

# Eosinophilic Oesophagitis (EoE)



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Publisher

DR. FALK PHARMA GmbH



Leinenweberstr. 5  
79108 Freiburg  
Germany

[www.drfalkpharma.com](http://www.drfalkpharma.com)

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2nd edition 2020

**The information in this booklet is not intended to be a substitute for professional medical advice, diagnosis or treatment. If you have any questions about your EoE or its treatment, make sure you speak to your GP or EoE specialist.**

## Eosinophilic Oesophagitis (EoE)

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Advances in clinical management of eosinophilic oesophagitis, 1238–54,

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## GENERAL INFORMATION CONCERNING EoE

### > What is eosinophilic oesophagitis?

Eosinophilic oesophagitis (abbreviated EoE) is a chronic, inflammatory disease of the oesophagus whose origins and causes are not yet fully understood. This inflammation of the oesophagus (as denoted by the "itis" at the end of oesophagitis) is characterised by the presence of a certain type of white blood cells in the mucosa, the so-called eosinophils. This is why the disease is called eosinophilic oesophagitis. The most commonly reported symptoms include difficulty swallowing (whereby food may potentially become lodged in the oesophagus) and pain during swallowing.

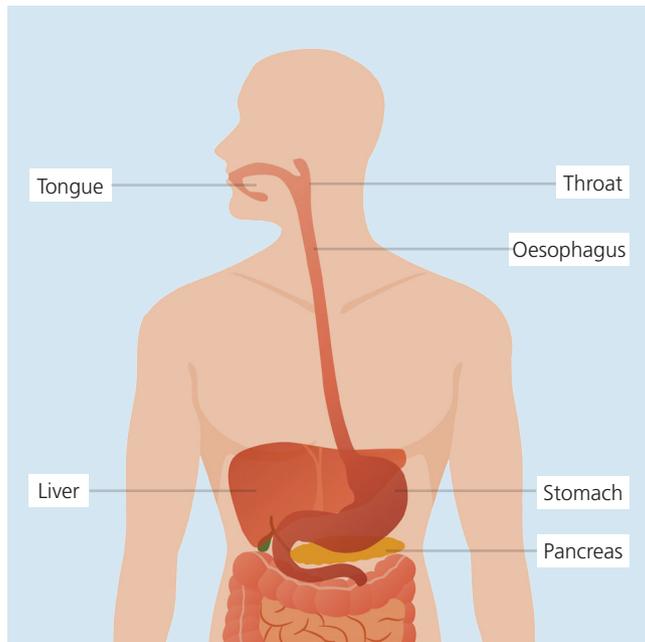


Fig. 1: The oesophagus connects the mouth to the stomach

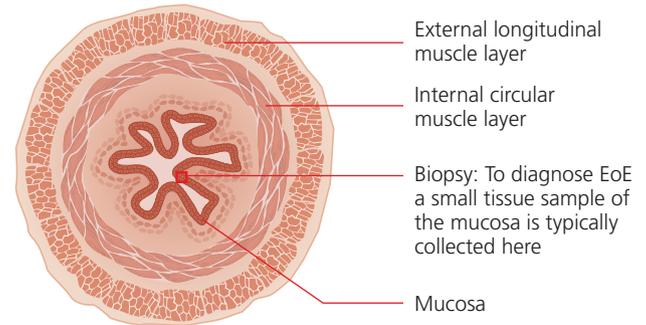


Fig. 2: Cross-section of the oesophagus.

### > What are the causes of EoE?

The oesophagus is about 25 cm long with a diameter of about 2.5 cm. It connects the oral cavity (mouth) to the stomach and is responsible for transporting food from the throat to the stomach. Based on this function, the oesophagus comes into contact with all the food we consume.

In EoE patients, certain food components (so-called allergens) are suspected of triggering inflammation in the oesophagus.

