What you should know about gallstone treatment
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Preface

Dear Patient,

Gallstones are much more common than you might think: Around one in every five adults in Western industrial nations will have stones form in their gallbladder over the course of their life, and in rare cases also in their bile ducts.

But many of these people are unaware, as only 20% of those affected suffer from the typical complaints. The majority have what we call “silent gallstones” – although these do not necessarily stay silent: Cramp-like pain, colic, fever and possibly impaired functioning of the gallbladder, liver or pancreas demand a correct diagnosis and in some cases rapid treatment.
How do gallstones develop and what should you do?

Surgery, i.e. removing the gallbladder together with the gallstones?

Attempts to break up the gallstones using medication?

Is it possible to prevent new gallstones from forming?

This brochure will answer these questions for you and inform you about the latest in gallstone treatment.

You’ll not only learn how your gallbladder functions, but will also get an overview of the treatment options available.

If you still have questions after reading the brochure, please contact your doctor, who will certainly be happy to help.

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Location and function of the gallbladder

The gallbladder is found in the upper right abdomen, just below the liver. It has a very straightforward function: collecting and concentrating bile, which is formed in the liver cells and flows via the bile ducts into the gallbladder. At mealtimes, the gallbladder then passes this concentrated digestive juice on to the duodenum (the first section of the small bowel) in controlled doses to aid digestion.
Diagram of gallbladder, stomach and liver.
Why does the gallbladder have this reservoir function?

Our liver produces around 1 liter of bile every day. The main substances that make up bile are shown in the figure.

![Composition of bile](image)

The bile is secreted into small bile canaliculi (thin tubes) in the liver. The small bile canaliculi lead into larger passages and finally into the two hepatic ducts (left and right) in the liver. These two ducts meet and lead into the common bile duct. A muscle (sphincter) closes the bile duct at the point (known as a papilla) where it opens into the second part of the duodenum. The gallbladder is connected to the common bile duct via a small bile duct known as the cystic duct. While the sphincter remains closed, the bile formed by the liver is stored in the gallbladder and becomes increasingly concentrated. This takes place in particular when the stomach is empty for long periods of time, mainly at night.
If the sphincter of the bile duct opens in a timely manner after eating and the gallbladder contracts at the same time, the bile stored and concentrated there can mix with the semi-digested food and enable important nutrients to be absorbed. As humans are omnivores, i.e. we eat both animal products and plant-based foods, we need bile in order to be able to optimally break down our food and extract nutrients from it. Thorough chewing, gastric juices and properly functioning bowels are also important.
Since we eat different amounts at different times of day, we need to have enough bile and digestive juices stored to meet a range of different digestion requirements.

Bile makes it easier for the body to absorb dietary fat and fat-soluble vitamins in particular, as well as many medications. After a meal, the gallbladder contracts and pushes the concentrated bile through the bile duct into the duodenum, where it mixes with the semi-digested food.

To fulfill this function, bile is mostly made up of emulsifying substances (solubilizers which make dissolving and mixing easier), such as bile acids, as well as cholesterol, pigments, proteins, lecithins, salts and water.
How do gallstones develop?

The main trigger for gallstones is an imbalance in the composition of the bile, which can have a variety of causes.

Bile is made up of many different substances, and these will only stay mixed together in a solution so long as the proportions of cholesterol, bile acids and other substances are exactly right and everything is well mixed by regular contracting and emptying of the gallbladder.

An imbalance in the individual substances can be caused by a number of factors:

- hereditary (genetic) changes,
- disruptions to production or transport in the liver, where the bile is formed, e.g. caused by eating too much fatty food,
- disruptions to the process of concentrating the bile in the gallbladder, inadequate mixing of the bile, e.g. in diabetes patients, other metabolic disorders,
- loss of bile acids, e.g. after surgery on the small intestine for Crohn’s disease or similar.

These disorders initially cause microscopically small crystals to settle in the gallbladder. Once small gallstone crystals have formed, they can continue to grow over the course of months and years – and usually you won’t notice a thing. Eventually the gallbladder will no longer be able to contract properly, the opening of the gallbladder or the duct leading out of it will be partly or completely blocked by a stone, causing the bile to become backed up. That’s when the painful symptoms will start.
Who has an increased risk of developing gallstones?

