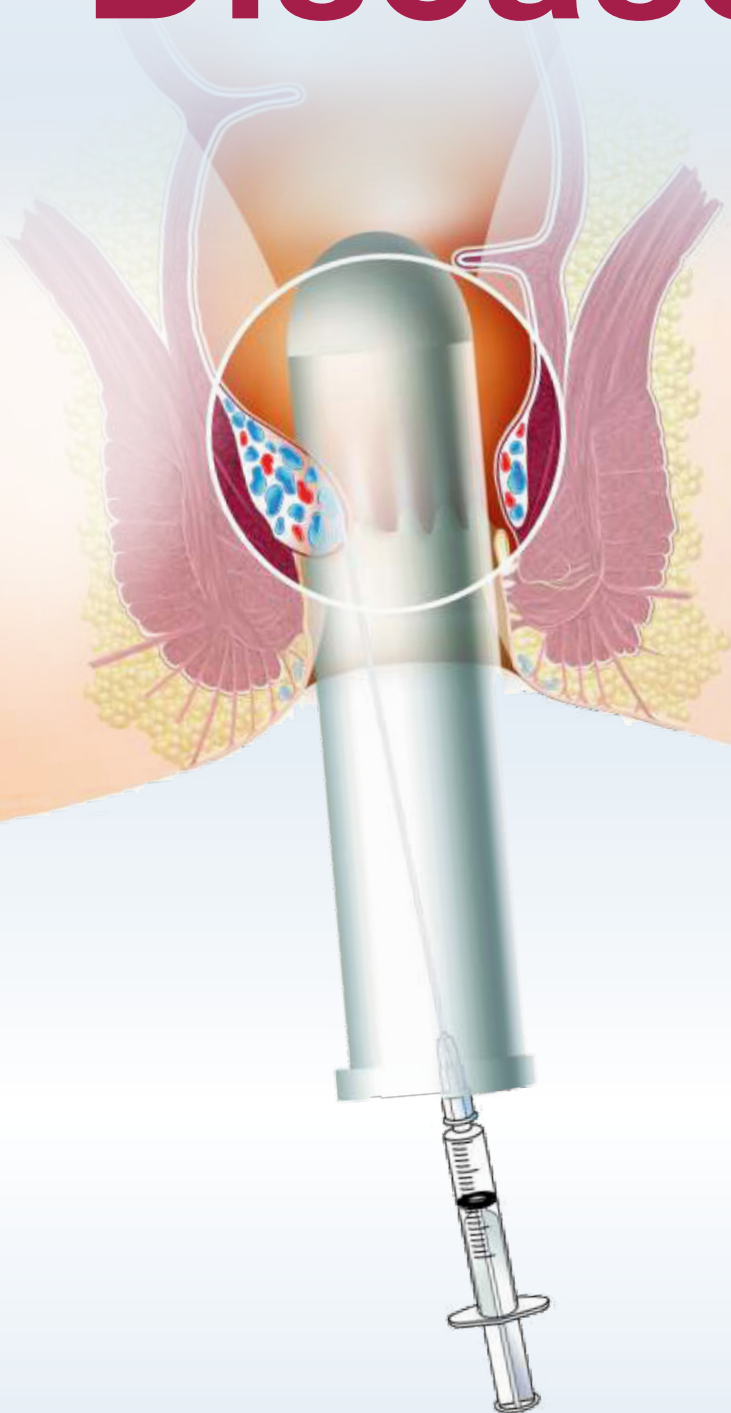
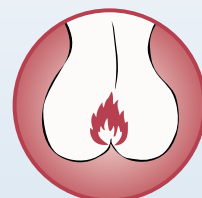


A PRACTICAL GUIDE FOR PHYSICIANS

# [Haemorrhoidal Disease]



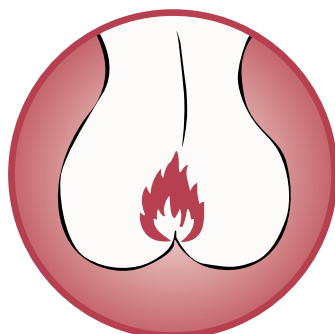
**INTERNATIONAL  
RECOMMENDATIONS**  
FOR THE TREATMENT OF  
HAEMORRHOIDAL DISEASE  
WITH **SCLEROTHERAPY**

Based on the first international expert meeting  
on sclerotherapy for haemorrhoidal disease  
held in Wiesbaden on 18 January 2020

**kreussler**  
PHARMA

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# 1. Introduction

In Germany, sclerotherapy with Aethoxysklerol® (active ingredient polidocanol) has been registered for the treatment of haemorrhoidal disease since 1966. Sclerotherapy with liquid polidocanol is the treatment of choice for first-degree haemorrhoidal disease and a good treatment option for second-degree disease. Polidocanol is also often used in combination with rubber band ligation.

Sclerotherapy with foamed polidocanol for the treatment of varicose veins has evolved and improved continuously since the 1990s and the superior efficacy of foam sclerotherapy has been successfully demonstrated in various clinical trials.

In contrast, the first reports on the use of foam sclerotherapy for haemorrhoidal disease did not appear until 2006. By now, several studies looking at the use of foam sclerotherapy in haemorrhoidal disease have been conducted with promising results and the use of foam has started to attract more and more interest worldwide.

Regardless of whether liquid or foam is used, the techniques used for sclerotherapy vary, both within the same country and between different countries.

For this reason, Kreussler Pharma set up an initial meeting to discuss the treatment of haemorrhoidal disease with key opinion leaders from Germany, Italy and Poland at the beginning of 2020.

**The aim of the meeting was to reach a consensus on the essential diagnostic measures and the most appropriate injection techniques for sclerotherapy. During the meeting, the experts agreed on the following recommendations and basic procedures for performing sclerotherapy with liquid and foamed polidocanol in haemorrhoidal disease.**



The experts of the meeting and the Kreussler team

## 2. Authors and participants of the meeting



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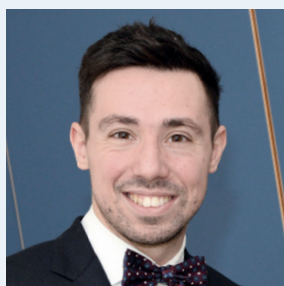
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- Performed the first foam study in the treatment of haemorrhoidal disease
- Invited speaker in more than 50 national and international colorectal/surgical congresses
- Published about 35 papers in indexed journals
- Member of the German Professional Association of Coloproctology (BCD) and the German Society of Coloproctology (DGK)



## 3. Basics

### Definition of haemorrhoids

**Haemorrhoids are normal structural components of the intestine and an important part of the anal continence organ. They contribute to fine-tuning the anus seal.**

Synonyms used: haemorrhoidal plexus, haemorrhoidal cushions, haemorrhoidal nodes, corpus/plexus cavernosum recti, piles

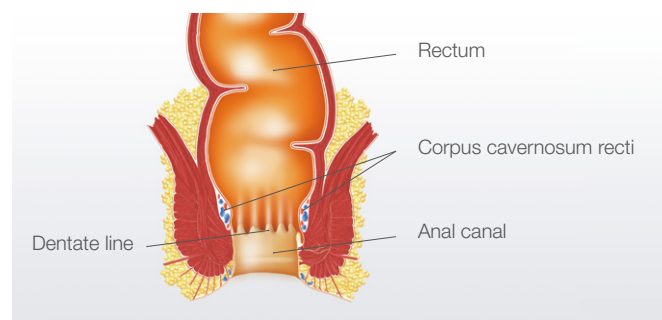


Figure 1: Corpus cavernosum recti in the distal rectum

In Germany, the term “corpus cavernosum recti” is normally used to describe the physiological state, whereas the term “haemorrhoid” is mainly used to describe enlargement of the haemorrhoidal cushions without symptoms. According to the Italian experts, both corpus cavernosum recti and haemorrhoids represent the physiological state (Gallo et al., 2020).

The term “haemorrhoidal disease” is used when the haemorrhoids cause symptoms (see definition and classification into degrees below).

