum bile acid test. It is possible to have a normal liver blood test result with a raised bile acid, so a bile acid test is important for diagnosing the condition. However, an abnormal liver blood test result with a normal bile acid does not confirm ICP.

Liver blood tests are performed to gain an idea of how your liver is functioning. A number of separate properties of your blood will be examined. Your doctor should use **pregnancy-specific** reference ranges to interpret your blood test results.

In ICP, doctors will be looking for abnormal levels of the liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Sometimes levels of another enzyme, gamma-glutamyl transferase (GGT), will also be raised but this substance is generally not considered in the diagnosis of ICP.

The most specific test involves measuring serum bile acids. In UK hospitals, the reference range can vary but typically, raised levels would be a measurement of greater than $14\mu\text{mol/L}$. However, some hospitals may ask you to fast before the test. In this case, a fasting level of greater than $10\mu\text{mol/L}$ would support the diagnosis of ICP.

If the tests are within normal limits and you carry on itching, it is important that the tests are repeated. Unfortunately the serum bile acid test is not available in all hospitals. Your doctor may need to send a sample to another hospital for diagnosis.

Excluding other liver conditions

If liver blood tests are abnormal, doctors will carry out screening to eliminate other causes, such as viral hepatitis and autoimmune disease, before diagnosing ICP.

This may involve an ultrasound scan to look for any sign of liver abnormality. Doctors may also use ultrasound to check for gallstones (see 'Useful words' section), as research suggests these occur more often with ICP.

Women with hepatitis C are at increased risk of developing ICP during pregnancy. A small number of women with ICP may therefore have undiagnosed hepatitis C. If your test results do show that you have viral hepatitis, or another liver condition, you will then be able to be referred to a specialist in liver disease (hepatologist) and receive treatment.

The presence of itching helps to distinguish ICP from other liver diseases of pregnancy, such as HELLP syndrome, acute fatty liver of pregnancy or pre-eclampsia (see 'Useful words' section).

ICP is only completely confirmed when symptoms disappear and liver tests go back to normal after delivery.

Treatment

There is no cure for ICP. Doctors will monitor your condition, treat symptoms and may advise delivering your baby early.

Monitoring your liver function

Following diagnosis of ICP, doctors should carry out liver blood tests and bile acid tests on a weekly basis to monitor your condition. This may involve more trips to hospital which can be either reassuring or unsettling at this time. If your itching persists, doctors are advised to run these tests every one or two weeks.

Relieving the itch and lowering your bile acids

Topical creams such as calamine lotion and aqueous cream with menthol, are safe and may provide some temporary relief from itching for some women.

A number of medications may be used in your treatment. As yet, a specific medication to manage ICP is not available, although clinical studies are in progress. Medication is currently aimed at reducing the build-up of bile acids in your blood, to relieve the itching and to protect your baby. Some of the medications listed below are primarily used for other conditions and agreement about their effectiveness in ICP is still being discussed and investigated.

- Ursodeoxycholic acid (URSO or UDCA) is a naturally occurring bile acid which accounts for 1% of circulating bile acids in your body. It provides protection for the liver by displacing more harmful bile acids, improving the flow of bile and decreasing the delivery of bile acids to the baby.

URSO is the most commonly prescribed medication to relieve itching caused by ICP. It is still being evaluated for use in pregnancy and is prescribed with 'informed consent' (that is, taken with the knowledge that it is not licensed).

One study has shown that URSO is particularly effective in ICP cases with higher levels of bile salts (greater than $40\mu\text{mol/L}$). URSO has been used for many years and although there have been no reports of adverse effects for the unborn baby when the mother takes URSO, there have been no studies to look into this and wider research studies need to be carried out.

- **Rifampicin**
Rifampicin is a very powerful antibiotic that has been used in addition to UDCA for those women whose bile acids do not improve on UDCA alone. It has been shown to be effective in around a third of the women who take it but still requires further testing. A trial of the drug is currently underway in Australia, the UK and other countries.
- **Dexamethasone (Decadron)** is a steroid sometimes prescribed for a few days to increase the maturity of the baby's lungs so the baby can be delivered earlier. It has also been previously used to attempt to reduce the mother's level of hormone production and to help relieve itching. However, continuous use of steroids in pregnancy is now thought not to be good for the baby and very few clinicians will treat ICP with this drug.
- **Chlorpheniramine (Piriton)** is an antihistamine that may be prescribed to help you sleep at night by making you drowsy but is not considered to have any effect on your itching.
- **Cholestyramine** has been proven to reduce itching in some women but does not improve liver function or bile acid levels and may lead to vitamin K deficiency. It also binds bile acids and so should not be taken at the same time as URSO. For these reasons it is not in clinical use.