A significant number of people with gallstones have a diet that’s high in calories and especially in fat.

But relatively long periods of fasting can also lead to high levels of cholesterol in the bile. Eating a diet that’s low in fat means the gallbladder empties less often, causing the bile to thicken as it sits there. Generally speaking, gallstones are more likely to form when high cholesterol levels in the bile are not balanced out by an increase in the amount of bile acids produced.

Loss of these crucial bile acids can be the result of chronic conditions affecting the large or small bowel (Crohn’s disease, ulcerative colitis) or of surgery.

The following groups have a higher risk of developing gallstones:

- people with a family history of gallstones,
- women, compared to men,
- people who are obese or who overeat,
- people with metabolic diseases,
- people with diabetes,
- people with liver diseases (cirrhosis, hepatitis),
- people with bowel disease (affecting the small or large bowel),
- people following a strict weight loss diet,
- people who have had stomach surgery to aid weight loss,
- pregnant women.
The increased risk of gallstones during pregnancy is probably due to the way the body’s processes change during pregnancy, e.g.:
– the hormonal balance changes,
– the gallbladder is less able to contract due to the space taken up by the unborn baby.

Probably as a result of their hormonal balance, women have an overall higher risk of developing gallstones compared to men.

In recent years, clear genetic (hereditary) factors have also been identified which could cause a higher likelihood of gallstone formation to run in families. There is also a clear link to age.

We have looked at the various possible causes of gallstone formation. In the next section, we’ll see what different types of stone exist and how different types of treatment have been developed accordingly.
Composition of gallstones

Depending on the type of imbalance in the bile, the gallstones that form may be mostly made up of cholesterol or of pigments (bilirubin), and may also contain different amounts of salts (e.g. calcium), substances that make up mucus (mucins) and proteins.

All sorts of combinations are possible, meaning there is a huge range of different kinds of stones which vary from patient to patient.

The table and illustration below give an overview of the different types of gallstone.

<table>
<thead>
<tr>
<th>Type</th>
<th>Main component</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol stone</td>
<td>Cholesterol</td>
<td>70–90%</td>
</tr>
<tr>
<td>Mixed stone</td>
<td>Cholesterol, pigments</td>
<td>10–30%</td>
</tr>
<tr>
<td>Pigment stone</td>
<td>Pigments, calcium, mucins</td>
<td>5–10%</td>
</tr>
</tbody>
</table>
Gallstone composition

These differences in the composition of gallstones have consequences for treatment, as you will see shortly.

Different types of gallstone in humans.
Gallstone treatment options

The treatment options are based on the composition of the gallstones and the severity of the condition. In individual cases, of course, the patient’s constitution may also make a particular kind of treatment more suitable.

Generally speaking, there are a number of medical treatment options available these days, which you can read about in the following sections:

– surgical procedures,
– dissolving stones with medication,
– following nutrition guidelines.

It is important to note that these days “silent”, i.e. symptom-free, gallbladder stones are generally only monitored, not treated.

Gallbladder stones are only treated if they have begun to cause troublesome symptoms. On the other hand, stones in the bile ducts must (almost) always be rapidly treated/removed.
Surgery for stones in the gallbladder

If you are advised to have surgery, you should know:

- Surgically removing the gallbladder (a “cholecystectomy”) is currently the first-line (preferred) treatment for patients suffering from gallbladder stones.
- Removing the gallbladder is one of the most common and safest of all modern surgical procedures.
- For many patients who are admitted to hospital with very acute symptoms, an operation is often the only sensible course of action, and can save their life. In these cases, the operation should generally take place as quickly as possible.

*Acute inflammation of the gallbladder (ultrasound image): wall thickening (A), sludge (“detritus”) in the gallbladder.*
Gallbladder removal is a routine procedure in modern surgery, with just under 200,000 operations per year in Germany. Of course, like any surgical procedure, this operation can appear less straightforward to some individual patients. An in-depth conversation with your doctor before surgery of this kind is the best way to resolve all of your concerns and questions. It is also an opportunity for your doctor to thoroughly explain why the operation is necessary and what it involves.