#### Common triggers of EoE include<sup>1</sup>

- > Milk and wheat (most common)
- > Soya
- > Eggs
- > Nuts
- > Fish and seafood



The inflammatory reaction is highly similar to asthma, a chronic, inflammatory condition of the respiratory tract that is triggered by allergens in the air. Therefore, EoE is often referred to as "asthma of the oesophagus". Similar to asthma, airborne allergens are also suspected of potentially triggering EoE.



**EoE is presumed to involve a chronic, inflammatory reaction triggered by certain allergens in foods and in the air.**

In addition, EoE patients also commonly suffer from allergic diseases, such as hay fever, asthma or rash and food allergies in general. Yet, the connection between EoE and these disorders remains unclear. The exact causes and pathogenic processes of EoE are also not completely understood and thus form the focus of current research.

### > What are the symptoms of EoE?

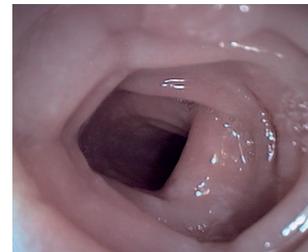
The main symptoms of EoE in adults include difficulty swallowing (so-called "dysphagia") and/or pain during swallowing, also known as "odynophagia", chest pain, and heartburn. In a worst-case scenario, EoE can even result in a prolonged obstruction of the oesophagus, a so called food bolus impaction. In this circumstance a bite of food gets stuck on its way through the oesophagus (see Figure 3). In some cases, the food can no longer be coughed up or regurgitated and requires removal from the oesophagus by a physician. In children, the symptoms are significantly less consistent and EoE often manifests indirectly with vomiting, reduced appetite or growth disorders. As a result, a diagnosis is often difficult and may be significantly delayed after the initial occurrence of symptoms – taking years in some cases.



Normal



Inflammation: white deposits



Strictures (narrowing) with typical ring formation



Acutely inflamed EoE with lengthwise reddish furrows



Mucosal tear following successful dilatation



Obstruction of the oesophagus with a piece of meat (arrow)

*Fig. 3: Endoscopic findings in the oesophagus. In 10-25% of EoE patients, the oesophagus appears normal despite the presence of microscopic inflammation.<sup>2</sup> Signs of acute inflammation (white deposits, mucosal swelling, elongated striations) and signs of scarring (ring formations with narrowing of the diameter of the oesophagus in some cases) are distinguished.*

In addition, pronounced avoidance strategies have been observed, especially in adolescent and adult patients, including:

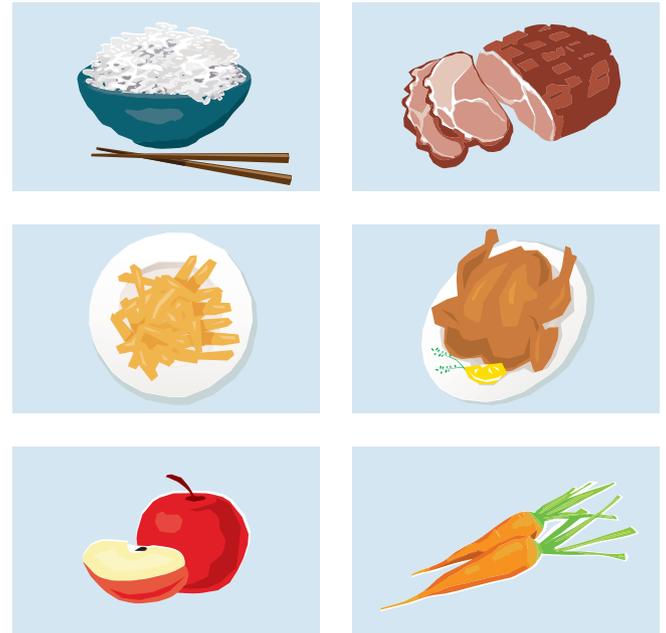
- Avoidance of certain foods or even avoiding restaurants altogether.
- Thoroughly chewing food and consuming food in small bites only.
- Plentiful drinking in order to minimise or prevent difficulty swallowing.



