



# How to manage anal ulcerations and anorectal stenosis in Crohn's disease: algorithm-based decision making

French National Working Group Consensus 2018

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## Abstract

The French National Society of Coloproctology established national recommendations for the treatment of anoperineal lesions associated with Crohn's disease. Treatment strategies for anal ulcerations and anorectal stenosis are suggested. Recommendations have been graded following international recommendations, and when absent professional agreement was established. For each situation, practical algorithms have been drawn.

**Keywords** Crohn's disease · Anal ulcerations · Anorectal stenosis · Treatment

## Abbreviations

AUC	Anal ulceration of Crohn's disease
APL	Ano-perineal lesion
CD	Crohn's disease
PA	Professional agreement
EA	Expert agreement
MRI	Nuclear magnetic resonance imaging
IS	Immunosuppressant

## Methodology

The management of anoperineal lesions (APL) in patients with Crohn's disease (CD) is often complex and the existing recommendations date back to 2014 and do not cover all types of lesions [1]. A working group of 14 national experts in the management of APL associated with CD was formed in January 2017. Work on the development of recommendations took place between February and November 2017 and used the DELPHI methodology. For each clinical situation, the group developed a management decision algorithm based on the international recommendations, French clinical practice recommendations, available publications, and clinical/surgical experience, with graded recommendations (Table 1). The first draft was initially submitted to all group members. A summary of the corrections was made by a panel of 4 members of the group. In November 2017, all 9 decision algorithms were circulated to all members of the French National Society of Coloproctology. At the society's national conference on November 26, 2017, the issues that were not the subject of consensus were put to the vote of the 300 delegates present. These responses were then integrated into the algorithms as "professional agreements" (PA).

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**Table 1** Grades of recommendations

A	Directly based on Level I evidence
B	Directly based on Level II evidence or extrapolated recommendations from Level I evidence
C	Directly based on Level III evidence or extrapolated recommendations from Level I or II evidence
D	Directly based on Level IV evidence or extrapolated recommendations from Level I, II, or III evidence

## Definitions

Mucosal or cutaneous anal ulcerations associated with CD are the primary lesions due to this disease.

In children, CD may not have the same evolution as in adults and the treatment approach may be different. The impact on nutrition and growth greatly influences its management [7].

The clinical presentation is polymorphous, but differs from classical anal fissures in the pitted aspect, prominent margins and inflammatory character of the lesions; and they are sometimes associated with inflammatory markers. Their locations may be non-commissural, occasionally multiple, and readily extend above the dentate line of the lower rectum or below the anal margin or perineum. These primary lesions of Crohn's disease can be graded according to Cardiff's classification as U0 (no lesion), U1 (fissure or superficial ulceration) and U2 (ulcer) [2]. This grading scale established in one specialized center was based on the clinical aspect of the lesion and also on the observed evolution. U2 lesions have the poorest prognosis [2]. The cumulative probability of an AUC at 10 years after the initial diagnosis of CD is greater than 20% [3]. These lesions are an indication of disease severity and are frequently associated with ileal and especially rectal involvement [4, 5]. However, the spontaneous evolution of these lesions is poorly understood because it is rarely described in the literature.

In France, the prevalence of CD-related anal lesions in children has been studied in a population-based cohort analysis of the EPIMAD register [8]. It included 404 children (0–17 years old) followed for more than 2 years (median follow-up 84 months). The prevalence of anal lesions was 9% at the time of diagnosis of CD and 27% at the end of the follow-up period.

The anatomo-clinical description of anal lesions associated with CD can be made using Cardiff's classification [2].

Ulceration is considered to be deep if it exposes the underlying muscle fibers, if there is granulation tissue, or if its margins are raised and inflammatory. It is cavitating if it is deep, decaying and destructive [6].

Cardiff's classification identifies three types of perianal lesions: ulceration, fistula/abscess, and stricture/stenosis, and grades them according to their severity. This is supplemented by an appendix grading the activity of the lesions and describing possible associated lesions.

## Ulcerations and fissures

### Evaluation

AUCs can be painful when they are extensive or cavitating, can be complicated by anal abscesses or fistulae, and potentially lead to sphincter destruction or anal stenosis.

The evaluation of an anal ulceration in the context of Crohn's disease (AUC) can be only be done by a complete proctologic examination including a systematic anoscopy

and if necessary an examination under general anesthesia (GA) if an examination is impossible otherwise.

An magnetic resonance imaging (MRI) evaluation is indicated for AUC with suspected or proven associated suppuration. Grade B

## Treatment

The surgical treatment of an anal fissure, even of a banal presentation, should be avoided during CD that is not in complete and prolonged remission. PA

Even for a classical anal fissure occurring in the context of Crohn's disease, surgical treatment should be avoided, as it could fail to heal, or lead to suppuration or secondary incontinence (PA). Due to the risk of anal incontinence, it is not recommended to perform a sphincterotomy (PA).