Today, in the vast majority of cases, the gallbladder is removed through a number of very small incisions (cuts) in the skin of the abdomen or the navel (“keyhole surgery”, using what are known as endoscopic or laparoscopic surgical techniques). This usually avoids the large, unsightly scars which were caused by the type of gallbladder surgery used in the past. And it has considerably reduced the amount of time that patients need to stay in hospital after surgery, now usually a few days at most.

The risk involved in laparoscopic gallbladder surgery is very much dependent on any other conditions the patient has. It is extremely rare for the bile duct to be damaged, as some patients may fear.
Dissolving gallstones with medication

Dissolving gallstones with medication (a process called “litholysis”) is only recommended these days for patients who meet strict criteria and who have been informed about the risk of developing gallstones again in the future. Surgical gallbladder removal is a low-risk, definitive method of treatment.

The principle: reversing gallstone formation

Our liver produces important bile acids which allow bile to emulsify cholesterol (make it more soluble).

Gallstones that have formed mostly from cholesterol crystals can be dissolved by regularly taking a highly pure form of bile acids with a litholytic (stone-dissolving) effect. So the process of stone formation is in effect reversed.

The bile acid ursodeoxycholic acid has proved to be especially suitable for this form of treatment.

Which gallstones is medication treatment best for?

Only patients with gallstones made up mostly of cholesterol respond to treatment with ursodeoxycholic acid. These stones can be detected and located by ultrasound.
Cholesterol stone. It is light colored and somewhat translucent.

Small stones in the gallbladder, which is filled with bile and has thin walls (ultrasound image).
Medication treatment is **ideal** for “floating” stones. These have a similar density to bile, meaning that they don’t settle at the bottom of the gallbladder.

Using ursodeoxycholic acid to dissolve gallstones is only possible in certain cases:

- The stones should have a maximum diameter of 5 mm.
- Only stones containing mostly cholesterol can be dissolved.
- Less than one third of the gallbladder should be filled with stones.
- The gallbladder must be fully functioning, i.e. must contract properly after a test meal (e.g. chocolate, an egg).
- The bile ducts must not be blocked.
- Certain medications should not be combined with the stone dissolution treatment (clofibrate, antacids, cholestyramine, estrogen preparations).

**What should you bear in mind when taking medication to dissolve gallstones?**

**First of all: Patience is key.** Gallstones often take months or years to form, so they can’t be dissolved by the bile acid mentioned above overnight.

**Duration of medication treatment**

Depending on the size and quantity of the stones, this treatment can take from 3 months to 1 year. The duration of treatment is dependent above all on the maximum stone size.
Taking your medication regularly and consistently is absolutely essential to ensure the stones can be successfully dissolved. It’s best to take your medication in the evenings, as nighttime in particular is when the liver produces bile with a slightly higher tendency to form gallstones.

Severe stomach pains, fever or chills and shivering, as well as dark urine, can be a sign that a stone is stuck in the bile ducts. This causes the flow of bile to be disrupted, so that it backs up in the liver. If you experience these symptoms you should seek immediate medical help!

Drastic (fat-free) diets leading to rapid weight loss create a high risk of developing gallstones. The risk is also high in the first months after stomach bypass surgery to aid weight loss. This risk can be reduced by treatment with ursodeoxycholic acid – in consultation with your doctor. This therapy should be continued at least until your weight has stabilized.
Advantages of medication treatment

Treatment with ursodeoxycholic acid has almost no side effects and has been proven to be safe and successful in many international clinical studies.

This form of treatment is without a doubt the least invasive way of removing gallstones.

Compared to other forms of treatment, especially surgery, it has a range of advantages for the patient:

- no risks/after-effects of surgery (anesthesia, complications, scarring, diet restrictions),
- no pain or time off work for recovery.

Success rates and follow-ups for treatment to dissolve stones using medication

If the medication is taken regularly, the gallstones it targets can be dissolved in 30–70% of cases.