The corpus cavernosum recti is located immediately above the dentate line in the submucosa of the distal rectum (figure 1) and consists of spongy connective tissue cushions surrounding a network of direct arterio-venous communications. On the basis of scanning electron microscopy studies, some authors have suggested that the network may consist mainly of veins with small sphincters (Aigner et al., 2009).

The term “internal haemorrhoids” is used in many countries to describe the haemorrhoidal cushions above the dentate line.

The term “external haemorrhoids” is sometimes used to refer to anal venous thrombosis (outside the anus), but is a different condition. To avoid misunderstandings, the term should not be used in this case.

### Definition of haemorrhoidal disease

The German experts define haemorrhoidal disease as follows: If the haemorrhoids become enlarged and/or displaced and are symptomatic, this is referred to as haemorrhoidal disease.

According to the Italian experts, haemorrhoidal disease is defined as the symptomatic enlargement and distal displacement of the anal cushions (Lohsiriwat, 2012).

Patients often understand haemorrhoids to mean the pathologically enlarged haemorrhoidal plexus with symptoms and therefore use the term “haemorrhoid” to refer to the disease.

Haemorrhoidal disease is progressive in most cases.

### Goligher's classification of haemorrhoidal pathology

Continued enlargement of the haemorrhoids can lead to distal dislocation and, ultimately, prolapse. The most commonly used classification system for haemorrhoidal disease worldwide is still the system proposed by

Goligher (figure 2), which classifies haemorrhoids based on their location and degree of prolapse (Rubini and Ascanelli, 2019).



Figure 2: Goligher's classification of haemorrhoidal pathology

**First-degree/grade 1 haemorrhoidal disease:**

The haemorrhoids begin to bulge into the anal canal, but are not visible externally and can only be diagnosed with proctoscopy.

**Second-degree/grade 2 haemorrhoidal disease:**

The haemorrhoids prolapse on defaecation and return spontaneously after defaecation.

**Third-degree/grade 3 haemorrhoidal disease:**

The haemorrhoids prolapse on defaecation, during strenuous activity and in response to a rise in intra-abdominal pressure and require manual replacement.

**Fourth-degree/grade 4 haemorrhoidal disease:**

At this final stage, the haemorrhoids are permanently prolapsed and cannot be repositioned (permanent anal prolapse).

Goligher's classification may lead to confusion, because haemorrhoidal prolapse often occurs in combination with anal prolapse.

Other haemorrhoidal disease scores that are based on symptoms and health-related quality of life may become an option in the future.

For scientific research, clinical studies and specific comparisons between different countries, it is advisable to use validated symptom scores and to include a quality-of-life index (Gallo et al., 2020).

However, Goligher's classification is sufficient for everyday practice.

## Description of haemorrhoidal disease

In routine clinical practice, haemorrhoidal disease is described with reference to an imaginary clock-face ("anal clock"), when the patient is examined in the lithotomy position (figure 3).

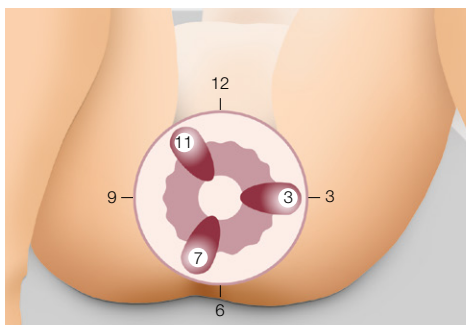


Figure 3: "Anal clock" in the lithotomy position

It is often claimed that enlarged haemorrhoids are only found at the 3, 7 and 11 o'clock positions, where the terminal branches of the superior rectal artery join the haemorrhoidal cushions. However, it has been shown that the entry point of this artery shows considerable variation between individuals and that there may be more than three terminal branches. Consequently, enlarged haemorrhoidal nodes can be found anywhere around the circumference of the anus, although they are most commonly found at the 3, 7 and 11 o'clock positions (Thomson, 1975).

Patients may present with different degrees of haemorrhoidal disease simultaneously, for example, second-degree disease at the 3 o'clock position and first-degree disease at the 11 o'clock position.

## Symptoms of haemorrhoidal disease

Most symptoms of haemorrhoidal disease are nonspecific and may also occur in other diseases:

- Bleeding during or at the end of defaecation: bright red blood may drip into the toilet, coat the stool or stain the toilet paper
- Itching (pruritus ani)
- Burning
- Anal discomfort and a feeling of dull internal pressure
- Prolapse (may cause irritation and inflammation)
- Leakage of mucus or faecal secretion

According to the experience of the experts, the size of the haemorrhoids does not necessarily correlate with the symptoms.

**Bleeding** may occur once, recurrently or continuously over longer periods. Haemorrhoidal bleeding most likely arises from the superficial vessels of the anal transitional zone (interposed between the columnar epithelium of the mucosa and the squamous epithelium of the anoderm). When the blood flow to or from a permanently prolapsed haemorrhoid is cut off, the haemorrhoid may become "strangulated", which can lead to complications such as incarceration and thrombosis. This condition is very painful and should always be treated as an emergency case.

**Pain** is not a typical symptom of haemorrhoidal disease but can be a sign of complications such as incarcerated and/or thrombosed prolapse or may indicate the presence of another disease.

## 4. Recommendations for diagnosis and standardised examination procedure

An accurate diagnosis is essential to distinguish haemorrhoidal disease from other diseases of the anorectal region that may present with similar symptoms and to exclude cancer. In addition, the degree of the disease has to be defined in order to consider treatment options.

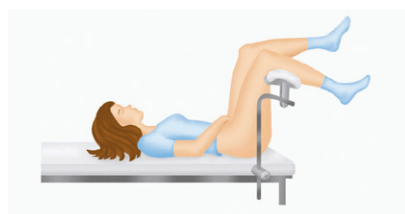
### Obligatory components of a proctological examination:

- Medical history
- Inspection
- Digital examination and anal palpation
- Proctoscopy: sufficient for diagnosing haemorrhoidal disease
- Rectoscopy: should be performed to exclude other diseases

In addition, colonoscopy for cancer screening should be considered (Gallo et al., 2020).

The proctological examination is carried out with the patient in the lithotomy (supine) position, lying on the left side (Sims position) or, less frequently, in the knee-elbow position (figure 4).

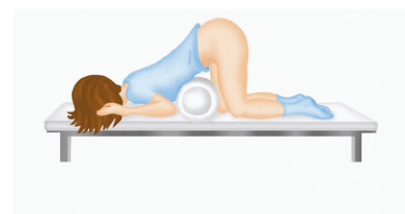
Faecal occult blood tests are not suitable for diagnosing haemorrhoidal disease, but haemorrhoidal bleeding may lead to a positive test result.



Lithotomy position



Sims position



Knee-elbow position

Figure 4: Different positions

**Medical history:** The medical history is essential to help narrow down the differential diagnosis and should include a detailed description of the symptoms experienced by the patient in the anus and anal region (nature, extent, duration and course of the complaints). The patient should be asked about bleeding, pruritus, prolapse, incontinence, pain, bowel habits (frequency, consistency and defaecation), eating habits, fluid intake and family history of colorectal carcinoma.

**Inspection:** The examination begins with an inspection of the anal and perianal area – if necessary, with separation of the buttocks. Anal eczema and irreducible prolapse can be diagnosed by inspection. The patient should be asked to strain in order to check whether prolapse occurs in response to a rise in abdominal pressure.

Anal prolapse (covered by anoderm) and rectal prolapse (covered by mucosa) must be differentiated from haemorrhoidal prolapse. Prolapsed haemorrhoids may be covered by mucosa of the rectum and tissue of the transitional zone only, or by anoderm as well (prolapsed haemorrhoids in combination with anal prolapse).