Other drugs are currently being investigated for use in ICP including heparin, and not-UDCA.

The role of vitamin K

Vitamin K is a fat-soluble vitamin, absorbed in your diet, that is essential for blood coagulation (clotting).

Absorption of fats can be reduced in ICP and this could affect the uptake of vitamin K.

A lack of vitamin K can affect your bloods clotting mechanism and could result in increased blood loss during delivery. Many doctors will check how your blood is clotting and if necessary prescribe a daily supplement of vitamin K, in the form of an oral water-soluble tablet, to try and reduce the risk of a severe bleed after delivery. However, there is no research at present to confirm that taking oral vitamin K will do this, but neither is it thought to harm your baby.

Following the birth, it is recommended that your baby be given vitamin K, usually in the form of an injection. This is standard practice for all newborns (whether from an ICP pregnancy or not) as many are deficient in vitamin K.

Deciding whether to deliver early

If you have ICP, the practice in most obstetric units is to monitor you closely (checking your liver enzymes and bile acid levels) and for your baby to be delivered between 37-38 weeks of pregnancy.

Research has shown that mothers with fasting bile acid levels greater than $40\mu\text{mol/L}$ are at most risk of going into premature labour and their babies showing symptoms of distress. More recent research has suggested that the increased risk of stillbirth is particularly associated with bile acid levels >100 micromol/L and this may mean that some women could have their babies later than 38 weeks of pregnancy. This will require further research.

Bile acid levels usually rise as the pregnancy continues. The weekly monitoring of your blood tests will help your doctor to see if levels are rising and make decisions about any increased risks.

Your obstetrician should discuss fully the possible risks and benefits of early delivery with you. Some premature babies may need to be admitted to a special care baby unit.

Other monitoring may include having regular tests to monitor your baby's heartbeat (cardiotocography or CTG) and scans (to look at oxygen flow and the growth of your baby). Neither of these procedures have been shown to be able to predict a baby that may be at risk from ICP, however, many women find it reassuring to have them.

With 'active' management (such as monitoring, symptom treatment and early delivery) the risk of stillbirth for women with ICP and bile acid <100 is thought to be the same as that for normal pregnancy (around 1%). It is not currently known which aspects of 'active' management are of most benefit. A UK trial is currently trying to establish whether ursodeoxycholic acid and/or delivery between 37-38 weeks of pregnancy contribute to improving outcomes for the baby.

Aftercare

You and your baby should receive the standard health checks after birth. After the delivery the itching should disappear relatively quickly. There are no known developmental problems for the baby. The risk of developing neonatal jaundice is the same as for other babies. It is thought that there is no major damage caused to the liver of either mother or baby.

Women with a previous history of ICP are more likely to have gallstones and some other forms of liver impairment in later life. Specifically a small proportion of women who have had ICP may develop autoimmune forms of liver disease, such as autoimmune hepatitis or primary biliary cholangitis (see our disease specific publications for more information on these conditions).

Some women who have had ICP also develop cholestasis outside of pregnancy when taking some medications such as antibiotics or the contraceptive pill (see the 'Looking after yourself' section for advice).

You should have a blood test before you are discharged from hospital to check your liver function and bile acids. However, liver blood tests can be raised for the first 10 days after birth in normal pregnancy. You should have a follow-up post natal check to confirm that symptoms have resolved and the diagnosis was correct. At your appointment your doctor will be keen to establish that the itching has gone away and carry out a liver blood test and serum bile acid test, to see if these have returned to normal. Levels should improve over time but it may take up to 12 weeks for liver blood tests to go back to normal.

If there are any abnormal results you will need to have further tests. These are to determine whether your liver is taking extra time to settle down or, more rarely, whether you have an underlying liver problem.

If the latter is the case, you may be referred to a hepatologist (liver specialist), or perhaps a gastroenterologist (specialist in disorders of the digestive tract) with knowledge of liver problems. In general, if you continue to itch after six months, a referral to a liver specialist should be sought.

Looking after yourself

Should I change my diet?

There are no special foods to eat or to avoid. As with all pregnant women, it is important that you eat a well-balanced diet which includes lots of vegetables, fruit and whole wheat cereals, including bread. As the flow of bile into the gut is reduced, you may find you cannot tolerate the same amount of fat as normal. You may therefore find that it helps to lower your fat intake.