**Although these avoidance strategies seriously restrict the quality of life, many patients are often unaware that they are suffering from a disease of the oesophagus because they consider their condition to be normal.**

If EoE remains untreated, the oesophagus may often continue to constrict over the years (reducing the diameter of the oesophagus). The difficulty swallowing typical of EoE is either the result of an active inflammation or a narrowing of the oesophagus. This difficulty occurs especially with solid foods (see Figure 4). But it is also possible that the disease suddenly manifests even though a person never experienced difficulty swallowing when a piece of food becomes stuck in the oesophagus.

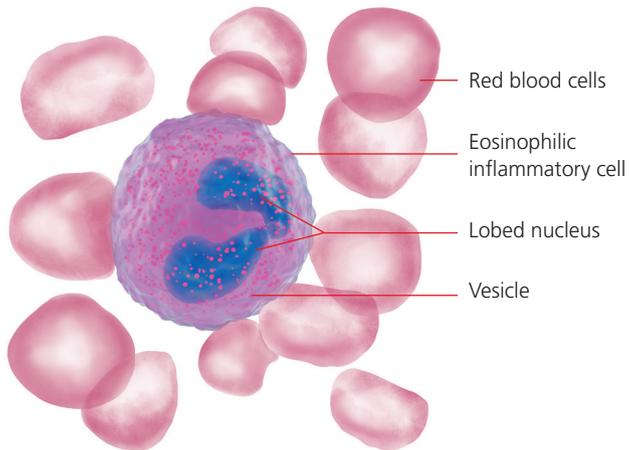
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*Fig. 4: Typical foods that cause difficulty swallowing include dry rice, meat, raw fruits and vegetables (e.g. carrots, apples) or French fries. Patients experience difficulty swallowing because these foods are very solid, not because they trigger acute allergies.*

#### ➤ How can EoE be diagnosed?

EoE can only be definitively diagnosed by a gastroenterologist. In addition to recognising the symptoms described above, EoE is diagnosed by endoscopic examination of the oesophagus with simultaneous collection of tissue samples. The oesophagus commonly exhibits signs of acute inflammation (see Figure 3), but only a high number of eosinophils in the mucosa of the oesophagus is considered decisive evidence of EoE (see Figures 5 and 6).



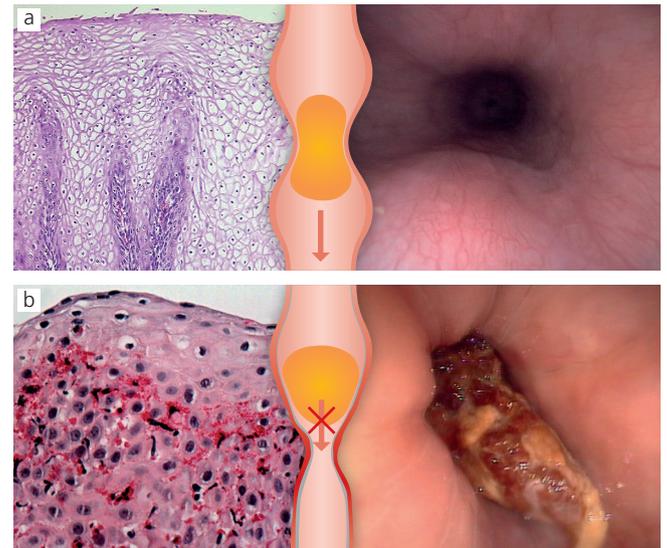
*Fig. 5: An eosinophil (specialised white blood cell) surrounded by red blood cells. Inside the cell is a lobed nucleus (compartment where genetic material is stored) and numerous vesicles (small bubbles or granules) containing various inflammatory substances. Every human has small numbers of eosinophilic inflammatory cells circulating in the blood. These form an important line of defense against parasites (e.g. worms) and in the case of allergies. The mucosa of the oesophagus is normally completely free of eosinophilic inflammatory cells.*