**Digital examination and anal palpation:** Inspection is followed by a digital examination (figure 5), which is used

to check for abnormalities of the anal canal and the lower rectum. For the digital examination, the examining finger is sheathed in a rubber glove and should be moistened with an adequate quantity of anaesthetic lubricant. Then, the finger is gently inserted into the anal canal, where indurations or unusual masses, narrowing of the lumen or loss of continuity of the sphincter muscles can be felt. The cervix and prostate are readily palpable through the rectal wall and should also be assessed. The finger should be rotated through a full 360 degrees to ensure that all structures are fully evaluated.

Enlarged haemorrhoids are not generally palpable but may be felt as soft cushions in some cases.

The competency of the external anal sphincter should be evaluated by asking the patient to simulate interrupting a bowel movement.

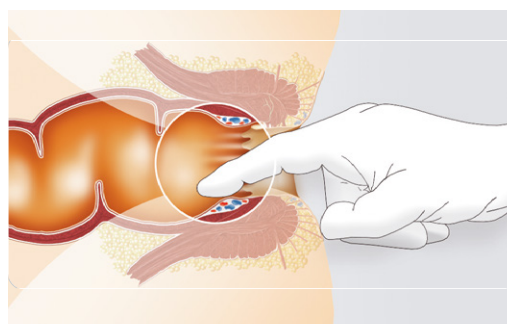


Figure 5: Digital examination



**Proctoscopy:** Proctoscopy (figure 6) is required to diagnose first-degree haemorrhoidal disease and is an essential component of a sound medical assessment.

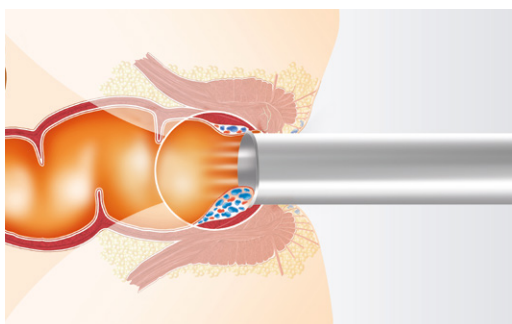


Figure 6: Proctoscopy for diagnosis

It allows the entire anal canal and parts of the lower rectum to be examined and does not normally require any special preparation such as enemas or laxatives.

The tip of the proctoscope can be dipped into an anaesthetic lubricant first (not mandatory), before being introduced into the anal canal using slight pressure. Intubation should not be carried out blindly against resistance. The proctoscope should be inserted as far as is necessary to ensure a full assessment of the anal canal. If there is an internal obturator, this is then removed, a cold light source is attached and the proctoscope is slowly withdrawn with rotatory movements that allow the entire circumference to be visualised.

If the proctoscope has a lateral window, it has to be rotated in a full circle so that each part of the anal canal and lower rectum can be seen in the window.

Before the proctoscope is withdrawn through the anal canal, the patient should be asked to press when it reaches the level of the haemorrhoidal nodes to assess the degree of prolapse.

**Proctoscopes:** In general, disposable or non-disposable proctoscopes measuring 10–15 cm in length that have a lateral window (Blond proctoscope) or are open in front (truncated or bevelled (figure 7)) can be used.



Figure 7: Different proctoscopes with open front used for the treatment of haemorrhoidal disease

Proctoscopes with a lateral window have the advantage that any enlarged haemorrhoids will bulge more or less distinctly into the lumen of the proctoscope. However, because of the small size of the lateral window, it may not be possible to see the entire mass.

Proctoscopes that are open in front provide a better overall view of each part of the anorectal circumference during the examination and are therefore well suited for diagnosis. Proctoscopes with a bevelled end allow the operator to inspect the circumference of the anus by rotating the scope rather than having to repeatedly reinsert it.

**For diagnosis, proctoscopes with a distal opening should be preferred.**

An anoscope is shorter than a proctoscope (5–10 cm) and can be used to inspect the anal canal and the lower rectum.

Rectoscopes or flexible endoscopes are not suitable for diagnosing haemorrhoidal disease.

**Rectoscopy:** Rectoscopy is an important component of the proctological examination and should be performed to exclude diseases of the rectum and to generate a differential diagnosis.

Rectoscopy is suitable for diagnosing rectal ulcers and inflammatory and neoplastic changes, which can be confirmed with biopsies.

Rectoscopy does not necessarily require any special preparation. However, enemas or laxative suppositories can be administered shortly before the examination if appropriate.

The rectoscope with obturator in place is moistened with a lubricant and introduced into the anal canal using slight pressure. Once the obturator has been removed and the fibre-optic cable has been mounted, air can be insufflated with a balloon to expand the rectum. With visualisation and illumination provided via the attached optical fibre, the rectoscope can be advanced as far as the lower sigmoid colon. The operator examines the mucosa carefully while withdrawing the rectoscope.

**Colonoscopy:** In addition, colonoscopy should be considered, to screen for cancer and to rule out the possibility that the symptoms are due to other diseases of the bowel above the rectum.

## 5. Differential diagnosis

Several anorectal conditions can cause symptoms similar to those associated with enlarged haemorrhoids and can also have a similar appearance. Haemorrhoidal disease also occurs in combination with the following findings and diseases.

The most important differential diagnoses are described below:

- Anal skin tags (figure 8)
- Anal venous thrombosis (figure 9)
- Condyloma acuminata (anal warts) (figure 10)
- Anal fissure (figure 11)
- Anal eczema (figure 12)
- Hypertrophied anal papilla (anal fibroma) (figure 13)
- Anal abscess and anal fistula
- Cryptitis (inflammation of the proctodeal glands)
- Anal prolapse (anodermal prolapse)
- Anal (canal) carcinoma and carcinoma of the perianal area
- Proctitis
- Anorectal melanoma
- Perianal Crohn's disease and colitis
- Rectal prolapse (figure 14)
- Rectal polyps (figure 15)
- Rectal carcinoma (figure 16)
- Solitary rectal ulcers
- Rectal varices

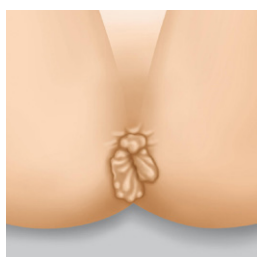


Figure 8: Anal skin tags

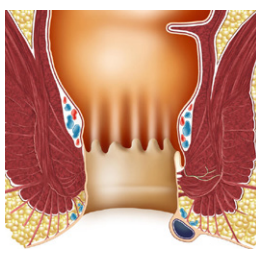


Figure 9: Anal venous thrombosis

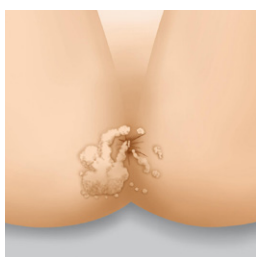


Figure 10: Condyloma acuminata (anal warts)

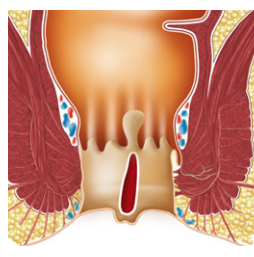


Figure 11: Anal fissure

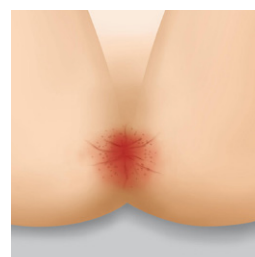


Figure 12: Anal eczema

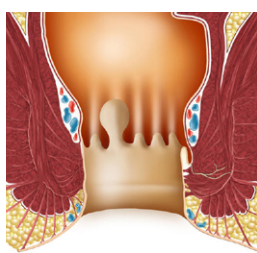


Figure 13: Hypertrophied anal papilla (anal fibroma)

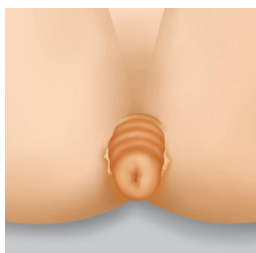


Figure 14: Rectal prolapse

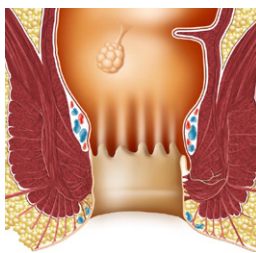


Figure 15: Rectal polyps

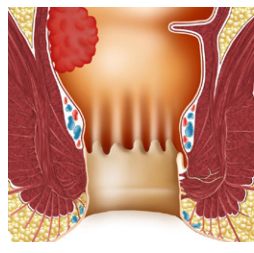


Figure 16: Rectal carcinoma

**Severe pain** usually indicates an anal fissure or anal venous thrombosis. Chronic increasing pain that is perceived as dull and diffuse occurs in cases of abscess, fistula and other inflammatory diseases, but also in anal carcinoma.