What can I do to relieve itching?

To help with itching you may find the following suggestions from other mothers helpful.

- Have frequent tepid baths.
- Try not to get too hot.
- Use lotions such as calamine and aqueous cream with menthol.
- Wear loose cotton clothing.
- Gently scratch your skin with a baby's hairbrush.

Can I drink alcohol?

ICP is not caused or made worse by alcohol. However, the Department of Health recommends that if you are pregnant or are planning a pregnancy, you should avoid drinking alcohol to minimise harm to your baby.

When you drink, the alcohol passes across the placenta to the baby. A baby cannot process alcohol in the same way that you can and this can seriously affect the baby's development.

If you do choose to drink, in order to minimise the risk to your baby you should limit this to no more than one or two units of alcohol once or twice a week. You should avoid getting drunk.

Additionally, it is recommended to avoid alcohol completely in the first three months of pregnancy as it increases the risk of miscarriage.

Will ICP damage my liver?

ICP is not thought to cause any lasting liver damage in the majority of cases. However, it may leave your liver more sensitive to normal changes in the level of your hormones, and a few women report what is known as 'cyclical itching' during the menstrual cycle. This can happen just before ovulation or just prior to a period.

This type of itching is usually only mild and stops either when ovulation has taken place or your period has started.

Can I breastfeed?

ICP should not influence your ability to breastfeed.

What about future pregnancies?

It is highly possible that you may have ICP in future pregnancies. Research suggests that it is between 60-90%. If ICP does recur, it may not necessarily follow the same pattern.

It is important that any future pregnancies are carefully managed by a consultant obstetrician who is familiar with the condition. This may involve checking your bile acid levels and liver blood tests early in pregnancy and then at 28 weeks. If itching occurs, blood tests should be checked sooner.

If you are worried that you may have ICP, you must contact your doctor or midwife.

As ICP can run in families, it is important to make family members aware of the increased risk.

Can I use the contraceptive pill?

Until it is proven that the hormones oestrogen and progesterone do not have an effect on the liver in ICP, it would seem sensible to approach hormonal contraception (the 'pill') with caution or avoid it completely.

However, this may not be realistic or practical for all women and it may be best to discuss the options with your doctor or a suitable healthcare professional. Use of contraception after ICP is still a new area and may involve some trial and error in choosing what is right for you.

There is anecdotal evidence that a number of women can tolerate the mini pill and that others are also able to use a low dose combined oral contraceptive pill.

You might also consider intrauterine contraceptive devices (IUCDs). Some IUDs release a lower dose of hormones which avoid the liver by going directly into the womb, rather than into the bloodstream. Some women are unable to tolerate even low doses of localised hormones from the IUD.

If you do proceed with hormonal contraception, a liver blood test should be undertaken beforehand to establish that your liver function is normal. You should have the test repeated six weeks later.

If you have any concerns, there are other forms of contraception available.

Can I take antibiotics?

Because they have the potential to cause cholestasis, it may be advisable to avoid the antibiotics erythromycin and augmentin following an ICP pregnancy. Other antibiotic treatments are likely to prove just as effective and should be used if possible. Your doctor should be able to determine which antibiotics the organism causing your infection is sensitive to and prescribe accordingly.

How can friends and family help?

It goes without saying that the anxiety of an ICP pregnancy can be extreme. It is important that concerns are acknowledged by both healthcare professionals and friends and family. Being told everything will be okay can be counter-productive and can often make women feel more anxious.

Family and partners can reduce anxiety by reading up on the condition so that they understand concerns and provide support during hospital appointments and GP visits (further copies of this leaflet are available from the Trust).

Some women experience bouts of severe itching which could be dangerous while driving, so support with transport may be valuable.

Partners need to be aware that the effects of sleep deprivation can add to an already delicate emotional state and be sympathetic to the resultant fatigue. They need to be prepared for being woken up a lot in the night when itching is often at its worst. Offering to get up and make a hot drink in the middle of the night can be very helpful. It is not helpful to tell someone to 'stop scratching'. It is impossible!

You may wish to participate in a research project into the condition. Details of what it involves and how to take part can be found on the ICP Support website.

Where else can I get emotional support?

Many women say that they often feel very isolated with ICP. It is important not to push friends and family away. Let people know how you are feeling and ask for support.