Targeted surgeries (resection, fissurectomy, sphincterotomy) have only been reported in very limited, uncontrolled series and these procedures were performed before the era of biotherapy [9–11].

Before initiating medical treatment, one must first rule out abscess or associated complex fistula. If there is the slightest doubt of associated suppuration, an MRI examination with or without a clinical EUA is the strategy of choice for a thorough assessment of the AUC, particularly when there is suspicion of associated AUC.

In a patient with AUC the only surgical treatment recommended is the drainage of any associated anorectal suppuration, abscess or fistula. This must be done before initiating immunosuppressive therapy or biotherapy. Grade B.  
Once drainage is complete, treatment with anti-tumor necrosis factor (TNF) +/- immunosuppressors should be started without delay. EA

The indication for medical treatment of an AUC will depend not only on its symptomatic character, but also and independently of its cavitating/extensive aspect, its evolution and the presence of factors of indicating severity, in particular proctitis, stenosis or suppuration. EA

The goal of treatment is to improve the patient's quality of life and to avoid the occurrence of complications, such as suppuration, sphincter destruction or secondary stenosis.

There is no evidence in the literature to recommend early treatment of AUCs that are at a superficial stage and limited to Cardiff stage UI. However, depending on the overall context, treatment must be early enough to prevent the development of potentially invalidating lesions.

The only medical treatment of AUCs that has proven effectiveness is based on anti-TNF+/- and an immunosuppressor. Grade C

Medical treatment with anti-TNF that induces remission must be continued as maintenance therapy. Grade C

When initiating or restarting anti-TNF in adults, it is advisable to add an immunosuppressor for 6–12 months. Combo-therapy may increase the effectiveness of infliximab and adalimumab. Above all, it reduces the immunogenicity of anti-TNF treatment. It is advisable to immediately put in place the optimal conditions of use of anti-TNFs because, at present, they are the only molecules that have proven effectiveness on APL of CD. EA

To date, there is no study specifically evaluating the efficacy of other biotherapies in the treatment of AUC.

A retrospective study has evaluated the efficacy of infliximab administered by perfusion at 0, 2, and 6 weeks on 27 patients with CD-related anal ulceration, with a short follow-up. At week 8, 48% and at week 24, 50% of patients had healed [12]. In a large retrospective two-center series

( $n = 99$ ) with a follow-up of more than 3 years, a similar rate (42%) of healing of the AUC was observed at 12 weeks after the introduction of infliximab. In the long term (175 weeks on average), 72% (42/94) of the patients no longer presented anal ulceration, with 71% U1 classified lesions healed and 83% U2 classified lesions healed. The combination of infliximab and thiopurines was associated with better long-term healing of cavitating AUCs ( $p = 0.017$ ), in contrast to more superficial anal ulcers whose evolution was not influenced by dual therapy. In 94% of patients who received maintenance treatment, induction-induced remission was maintained [13]. This potential superiority of the combination over monotherapy for CD-related anal ulcers is consistent with that observed in other severe lesions of CD such as luminal ulcerations [14] or anoperineal fistulas [15]. No data are available on the combination of infliximab and methotrexate in the treatment of AUC.

Thiopurines administered alone may possibly have some moderate efficacy on APL associated with CD. Grade C  
Therefore, they are rarely indicated alone, and then only in the case of a single, superficial, limited AUC with few symptoms, in the absence of proctitis and subject to careful clinical monitoring. EA

There are no studies evaluating the effectiveness of thiopurines in the healing of AUC. Only one multicenter open-label study suggested a significant reduction in the risk of occurrence of an anal lesion, including fissure and ulceration, when azathioprine was introduced immediately after the diagnosis of luminal CD, compared to secondary introduction in the event of unfavorable evolution [16].

In children with CD, antibiotics may be proposed to reduce the symptoms of ulceration and also suppurations during CD. Grade C.  
They should not be a substitute for surgical drainage, which has to be associated with the above treatment in case of abscess/fistula. EA

Metronidazole treatment initiated in 53 children in the ‘Ontario cohort’ reduced complaints in 38; two-thirds of children with a fistula or abscess showed a response to the treatment; and the response was comparable in those with ulcerations [17].

In children with this indication, the European Crohn’s and Colitis Organisation (ECCO) group recommends the use of ciprofloxacin or metronidazole antibiotics [18].

In the event of failure of medical treatment in highly symptomatic, severe and disabling AUC, a diversion stoma with or without proctectomy should be considered as a last resort. PA

In small, open or retrospective case series, digestive diversion stoma was found to improve “refractory” Crohn’s APLs [19–23] as well as when taken together in a meta-analysis [24].