**Anal bleeding** is typically present in haemorrhoidal disease and anal fissures but can also be caused by many other conditions, for example, polyps and colorectal or anal carcinoma.

## 6. Recommendations for the treatment of first- and second-degree haemorrhoidal disease

**Haemorrhoidal disease should be treated by physicians experienced in coloproctology or proctology. Haemorrhoids without symptoms should not be treated.**

**Basic measures:** Patients should be informed about the benefit of a high-fibre diet which can make stools softer and easier to pass, thus relieving symptoms.

Alternatively, fibre preparations such as psyllium husks can be taken as a supplement. Bulking agents such as these swell when they come into contact with water and act as a natural laxative by stimulating the peristalsis and forward movement of the intestines and softening the stool. Chemical laxatives should be used sparingly, if at all.

Patients should also be informed about the benefit of optimal defaecation habits, including the avoidance of straining during and after defaecation and “long sessions” on the toilet.

The aim of both measures is to achieve one defaecation with normal stool consistency per day that should take no longer than two minutes. This will have a positive effect on the treatment of haemorrhoidal disease and should be a general recommendation.

**Symptomatic treatment:** Symptomatic treatment comprises oral treatment with flavonoids and topical treatment.

**Oral drugs** containing flavonoids like diosmin, rutoside or troxerutin are used in some countries as vasoprotective agents in the treatment of haemorrhoidal disease. Some studies show that flavonoids can increase vascular tone, reduce venous capacity, decrease capillary permeability, facilitate lymphatic drainage and reduce inflammation.

Flavonoids can be used to treat acute symptoms of haemorrhoidal disease or as an adjunctive therapy in combination with other treatment options.

**Topical treatment** includes the use of ointments, creams, suppositories and anal tampons. Anal tampons (suppositories with gauze pads) should be preferred because they remain in the anal canal after insertion to release their ingredients, whereas suppositories slip deep into the rectum.

The topical products contain antiphlogistics, NSAIDs, local anaesthetics, astringents or corticosteroids, either alone or in combination. Zinc oxide paste can also be used to treat pruritus and inflammation.

Topical treatment may be used to temporarily relieve acute inflammatory symptoms and pruritus or as an adjunctive therapy in combination with other treatment options.

**Minimally invasive treatment methods:** First- and second-degree haemorrhoidal disease (by definition symptomatic) should be treated using minimally invasive treatment methods.

The most widely used methods for treating first- and second-degree haemorrhoidal disease are sclerotherapy and rubber band ligation. Both are long-established treatment methods whose efficacy and safety have been proven in numerous clinical studies. There are country-specific differences with regard to the preferred method.

In Germany, sclerotherapy is mainly used to treat first- and second-degree haemorrhoidal disease. For first-degree haemorrhoidal disease, sclerotherapy is the most commonly used treatment, whereas rubber band ligation is mainly used for second-degree haemorrhoidal disease.

According to the Italian guidelines, injection sclerotherapy should be used to treat first- to second-degree haemorrhoidal disease as well as third-degree disease that fails to respond to conservative treatment (Gallo et al., 2020).

## 7. The treatment of haemorrhoidal disease with liquid sclerotherapy – recommendations and basic principles

**In proctology, sclerotherapy involves injecting a sclerosing agent into the bulging haemorrhoidal node or into the tissue at the base of the haemorrhoidal node.**

**The aim of treatment with sclerotherapy is to reduce and eliminate symptoms, to reduce or prevent prolapse and to maintain the haemorrhoidal tissue and anal continence.**

**In general, physicians should be familiar with the know-how required to diagnose haemorrhoidal disease and should be trained in key skills before starting to perform sclerotherapy.**

**Mode of action of sclerotherapy:** Sclerotherapy works primarily by causing sclerosis of the (bleeding) connective tissue at and near the injection site (especially if the sclerosant is injected into the haemorrhoidal cushions) and fixation of the mucosa to the underlying tissue, thus preventing prolapse (especially if the sclerosant is injected at the base). In addition, the sclerosant can diffuse from the injection site to obliterate small vessels.

All of these effects contribute to shrinking the haemorrhoids.

**The sclerosant polidocanol:** Polidocanol is the sclerosant of choice for haemorrhoidal disease. Although phenol solution is still used as sclerosant in some countries, it should no longer be used because of its carcinogenicity and teratogenicity.

The medicinal product containing the active substance polidocanol was approved in Germany under the name Aethoxysklerol® in 1966 and is currently approved for the treatment of haemorrhoidal disease in 27 countries and marketed in more than 50 countries.

As a modern sclerosant, polidocanol belongs to the class of non-ionic detergents.

It consists of a fatty alcohol part containing 12 C atoms and a chain of several oxyethylene units (-O-CH<sub>2</sub>-CH<sub>2</sub>) that are connected via ether (-O-) bonds (figure 17).

In Aethoxysklerol® the number of oxyethylene units is between 1 and 24 and the average number of oxyethylene units is 9, which is expressed by  $n = 9$ . Therefore, polidocanol is not a molecule with a single defined structure, but a mixture of molecules with different chain lengths.

From a chemical point of view polidocanol has an alcohol group (OH group) and belongs to the large group of alcohols. However, polidocanol is completely different to the chemical compound ethanol.

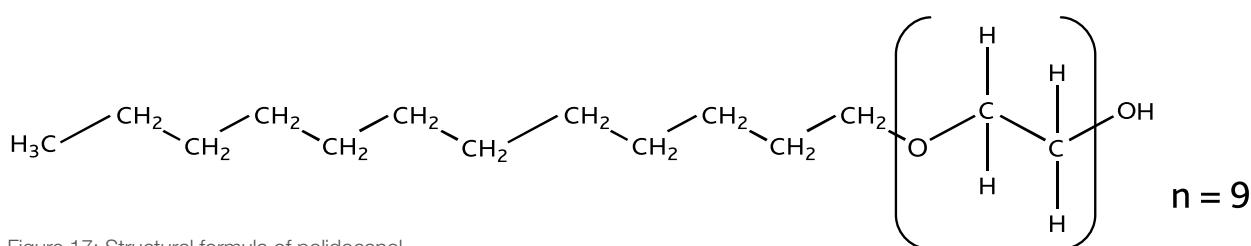


Figure 17: Structural formula of polidocanol

**Sclerosing effect of polidocanol:** The surface-active polidocanol molecules generate aggregations of molecules in the form of micelles that interact with the membrane of cells (figure 18). The micelles dissolve

essential molecules from the membrane, causing the affected cells to die. **Thus, above a certain concentration, sclerosing agents can destroy all types of cells.**