### > How frequently does EoE occur?

It is currently estimated EoE is prevalent at around 42 cases per 100,000 in adults and up to 34 cases/100 000 in children, although there are large geographic variations.<sup>3</sup>

### > What are the risk factors for EoE?

The majority of patients with EoE are male (approx. 60-80%).<sup>4,5</sup> EoE can occur at any age, but occurs most commonly between the ages of 30 and 50.<sup>4</sup> Patients with EoE often suffer from other allergic diseases, such as hay fever, allergic asthma, food allergies or atopic dermatitis. Hereditary risk factors are known, but have no influence on the diagnosis or treatment of EoE.



*Fig. 6: a) Normal oesophagus with no eosinophils  
b) Increased eosinophils in an EoE patient*

### > How does EoE progress if left untreated?

If left untreated, the persistent inflammation caused by the presence of eosinophilic cells, over the years can result in scarring and subsequent narrowing of the oesophagus (see Figure 6). Accordingly, EoE is a chronic disease for which there is currently no cure.



**Various therapies can minimise narrowing and scarring, prevent complications, such as obstruction of the oesophagus, and significantly improve the quality of life of patients.**

## THERAPEUTIC PRINCIPLES OF EoE

Three different treatment options are currently available: The first one is medication with locally acting steroid preparations, which reduce the inflammation, and proton pump inhibitors. The latter are usually used to inhibit the secretion of gastric acid. The second option involves special diets that avoid certain food allergens. The third option is dilation of the oesophagus with an endoscopic procedure.

### > Acute inflammation

Medications and diets are primarily applied in the case of acute inflammation. These therapies may minimise the risk of narrowing (also known as stricture formation) and potentially irreversible scarring of the oesophagus which is associated with prolonged untreated inflammation.

### > Advanced disease

If EoE has been diagnosed too late or the patient no longer responds to medications or diets and severe narrowing of the oesophagus has occurred dilation is applied. Here, the constricted segment is carefully dilated during an endoscopic procedure performed under deep sedation (without general anesthesia). Patients are typically pain- and symptom-free within 2-3 days after this procedure.

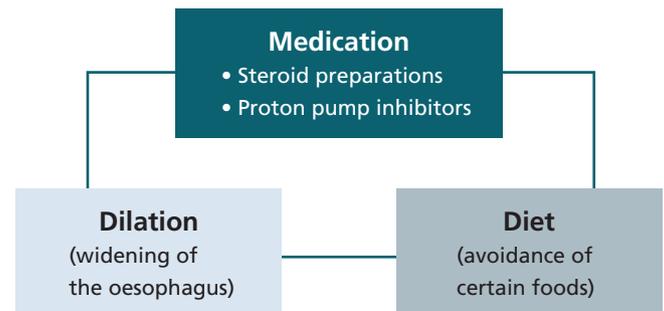


**The different treatment options are applied based on the clinical picture: Medications and diets in the case of acute inflammations, dilation in the advanced stage once the oesophagus has already narrowed.**

### > Long-term treatment is required

Currently, EoE cannot be cured with medications or diets. Unfortunately, if inflammation-inhibiting therapies are discontinued, the inflammation commonly flares up after a few months, accompanied by the known symptoms. As a result, the patient must remain in close contact with the treating physician, watch out for symptoms, and undergo regular check-ups.

But inflammation of the oesophagus is not necessarily accompanied by symptoms. It is possible to have oesophageal inflammation without ever noticing anything. Therefore, an endoscopic follow-up examination of the oesophagus should take place approx. 6-12 weeks following the start of treatment to verify therapeutic success.



## DIFFERENT THERAPEUTIC OPTIONS

### ➤ MEDICATIONS

#### Proton-pump inhibitors

##### **Efficacy:**

A minority of EoE patients respond to treatment with so-called proton-pump inhibitors. These medications suppress the formation of gastric acid and are approved for the treatment of heartburn and stomach ulcers but not EoE. The effect in EoE patients is probably not based on an inhibition of acid but may be an effect on the immune function in the oesophageal wall.