Pregnancy should be avoided during treatment, as a precaution.

Ultrasound is used to monitor the shrinking of the stones. Normally, ultrasound is used to check the effectiveness of medication treatment with ursodeoxycholic acid after 3–6 months, and treatment is only continued if the stones have shrunk significantly.

Before treatment begins, the patient must be given detailed information regarding alternative treatments (the standard being surgery) and in particular the risk that new stones will form even after successful medication treatment with ursodeoxycholic acid.
A final reminder:

Medication treatment to dissolve gallstones will only be successful if you take your medication consistently. Please do not change the dose, and under no circumstances stop the treatment without first discussing this with your doctor! In both situations, the stones would continue to grow and could cause such severe and acute symptoms that surgery might even become necessary.
Removing stones from the bile ducts

**Bile duct** stones are now usually removed using endoscopic techniques (“endoscopic retrograde cholangiopancreatography”, or ERCP). You may be familiar with the procedure of endoscopy from stomach or bowel examinations.

In **bile duct** stone treatment, the opening of the bile duct in the second part of the duodenum is opened up (a procedure known as a papillotomy) and an endoscope (a tube-like instrument) is used to introduce a small basket. This is opened to “catch” the stone and then removed again together with the stone. The stone is left in the small bowel and will leave your body when you go to the toilet. X-ray imaging is used to check the position of the stone and whether all of the stones have been removed.

**Bile duct** stones which are large, stuck or located deep in the liver or before a narrowing can also usually be broken up very safely and successfully using shock waves or with laser beams. They can then be removed in the same way as described above.

*X-ray of endoscope and stones in the bile duct.*
Is it possible to prevent new stones from forming?

Gallbladder stones can no longer develop after the gallbladder has been surgically removed. After medication treatment to dissolve gallstones – which today is only used in exceptional cases – around 50% of patients develop new stones in their gallbladder.

This is because gallstones are predominantly caused by disruptions to production in the liver, and the precise molecular, biochemical processes in the liver cells which make the bile produced more likely to form gallstones are still not at all fully understood, although they are the subject of intensive research.
Continuing medication treatment

As a result, after-treatment with ursodeoxycholic acid, in particular, should be continued for a period of around 3–6 months after a sonogram (ultrasound) has confirmed that the stones are gone.

It is currently being investigated whether a smaller dose of the medication over a longer period of time can reduce the risk of new stones forming. However, long-term results are not yet available.

Patients with a tendency to develop new gallstones will be advised to have their gallbladder surgically removed.

In 5–15% of patients, new **bile duct** stones can form months or years after the stones were completely removed via endoscope (“ERCP”). This is mainly caused by infections of the bile ducts, or by the flow of bile being impaired. No treatment options which are currently available can guarantee the prevention of new **bile duct** stones. The bile acid ursodeoxycholic acid, which is taken as medication to dissolve gall**bladder** stones, generally has no effect on **bile duct** stones.
Nutrition tips to help reduce stone formation

Following certain nutrition guidelines can help you reduce your level of risk and prevent stones from developing:

– Avoid excess weight, as overweight patients are particularly likely to develop gallstones.

– Reduce the amount of cholesterol in your diet. A low-cholesterol diet is an effective way for patients to remain “stone-free” for as long as possible.

– Have several small meals spaced out throughout the day, including a small evening snack (for example a glass of milk or a yoghurt). This causes the bile to mix well and the gallbladder to empty regularly, preventing stones from forming. Generally, patients who have had their gallbladder removed also find that having multiple small meals is easier on their digestion.

– A fiber-rich diet, e.g. including lots of vegetables, makes the digestion process easier and also helps to prevent stones from forming.

So our recommendation is: Talk to your doctor and follow their advice on diet and lifestyle.
A final word

Supporting patients and doctors in fighting liver, stomach, bowel and gallbladder diseases is the core mission of the Falk Foundation e.V.

This brochure should help you to understand more about modern treatment options, creating a stronger foundation of trust between doctors, patients, medical researchers, pharmaceutical manufacturers and the general public.

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