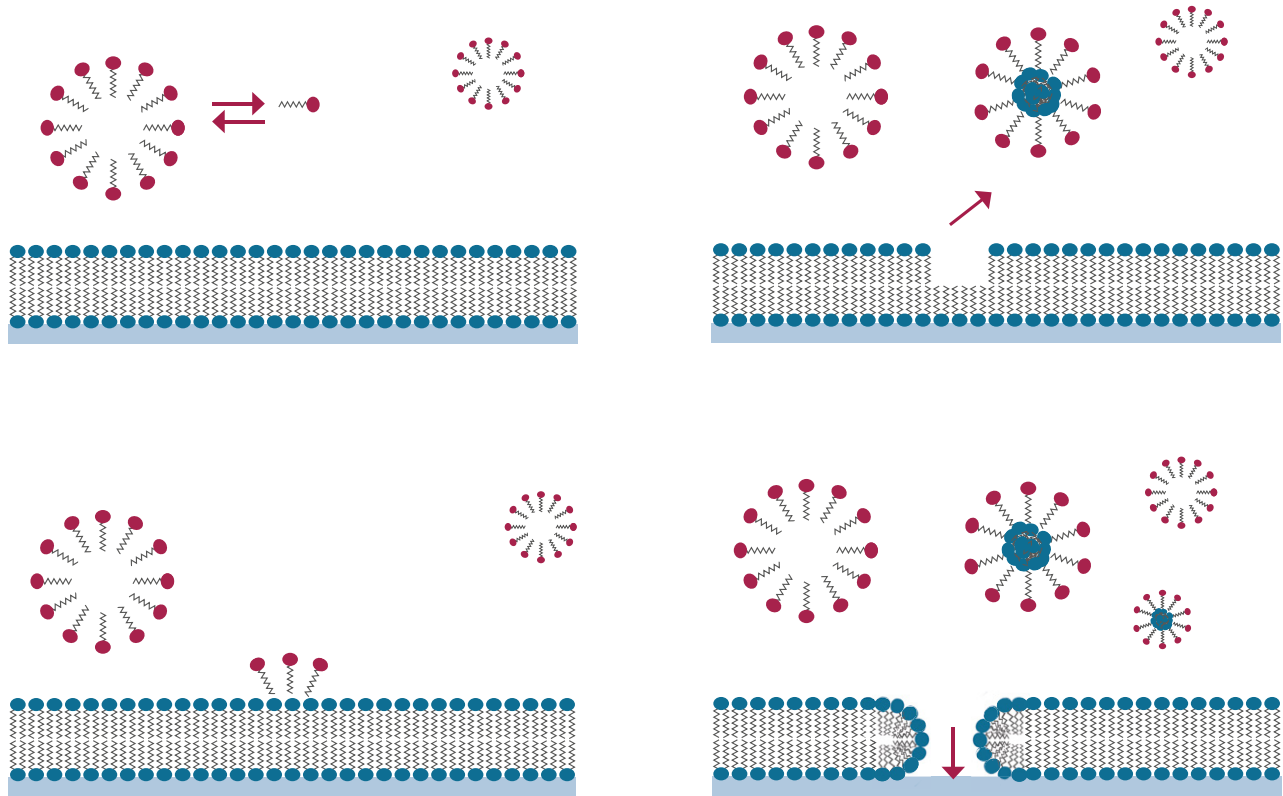


Figure 18: Schematic view of the effects of polidocanol on the cell membrane

In the case of haemorrhoidal disease, sclerotherapy results in the destruction of tissue cells and a deliberately induced, limited inflammatory reaction, which leads in

the long term to tissue fibrosis. In addition, sclerotherapy destroys the vessel walls near the injection site.



**Other important properties of polidocanol:** Polidocanol is the only sclerosant that has a local anaesthetic effect and reversibly suppresses the excitability of the pain-mediating receptors and the conduction capacity of the sensory nerve fibres. Therefore, polidocanol is often used in dermatological preparations and in cosmetics like shampoos and washing lotions because of its antipruritic effect and its emulsifying action. This is an important factor to consider in the case of allergic reactions.

Polidocanol should always be drawn up freshly and used promptly. It should be avoided to fill several syringes in the morning to use during the course of the day because of possible interactions between the polidocanol and the syringes. Polidocanol can dissolve syringe components such as silicone, which can make the syringes swell and stop moving smoothly.

**Indications:** Liquid polidocanol 3% (German trade name Aethoxysklerol® 3%) is approved for the treatment of first- and second-degree haemorrhoidal disease. In some cases, it may also be used to treat third-degree disease, for example, in patients who do not want to or cannot undergo surgical treatment due to comorbidities.

**Contraindications:** A complete list of contraindications to sclerotherapy of haemorrhoidal disease is included in the product information (summary of product characteristics, SmPC) for Aethoxysklerol® in the respective country.

#### **Most important absolute contraindications**

- Known allergy to polidocanol or any of the other ingredients
- Acute severe systemic disease (especially if untreated)
- Acute inflammation or diseases in the anal region or injection area

#### **Most important relative contraindications**

- Chronic inflammatory anorectal disease (e.g. Crohn's disease)

Anticoagulation therapy is not a contraindication, which makes sclerotherapy the treatment of choice for patients taking anticoagulants.

**Sclerotherapy during pregnancy:** The results of several animal studies did not provide any indication for teratogenic and mutagenic effects of Aethoxysklerol® under the given test conditions. However, there is insufficient clinical data on its use in pregnant women.

According to the product information, sclerotherapy must not be used during pregnancy unless clearly necessary.

Sclerotherapy in pregnant women who were not known to be pregnant at the time of injection is not considered to be a reason for termination of pregnancy.

**Sclerotherapy during breastfeeding:** Animal experiments suggest that a certain amount of polidocanol may be excreted into breast milk. As no studies in humans are available, breastfeeding should be discontinued for two to three days after sclerotherapy, as polidocanol is eliminated from the body within two days.

## Liquid sclerotherapy injection technique

There are two injection techniques for sclerotherapy of haemorrhoidal disease: the intrahaemorrhoidal method (formerly referred to as Blond's method) and the suprahaemorrhoidal method (formerly referred to as Blanchard's method). Both techniques produce good treatment results if used appropriately.

The application of both methods requires practice and experience because an inadequate technique can result in complications and treatment failures. The correct location and depth of the injection and the amount and concentration of the sclerosant are important factors.

In the treatment of haemorrhoidal disease, polidocanol is normally not injected into vessels, but into tissue. Although vessels within the haemorrhoid may be injected inadvertently, it is not possible to specifically inject individual vessels of the haemorrhoidal node.

### 1. Intrahaemorrhoidal method (formerly Blond's method)

With the help of the proctoscope, the sclerosant is injected directly into the surface of the bulging haemorrhoidal node (figure 19).

Usually, a proctoscope with a lateral window is used for intrahaemorrhoidal injection. However, a proctoscope or anoscope with an open front can also be used.

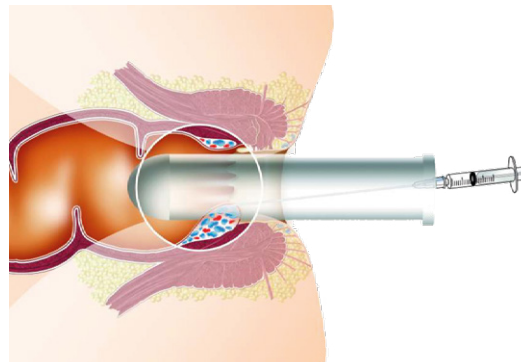


Figure 19: Intrahaemorrhoidal method

The sclerosant can be injected in two slightly different ways:

**1a Superficial:** The sclerosant is injected superficially and intramucosally (figure 20) to a depth of 1–2 mm.

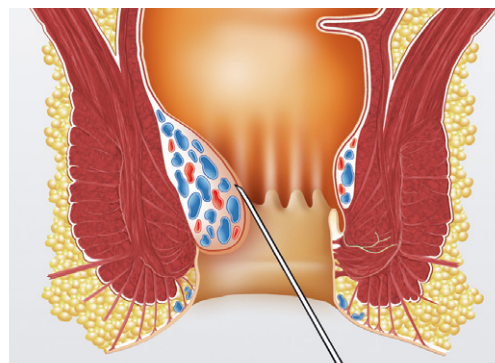


Figure 20: Superficial injection of the sclerosant

**1b Deep (submucosal):** The sclerosant is administered submucosally into the haemorrhoidal tissue (figure 21) to a depth of 5–6 mm.