**Due to the fact that there are not yet any studies comparing the treatment with placebo, more conclusive statements concerning efficacy cannot be made.**

##### **Intake:**

Standard therapeutic doses of proton pump inhibitors (PPIs) are used to treat some patients with Eosinophilic Oesophagitis.

##### **Side effects:**

Proton-pump inhibitors are considered relatively safe. Among the most common side effects are headache, abdominal pain, constipation, diarrhea, flatulence, nausea/vomiting and fundic gland polyps (benign).

##### **Treatment duration:**

Proton-pump inhibitors are typically administered for 6-8 weeks, but the exact duration should be in agreement with your doctor. If the patient does not experience any improvement, then other treatment strategies, such as local treatment with a steroid preparation or diet, must be considered.

#### Local steroid treatment of the oesophagus

##### **Efficacy:**

Locally acting steroid preparations (e.g. budesonide) work directly on the lining of the oesophagus and block several stages of the inflammatory process. They are usually well tolerated because they are rapidly inactivated in the liver and only tiny amounts of steroid actually get to other parts of the body via the bloodstream.



**In a recent study, 85% of patients experienced a reduction of inflammation and improvement of symptoms after 12 weeks of treatment.<sup>6</sup>**

##### **Intake:**

EoE used to be commonly treated with asthma sprays containing budesonide or similar active ingredients that were swallowed instead of being inhaled. But because these medications were developed to treat the respiratory tract, they are not ideal for coating the oesophagus. Recently, orodispersible tablets were developed for the treatment of EoE that specifically coat the oesophagus.

##### **Side effects:**

There is an increased risk for mild fungal infections (Candida) in the oral cavity or oesophagus. Fungal infections are relatively easy to treat with antifungal lozenges within a few days without the need to stop the local steroid treatment.

##### **Treatment duration:**

Budesonide treatment is typically applied for 6 weeks. Treatment may be extended to 12 weeks in patients who do not respond adequately to treatment within 6 weeks.

## > DIETS

Most EoE patients are allergic to more than one food. As a result, EoE is regarded as a special type of food allergy. If it is possible to eliminate the foods that cause an allergic reaction in the oesophagus from the diet, then the symptoms and inflammation may disappear without the use of medications. The most common foods that cause eosinophilic inflammation of the oesophagus include dairy products, wheat, eggs, soya, nuts, and fish/seafood (see Figure 7). Appropriate diets are therefore associated with massive restrictions on daily food choices and are rarely applied successfully over prolonged periods.



Fig. 7: Common food allergens

### Amino-acid-based nutrient solutions

#### Efficacy:

This diet dispenses with all conventional foods and instead involves the intake of a special nutrient solution. As a result, this diet is free of any allergy-triggering proteins and consists solely of the basic building blocks of dietary proteins, so-called amino acids, and other nutrients. These amino acids are produced as liquid food. Such protein-free diets have been found to be over 90% effective in reducing inflammation in adults with EoE.<sup>7</sup>

#### Procedure:

Adult patients are able to follow this diet at home, provided that they are able to drink the liquids. The taste is often described as unpleasant. Children/adolescents requiring treatment with an amino-acids-based diet usually do not tolerate the taste, which is why this diet is then administered via a feeding tube during an inpatient hospital stay.

#### Side effects:

Most patients find this diet to be extremely restrictive because they are not permitted to eat anything else. Adult patients rarely choose this diet.

#### Treatment duration:

This type of diet may be successful for 1-2 months, but is hardly feasible as a long-term therapy based on the associated restrictions.



**A diet of nutrient solutions is associated with a considerable loss of quality of life and is rarely feasible over the long term.**

## Empirical elimination diet

### Efficacy:

An elimination diet based on allergy testing results in an improvement in symptoms in only a very small number of patients. In EoE allergy tests are generally not specific, often misleading and are therefore not recommended by the current guidelines.