You may find it helpful to get in touch with others who have experience of ICP via online support groups, such as ICP Support, so that you can discuss your fears and worries in a safe and confidential environment. You may also access counselling services through your GP or via the British Association for Counselling & Psychotherapy (BACP).

You may find that you need to try a few different sources of support to find the right type for you, as everyone is affected differently. However, try not to remain isolated with any worries or concerns you have, and talk to your midwife or GP.

It is also important that your partner has someone to talk to. This can be an anxious time for everyone. Remember that the support sites are for them to use too!

Useful words

Acute fatty liver in pregnancy – a rare but serious condition which can occur in the last three months of pregnancy, causing rapid liver and kidney failure. Hospitalisation and immediate delivery of the baby is usually required.

ALT – alanine aminotransferase, a liver enzyme that enters the blood following liver damage. An ALT test is used to monitor and assess the degree of liver damage in patients with hepatitis of any cause including, for example, toxins and viruses.

AST – aspartate aminotransferase, a liver enzyme but less specific to the liver than ALT (see above). A raised AST level may also indicate muscle damage elsewhere in the body.

Cholestasis – a condition where the flow of bile from the liver is reduced.

Enzyme – a substance, usually a protein, produced by the body to help speed up a chemical reaction (which can be measured with liver function tests).

Fetal – relating to the unborn baby.

Gallstones – stones formed from bile that solidifies and hardens. Most gallstones are now known to be cholesterol gallstones, formed when the liver secretes bile that is abnormally saturated with cholesterol. Other stones can be formed from bile pigment (bilirubin). Gallstones become stored in the gallbladder or can find their way to the common bile duct.

Gene – a segment of a chromosome (or unit of DNA) that carries the instructions or code for making a specific protein or set of proteins responsible for, or contributing to, a specific physical trait or action.

GGT – gamma-glutamyl transferase, a liver enzyme in your blood that is measured to check for liver damage.

HELLP syndrome – hemolysis, elevated liver enzymes and low platelets, a group of symptoms that occur in pregnant women who have pre- eclampsia or eclampsia.

Hepatic – anything relating to the liver.

Hepatocyte – a liver cell.

Inferior vena cava – the large vein that carries blood back to the heart from the lower part of the body.

Intrahepatic – within the liver.

Jaundice – a condition in which the whites of the eyes go yellow and in more severe cases the skin also turns yellow. This is caused by accumulation in the blood of bilirubin, a yellow pigment and a waste product normally disposed of by the liver in bile

Mutation – an occurrence where a gene undergoes a change or variation in the base sequence of its DNA. Some mutations result in the gene no longer coding for the correct protein, or producing a reduced amount of the protein.

Pre-eclampsia – a condition in which a woman develops high blood pressure, excessive fluid retention and sometimes protein in her urine during pregnancy.

Serum – normally clear or yellowish, serum is the liquid that separates from blood when clotting occurs. Many chemical tests are carried out using serum.

Special thanks

Professor Catherine Williamson, Professor in
Obstetric Medicine, King's College London

Jenny Chambers, ICP Support

Further information

Please refer to the Trust website for details of patient organisations and support groups specialising in specific liver conditions, that you may find helpful.

The British Liver Trust publishes a large range of leaflets about the liver and liver problems written for the general public.

Leaflets that you may find particularly helpful include:

- *Autoimmune hepatitis*
- *Diet and liver disease*
- *Hepatitis C*
- *Liver disease tests explained*
- *Primary biliary cholangitis*

Contact us for more information:

Tel: 01425 481320

Helpline: 0800 652 7330

Email: info@britishlivertrust.org.uk

Web: britishlivertrust.org.uk

This leaflet is for information only. Professional, medical or other advice should be obtained before acting on anything contained in the leaflet as no responsibility can be accepted by the British Liver Trust as a result of action taken or not taken because of the contents.

We hope you have found this publication helpful

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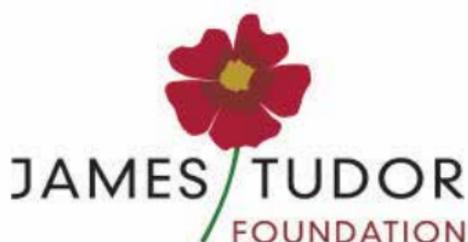
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Contact details

Call us: 01425 481320

Helpline: 0800 652 7330

Email us: info@britishlivertrust.org.uk

Visit our website: britishlivertrust.org.uk

Write to us: **British Liver Trust**, 6 Dean Park Crescent,
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