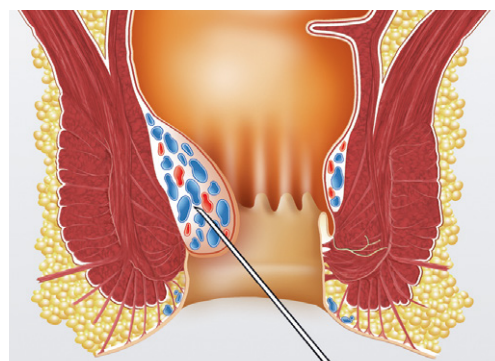


Figure 21: Deep injection of the sclerosant

## 2. Suprahaemorrhoidal method (formerly Blanchard's method)

The sclerosant is administered through a proctoscope with an open front, just above the haemorrhoidal node into the tissue at the base of the haemorrhoids (figure 22).

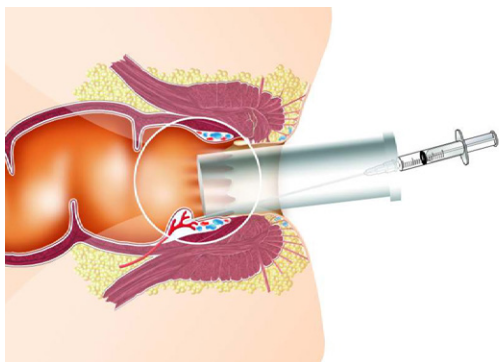


Figure 22: Suprahaemorrhoidal method

The injection is administered tangentially into the sub-mucosa of the rectal mucosa (figure 23). If the injection is too superficial, the treatment will not be fully effective.

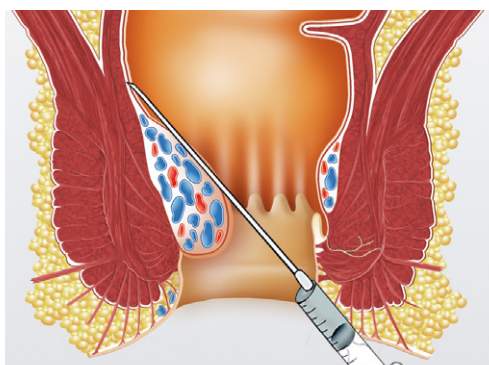


Figure 23: Injection into the submucosa of the rectal mucosa (suprahaemorrhoidal)

Both techniques can also be combined depending on the size of the haemorrhoidal nodes and the number of enlarged haemorrhoids.

An anoscope can be used instead of a proctoscope for injection.

### Further tips and recommendations:

- For reasons of hygiene, disposable needles and syringes are recommended.
- All enlarged haemorrhoidal nodes can be treated in one treatment session.
- One or more injections are administered into the enlarged haemorrhoids or at their base, depending on the size of the haemorrhoidal nodes.
- The sclerosant should only be injected into enlarged haemorrhoidal tissue and not into “normal” (not enlarged) haemorrhoids (for example, in a circular manner).

- **The sclerosant must not be injected to a depth greater than 5–6 mm to avoid injecting the muscular layer of the rectum and causing side effects.**
- The depth of the injection depends on the size of the haemorrhoid and the angle of the needle during the injection. The injection should be administered tangentially to the anal canal and the orientation of the needle should not be too vertical (in the vertical position, the needle penetrates more deeply into the tissue).
- If sclerotherapy is performed using the intrahaemorrhoidal method, the sclerosant is always injected into the haemorrhoidal nodes and it is impossible to inject the rectum if the injection is performed correctly.
- In some countries, patients with cardiac valve replacement receive prophylactic antibiotics at the day of treatment, depending on the recommendations of the cardiologists in the country in question. In Germany, antibiotics are not recommended.

### Materials required:

- Proctoscope/anoscope
- Anaesthetic lubricant
- Sclerosant
- Smooth-running disposable plastic syringe (1–3 ml)
- Disposable cannula (9–12 mm long)

**Dosage:** According to the product information (SmPC) the total quantity of 3 ml Aethoxysklerol® 3% should not be exceeded during one session and no more than 1 ml of Aethoxysklerol® 3% per haemorrhoid should be administered with the exception of the haemorrhoid at the 11 o'clock position: Here, no more than 0.5 ml should be injected because of the proximity to the prostate. Special care should be taken in the region of the internal sphincter muscle due to the risk of damage and subsequent incontinence problems.

Most physicians use less than 1 ml per injection and 1–3 ml per session. This also depends on the concentration of the sclerosant.

**Treatment sessions:** For best results, one to three treatments at intervals of three to four weeks may be necessary, depending on the severity of haemorrhoidal disease and the amount of sclerosant injected.

A follow-up visit should take place after one month. A further follow-up visit can be arranged after one year but is not mandatory. As a rule, patients will return to their doctor anyway if symptoms reappear. Patients without symptoms are not treated again.

### Side effects following sclerotherapy of haemorrhoidal disease:

In general, sclerotherapy is a very safe treatment method and the frequency of side effects is very low when compared with other methods.

Common reactions (frequency  $\geq 1\%$  and  $< 10\%$ ) include temporary pain, discomfort, burning and a sensation of pressure at the site of injection. According to the product information, allergic reactions such as allergic dermatitis, urticaria and other skin reactions are uncommon ( $\geq 0.1\%$  and  $< 1\%$ ) and, in most cases, mild. Other uncommon side effects include proctitis, pruritus and induration of the tissue around the injection site. In rare cases ( $\geq 0.01\%$  and  $< 0.1\%$ ), bleeding at the injection site, intra-haemorrhoidal haematoma, temporary urinary retention and necrosis (usually local) may occur. In single cases, necrosis may extend into the surrounding tissue and, in the worst case, cause pelvic sepsis. Systemic reactions such as nausea and fever are very rare ( $< 0.1\%$ ).

To date, no deep venous thrombosis or other thromboembolic events have been reported in connection with sclerotherapy of haemorrhoidal disease. The most likely reason for this is that polidocanol is injected into the tissue and not into vessels (most of the vessels in the region are too small for injection).

Sclerotherapy is normally painless when the proper technique is used because there are no pain fibres at the site of injection above the dentate line. Nevertheless, up to 10% of patients feel mild pain and a pressure sensation during and directly after the injection. This can happen, for example, if the injection is administered below the dentate line. Another possible reason is that not all pain fibres cease abruptly at the dentate line and that some sensitive nerve endings may extend above this line.

**A complete list of possible side effects is included in the product information (SmPC) for the respective country.**

**Post-sclerotherapy management:** As mentioned above, patients should be informed about the benefit of optimal defaecation habits. Patients can resume their normal daily activities immediately and return to work straight away.

Mild bleeding, which does not require further treatment, may occur within the first two days after the procedure.

Patients should be instructed to contact their treating proctologist without delay if they experience any unusual symptoms, for example, fever.

### Pros of sclerotherapy:

- Effective and safe treatment option.
- Most minimally invasive treatment.
- Normally painless.
- Can be performed as an outpatient procedure and requires no anaesthesia.
- No time off work is necessary.
- Takes just minutes to perform.
- Can be repeated as often as necessary.
- Lower complication rate compared with other treatment options (for example, rubber band ligation).
- Serious side effects are extremely rare.
- Haemorrhoidal tissue is preserved and remains intact.
- Patients taking anticoagulants can be treated as there is no severe bleeding after treatment.
- Most cost-effective treatment.
- Particularly suitable for first-degree haemorrhoidal disease if the haemorrhoidal node is so small that any rubber band may slip off.
- Can be combined with other treatment techniques.

### Cons of sclerotherapy:

- Several sessions may be necessary for an optimal treatment outcome.
- Recurrences may occur after some time and require further treatment.

**Combination with rubber band ligation:** A combination of rubber band ligation and sclerotherapy can be used for technical reasons and to decrease the risk of bleeding after ligation.

The sclerosant can be injected into the ligated node (figure 24, A) to increase the volume in the ligated node and to prevent the band from slipping off prematurely. In addition, or alternatively, the sclerosant can be injected around the base of the node (figure 24, B) to reduce the incidence of delayed bleeding after rubber band ligation.