Therefore, usually an empirical elimination diet is performed, which is based on excluding the 6 most common allergy-triggering foods with subsequent, controlled, step-wise reintroduction until the allergy-triggering “culprit” is identified. This diet has been proven effective in children and adults. In clinical studies, inflammation of the oesophagus has been successfully normalised in over 70% of patients on this diet.<sup>8</sup>

### Procedure:

This diet involves the complete elimination of dairy products, wheat, eggs, soya, nuts, and fish/seafood from the diet for 6-8 weeks. An endoscopic examination of the oesophagus is then performed, including the collection of tissue samples. In the best case, the inflammatory cells have then disappeared from the oesophagus. The individual foods are then reintroduced one after the other at 8-week intervals. Another endoscopic examination of the oesophagus is then performed at approximately 8 weeks following reintroduction of each new food category in order to determine whether it triggers an eosinophilic inflammation of the oesophagus. This procedure is continued until all allergy-triggering foods have been identified. Once an allergy-triggering food has been identified, it is eliminated from the diet.

During multiple sessions, a dietitian provides patients with instructions and advice on how these foods may be avoided. The diet is conducted on an outpatient basis.

In order to reduce the number of endoscopic inspections, a so-called step-up elimination diet may also be used in some cases, in which the first 2 foods (usually dairy and wheat) are eliminated and if there is no response, then 4 or ultimately 6 foods are eliminated from the diet. This step-up approach can reduce the number of endoscopic inspections by about 20% on average.<sup>9</sup>

### Limitations:

It can take up to about a year to identify the allergy-triggering food(s). It is also possible that a patient may require up to 8 endoscopic examinations of the oesophagus in order to identify the triggering allergens (see Figure 8). Each EoE patient must also attend multiple sessions with a dietitian when following the

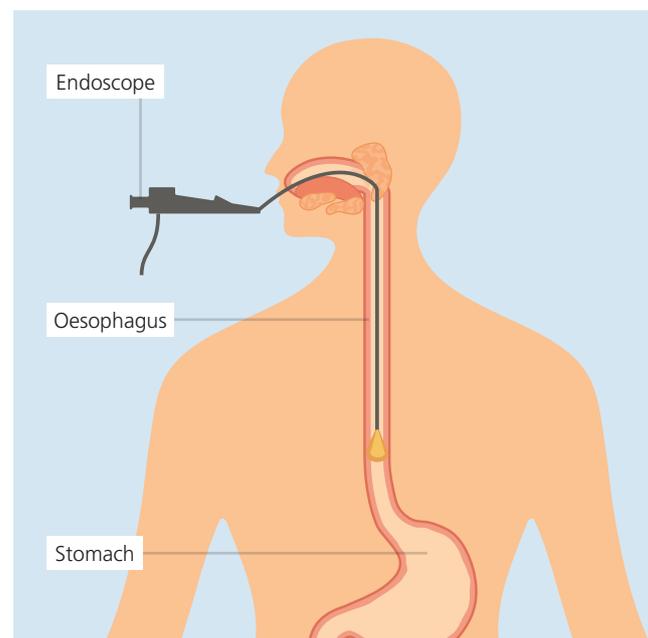


Fig. 8: Endoscopic examination of the oesophagus

empirical elimination diet. Patients are not permitted to consume allergy-triggering foods over the long term. This is sometimes associated with restrictions on the quality of life.

**Treatment duration:**

Patients in whom the triggering foods are successfully identified should follow the diet over the long term (for months or years).