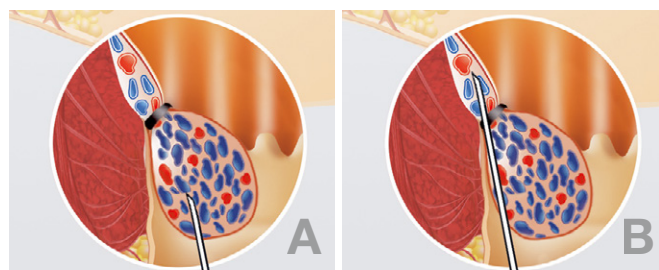


Figure 24: Injection of polidocanol into the ligated node (A) and at the base of the node (B)

If a patient presents with different degrees of haemorrhoidal disease simultaneously, it is possible, for example, to treat second-degree disease with rubber band ligation and first-degree haemorrhoidal disease with sclerotherapy in the same session.

#### **Efficacy of sclerotherapy with liquid polidocanol:**

In the last 25 years, few studies evaluating the efficacy of sclerotherapy with polidocanol have been performed. Below you will find the efficacy results for the most important recent studies.

Author	Country	Year	n	Degree	Success in %	Treatment sessions
Akerud	Sweden	1995	119	Mostly 1	88 97	1 2
Kohlstadt et al.	Germany	1999	603	1 and 2	Degree 1: 96 Degree 2: 52	5
Ahmet et al.	Turkey	1999	34	2	69	1
Brühl and Schmautz	Germany	2000	31	1	77	2
Petrin et al.	Italy	2000	80	2	79	Median 3
Yuksel et al.	Turkey	2008	62	1 and 2	68	1
Moser et al.	Germany	2013	64	1	69 92	1 2
Mukhopadhyay et al.	India	2014	58	1 and early 2	67 90	1 2
Mishra et al.	India	2020	75	1 and 2	61 95	1 2

According to the studies listed, the success rate of sclerotherapy is about 70 to 95% for first-degree haemorrhoidal disease and about 50 to 80% for second-degree disease. The number of treatment sessions usually ranges from one to three.

No reliable data is available on the recurrence rate after sclerotherapy and there is no unique definition of recurrences. Due to the progressive nature of the disease and because sclerotherapy preserves the haemorrhoidal tissue, there is a relatively high rate of symptom reappearance in the years following successful treatment (approximately 30 to 60%, based on estimates).

Patients should be informed that it may be necessary to repeat sclerotherapy after some time (if symptoms reappear) and that sclerotherapy can be repeated as often as necessary without any problems and with a good outcome. Treatment with sclerotherapy has the advantage that the haemorrhoidal tissue is preserved, which helps to maintain anal continence.

**Conclusion regarding liquid sclerotherapy:** Liquid sclerotherapy remains a reliable and successful treatment option for first- and second-degree haemorrhoidal disease.

We hope that the collected expert recommendations and tips will contribute to the standardisation of sclerotherapy in the future.



## 8. The treatment of haemorrhoidal disease with foam sclerotherapy – basic principles

Physicians started to use foamed polidocanol for ultrasound-guided sclerotherapy of varicose veins in the 1990s. Foam, which is produced by mixing air with liquid polidocanol, has the advantage that it displaces the blood in the veins, allowing better and more prolonged contact between the sclerosant and the wall of the vein. In contrast, liquid sclerosing agents are diluted rapidly by the blood flow in larger veins. Therefore, larger varicose veins can be treated more effectively with foam sclerotherapy.



As a result of the convincing clinical data, foam sclerotherapy has been approved as a new application method for the sclerotherapy of varicose veins in Germany and many other countries.

The results achieved in phlebology led to the assumption that foam could also increase success rates in the treatment of haemorrhoidal disease. There are no published results of foam sclerotherapy for haemorrhoidal disease before 2007.

### History of foam sclerotherapy in Germany:

Independent of the first Italian experiences with foam in 2006, Dr. Moser from Germany started to use foam for the treatment of haemorrhoidal disease in 2007. In the years that followed, he conducted a clinical study together with the Colorectal Centre in Mannheim to evaluate treatment with foam using a proctoscope (Moser et al., 2013).

This was the first GCP (Good Clinical Practice) compliant, randomised, prospective and controlled multicentre study to compare the efficacy and safety of liquid polidocanol with foam in the treatment of haemorrhoidal disease. Patients with bleeding first-degree haemorrhoidal disease were treated either with Aethoxysklerol® 3% liquid or foam. After three months, the treatment success after a single sclerotherapy session was significantly higher with foam (88%) than with liquid (69%). However, liquid sclerotherapy remained a reliable treatment option, with a 92% success rate after the second session compared to 98% with foam. Foam sclerotherapy required fewer treatment sessions and a smaller total amount of polidocanol for a successful treatment outcome. In addition, the study demonstrated a good safety profile for liquid and foam. Follow-up after six years showed a significantly lower recurrence rate with foam (46%) compared with liquid (67%).

From 2014 to 2017, Dr. Moser performed an additional retrospective analysis on 732 patients with first- and second-degree haemorrhoidal disease. After one year, 88% of the patients with first-degree disease and 77% of patients with second-degree disease had been treated successfully with foam. 86% of patients with first-degree disease required only one treatment session for successful treatment, compared with 36% of patients with second-degree disease. Of the latter group, 78% were treated successfully after two treatment sessions.

### **The Moser technique for foam sclerotherapy:**

- Standardised foam is prepared using the double syringe system EasyFoam® Kit.
- With the patient in the lithotomy position, the haemorrhoids are visualised during proctoscopy and injections are administered using an open-ended proctoscope.
- Using the suprahaemorrhoidal method, injections are administered submucosally into the tissue at the base of the haemorrhoids.
- As a rule, 2 ml of foam is slowly injected at the 3, 7 and 11 o'clock positions (6 ml per sclerotherapy session).
- Sclerotherapy sessions are performed until patients are free of bleeding and/or other symptoms.

### **History and studies of foam sclerotherapy in Italy:**

In 2006, Italian physicians started to use foam sclerotherapy for the treatment of first- to third-degree haemorrhoidal disease with the help of a flexible endoscope, which allowed retrograde visualisation of the haemorrhoidal nodes. The foam was injected through an endoscopic injection catheter that was passed via the biopsy channel to the tip of the video colonoscope, directly into the haemorrhoidal nodes. This technique, although successful, was not widely used because of the high costs of endoscopy and the skills needed for effective treatment.

In 2015, Italian experts (in particular Prof. Dodi and Dr. Lobascio) revisited the idea of using foam sclerotherapy to treat haemorrhoidal disease. In the years that followed, they started several foam studies, this time injecting the foam with the help of a proctoscope.

### **Studies in Italy:**

- Treatment of second-degree haemorrhoidal disease with Aethoxysklerol® 3% foam (with very satisfactory results, not yet published).
- Treatment of second- and third-degree haemorrhoidal disease with Aethoxysklerol® 3% foam:  
Initial results of the retrospective study have now been published (Lobascio et al., 2020). The overall success rate after one year was 79% after a single foam session and 86% after two treatments and no intra-operative complications or drug-related side effects occurred.
- Aethoxysklerol® 3% foam in comparison with rubber band ligation in the treatment of second- and third-degree haemorrhoidal disease (study to be completed in 2021).

### **The Italian technique for foam sclerotherapy:**

- Standardised foam is prepared using a double syringe system (EasyFoam® Kit or using Tessari's method).
- With the patient lying on the left side (Sims position), the haemorrhoids are visualised during anoscopy or proctoscopy.
- The intrahaemorrhoidal method is used and injections are administered directly into the three haemorrhoidal nodes at the 3, 7 and 11 o'clock positions.
- The Italian experts made the experience that the risk of damage to other structures may be lower with the intrahaemorrhoidal method.
- A maximum of 2 ml of foam is injected per node.  
A smaller volume of foam should be administered when treating the haemorrhoid at the 11 o'clock position because of its proximity to the prostate and special care should be taken not to inject too deeply.
- An anoscope or open-ended proctoscope is used. In most cases, a transparent disposable anoscope is used to provide a better overview of all structures.
- A 20 G needle (9 cm long) is used. Bleeding may occur during injection but stops soon after application of the foam.
- Injections can be repeated after three to four weeks.

Promising early results from the Italian studies have been presented at many congresses worldwide, which has triggered a sclerotherapy boom – not only in Italy, but in other countries as well.

Foam is also used to treat haemorrhoidal disease in Poland, Portugal, Spain and China.

# The treatment of haemorrhoidal disease with foam sclerotherapy – recommendations

## Rationale for using foam:

- Foam bubbles maximise the contact surface area within the haemorrhoid.
- The injection of foam may lead to vasospasm.
- Foam spreads locally in the haemorrhoidal tissue.
- Foam remains in the tissue longer than liquid.
- More micelles (which are responsible for efficacy) are formed.

Consequently, foam should result in better efficacy and a lower recurrence rate than liquid.

Sclerotherapy with foam leads to sclerosis as well as fixation and shrinkage of the haemorrhoidal tissue.

**Important information:** Foam sclerotherapy is not specifically approved as a new form of application for the treatment of haemorrhoidal disease at present. In principle, however, sclerotherapy with foam obtained from an approved sclerosing solution can be used because physicians are free to choose the most appropriate treatment approach for their patients.

Physicians should obtain the patient's explicit consent to foam sclerotherapy. Patients should be informed of the following:

- Foam sclerotherapy represents the further evolution of an existing method that uses a sclerosing agent that has been employed successfully for decades.
- The sclerosing foam is produced by mixing the liquid sclerosant and air in a standardised procedure.
- In experienced hands, foam sclerotherapy appears to be more effective for some indications and just as safe as liquid sclerotherapy, although there is more experience with the use of liquid sclerotherapy.
- The benefits and possible complications of foam sclerotherapy.

**Physician training:** Foam sclerotherapy is not recommended for physicians who are new to proctology. For safety reasons, only physicians who are familiar with the skills necessary for diagnosing and treating haemorrhoidal disease should start by using foam. It is recommended that physicians first gain experience with liquid sclerotherapy before they start with foam sclerotherapy, because inappropriate injection techniques may result in treatment failures and more side effects.

**Possible indications for foam sclerotherapy:** Foam is used for first- and second-degree haemorrhoidal disease. In Italy, foam is already used for bleeding third-degree haemorrhoidal disease if surgery is not possible due to comorbidities (Lobascio et al., 2020).

In general, however, the treatment of third-degree haemorrhoidal disease with foam is still being discussed and evaluated.

Foam sclerotherapy can be performed during colonoscopy for cancer screening and may become an interesting treatment option for gastroenterologists.

**Preparation of foam:** The foam is produced in accordance with the recommendations established for the treatment of varicose veins and can only be produced with detergent-type sclerosing agents such as polidocanol. **The foam is produced by mixing one part of the liquid sclerosant with four to five parts air (1 + 4–5) using a double syringe system.**

In the method used by Moser, the standardised foam was prepared using the EasyFoam® Kit double syringe system (figure 25) by mixing 1.6 ml of liquid polidocanol 3% and 7.4 ml of sterile air. This system consists of two silicone-reduced syringes connected by a special bidirectional check valve and is optimised for the generation of a fine-bubbled, homogenous and stable microfoam. One syringe is prefilled with sterile air and, after aspiration of liquid Aethoxysklerol® into the second syringe, the two syringes are connected and the entire content is pumped 20 times without interruption from one syringe to the other.

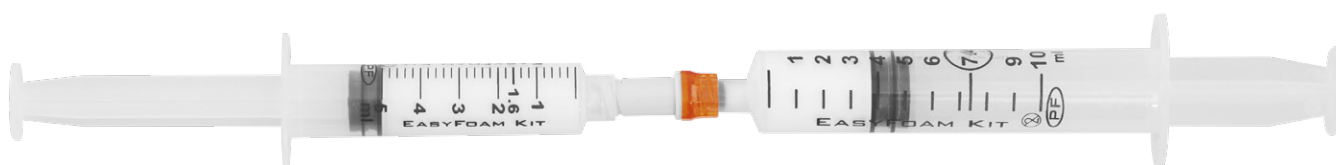


Figure 25: Preparation of foam with the EasyFoam® Kit

Foam can also be produced using a three-way stopcock (in the method described by Tessari) or other suitable double syringe systems and two-way connectors. **The foam must be injected immediately after production because of its short half-life.** Polidocanol can dissolve silicone out of the syringe, which can shorten the half-life of the foam. Therefore, silicone-reduced syringes should be used.

With practice, it takes less than one minute to prepare the foam.

## Foam sclerotherapy injection technique

**As with liquid sclerosant, foam can be injected using an intrahaemorrhoidal or suprahaemorrhoidal approach (see pages 16 and 17). A proctoscope with a lateral window or front opening or an anoscope can be used.**

**Important points to note for successful and safe sclerotherapy are the quality of the sclerosing foam, the site of injection, the injection technique and the amount of foam injected.**

Italian and Polish experts also use video-guided sclerotherapy with a special integrated video camera (video-anoscope). This is a safe method and very good for presentation and demonstration purposes.



**Dosage:** As with liquid sclerosant, the dose of 2 mg polidocanol per kg body weight per day should not be exceeded. Most physicians use polidocanol 3% foam for the treatment of haemorrhoidal disease. The recommended dose is up to 2 ml per injection and the most commonly used maximum total dose is 6 ml of foam per session.

### Further tips and recommendations:

- When injecting sclerosing foam, the gauge of the needle should be at least 25 G to prevent the foam from being destroyed as it passes through the needle.
- When injecting foam, the physician will feel less pressure than with liquid.
- When using the intrahaemorrhoidal method, the foam is usually applied using a combination of methods 1a and 1b. The injection is first administered tangentially to a depth of 5–6 mm (deepest possible point) and then more superficially at the end (most superficial point).
- **The intrahaemorrhoidal method has the advantage that there is no risk of injecting the muscular layer of the rectum. Therefore, the intrahaemorrhoidal method is recommended for physicians who are new to foam sclerotherapy.**
- After the foam has been injected, the needle should not be moved and the physician should wait approximately five seconds before removing the needle. Otherwise, foam and blood may leak out of the tissue.
- If the foam is injected too superficially, the view can be obscured by foam bubbles in the distal rectum and the anal canal, which can make it difficult to see where to inject.

**Specific side effects of foam sclerotherapy:** No problems with thromboembolic events or bubbles are to be expected when foam is injected into haemorrhoidal tissue or at the base of the haemorrhoidal nodes. To date, no specific side effects have been observed with foam.

**Pros of foam:**

- Foam appears to be more effective than liquid.
- Results to date have shown that foam sclerotherapy is more effective for the treatment of first- and second-degree haemorrhoidal disease and that it may be an alternative to surgical methods in the treatment of higher-degree disease.
- Less sclerosant is required for successful treatment.
- Fewer treatment sessions are required.
- There may be a lower recurrence rate.
- It is an interesting treatment option for physicians who would like to use a stronger sclerosing agent.
- The cost-benefit ratio may be favourable.

**Cons of foam:**

- Foam has not yet been officially approved as a new application method.
- It takes slightly longer (less than one minute) than liquid sclerotherapy (on the other hand, the foam can be prepared by an assistant).
- The evidence for efficacy and safety is not yet sufficient.

**Conclusion regarding the future of foam sclerotherapy:** It is an innovative and interesting non-surgical treatment method for haemorrhoidal disease. The results to date from clinical studies and the experience of experts indicate that foam sclerotherapy is more effective than liquid sclerotherapy for the treatment of first- and second-degree haemorrhoidal disease. It also requires a smaller volume of injected sclerosing agent and fewer treatment sessions. At the same time, foam sclerotherapy appears to be just as safe as the well-established liquid sclerotherapy method.

In addition, foam sclerotherapy may allow more advanced degrees of the disease to be treated using a minimally invasive method. Further studies are required to evaluate the long-term data on foam sclerotherapy and the efficacy and clinical relevance of using foam to treat more advanced degrees of haemorrhoidal disease.



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