**In many cases, the elimination diet may reduce symptoms and may also be maintained over a prolonged period.**

## DILATION OF THE OESOPHAGUS

**Efficacy:**

About 75% of patients, treated by dilatation, experience significantly improved symptoms.<sup>10</sup>

**Procedure:**

In the case of stricture formation (narrowing) of the oesophagus, the diameter may be enlarged through dilatation treatment. Here, an endoscopic examination is performed. The diameter of the oesophagus is then enlarged by deploying an inflatable balloon or by inserting a wire into the stomach and advancing bougies (candle-shaped plastic cylinders) of increasing diameter into the oesophagus via the instrument in use (endoscope).

Dilation takes about 10 minutes and is performed with the patient under deep sedation. The scar tissue that reduces the diameter of the oesophagus is mechanically dilated during the procedure. However, this procedure does not treat the underlying inflammation that is causing the narrowing of the oesophagus and dilation procedures possibly must be repeated as new strictures form over time.

**Side effects:**

Pain during swallowing may occur in some patients for 2-3 days following the procedure but this pain responds well to conventional relievers.<sup>11</sup> The risk of complications, especially a hole (perforation) in the oesophagus, is relatively low (<1%).<sup>12</sup> A hole in the oesophagus may be closed endoscopically with small metal staples or temporary stents that are then removed after a few weeks. Operations to treat the complications of dilatation procedures are very rarely necessary.

**Treatment duration:**

Dilations may be performed as often as necessary. Patients are usually required to undergo dilation treatment once a year if they are not additionally receiving anti-inflammatory treatment with medications or a diet.



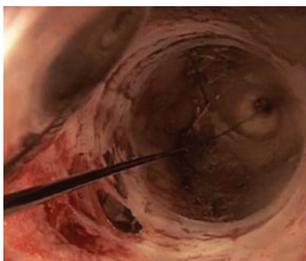
**Dilation does not treat the causes of EoE, but instead merely involves the mechanical expansion of the constricted oesophagus.**



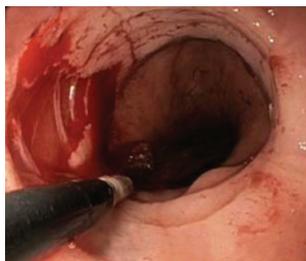
*Stricture in the oesophagus*



*Superficial laceration of the mucosa following attempted passage of a gastroscope*



*Insertion of an inflatable balloon via the accessory channel of the gastroscope. Balloon is inflated to a defined diameter.*



*The stricture is expanded, a superficial tear of the epithelium is visible. The gastroscope is then able to be pushed without difficulty.*

*Fig. 9*

## SUMMARY: CHARACTERISTICS OF THE DIFFERENT TREATMENTS

	MEDICATIONS		DIETS			DILATION
	Proton-pump inhibitors	Local steroid treatment of the oesophagus	Amino-acid-based nutrient solutions	Elimination diet based on allergy testing	Empirical elimination diet	Dilation treatment of the oesophagus
Reduces symptoms	●●	●●●	●●●	●	●●	●●●
Reduces endoscopically visible inflammation	●●	●●●	●●●	●	●●	—
Reduces microscopically visible inflammation	●●	●●●	●●●	●	●●	—
Reduces stricture formation (narrowing) in the oesophagus	—	●	—	—	—	●●●
Side effects	!	!	—	—	—	!
Limitations	—	—	!!	!	!	—
Notes	Effective in only a minority of EoE patients.	In a recent study, up to 85% of patients experienced a reduction of inflammation and improvement of symptoms. <sup>6</sup>	Rarely used, usually administered via a feeding tube.	Allergy tests that measure systemic immune responses accurately more often cannot predict food triggers for EoE. <sup>13</sup>	Roughly 70% chance that microscopically identifiable inflammation will be reduced. <sup>14</sup> Multiple endoscopies of the oesophagus required to identify the triggering food(s).	No treatment of the underlying inflammation. Treatment must be repeated approximately once a year without additional dietary or medicinal treatment.

### Legend:

- Strong effect and/or many side effects
- Moderate effect and/or moderate number of side effects
- Weak effect and/or few side effects
- No effect and/or no side effects

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