However, in the medium and long term, the rate of healing allowing the return of continence was low (20%), and the risk of proctectomy was high (about 40%). The presence of proctitis was an independent factor in the non-restoration of continence. These poor results do not seem to be improved by the addition of anti-TNF therapy [16, 24].

Proctectomy is indicated as a last resort for severe refractory anorectal lesions, after failure of other medical and surgical treatment. While it allows an improvement in the quality of life of patients, it is associated with a risk of about 20% of persistent perineal sinus and the frequency is increased if anoperineal suppuration is present [25] and management is challenging [19, 26].

## Anal or rectal stenosis

### Evaluation

The evaluation of an anal or rectal stenosis must specify the height of its lower verge with respect to the anal margin, its length, its size, its fixed or mobile character under anesthesia, the extent of perirectal fibrous infiltration, its impact on anorectal function, its symptomatic repercussions (Allan score), and its association with other lesions (ulceration, fistulae, abscesses). This assessment should include a clinical examination, possibly under general anesthesia, MRI and endoscopy with biopsies of the stenosis and upstream, possibly following dilation due to the risk of degeneration. PA

The evaluation of anorectal stenosis in CD requires clinical examination, sometimes under anesthesia, endoscopic examination and MRI, to describe the stenosis itself and to identify associated anoperineal lesions whether inflammatory, infectious or dysplastic.

It is recommended to accurately describe the stenosis (its position relative to the anal margin, its length and its size), to evaluate its clinical impact by looking for dyschezia or continence disorders, or using the Perianal Disease Activity Index (PDAI) [27] and to look for other anoperineal lesions (ulceration, fistula, abscess) (Figs. 1, 2).

According to the ECCO consensus, when a radiological assessment of Crohn’s APL is required, it is recommended to perform an MRI examination (Grade B) [28] to complement the clinical examination (under general anesthesia if needed); it is also recommended to carry out an assessment of luminalCd.

Despite the lack of specific epidemiological data on the frequency of stenotic cancers, biopsies are recommended to search for dysplasia or neoplasia.

This assessment is essential because the treatment depends on the characteristics of the stenosis, the existence, or not, of associated perineal disease, and the existence of luminal involvement in CD (activity, dysplasia).

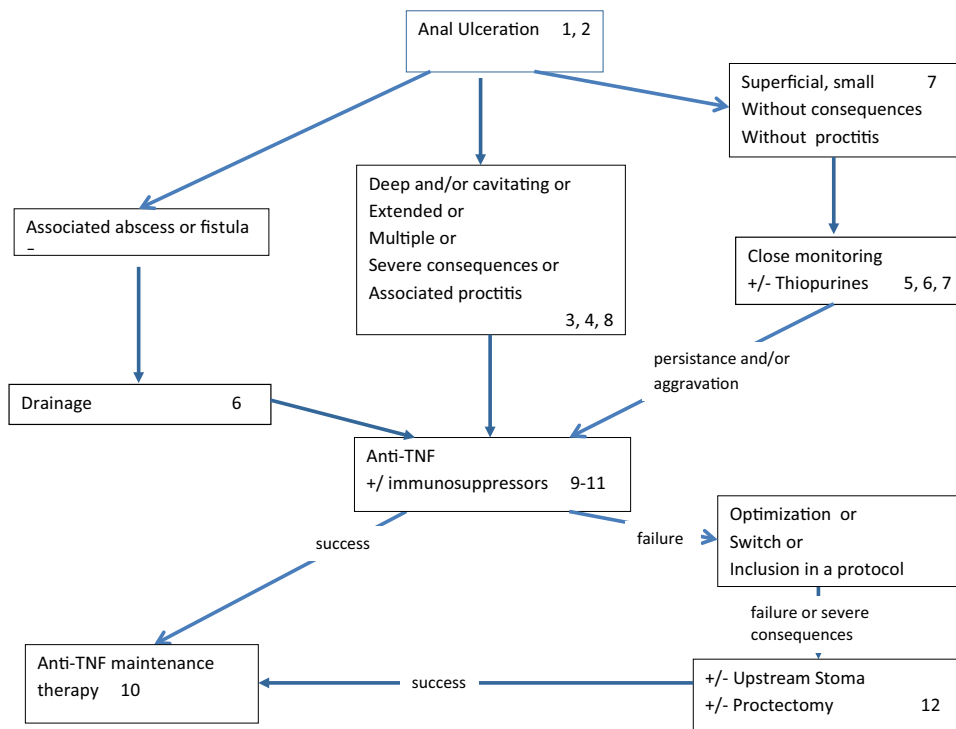
### Treatment

The indication for treatment of an anal or rectal stenosis must take into account the existence of signs of occlusion or of dyschezia, of incontinence and the possibility of performing an endoscopy with biopsies. EA

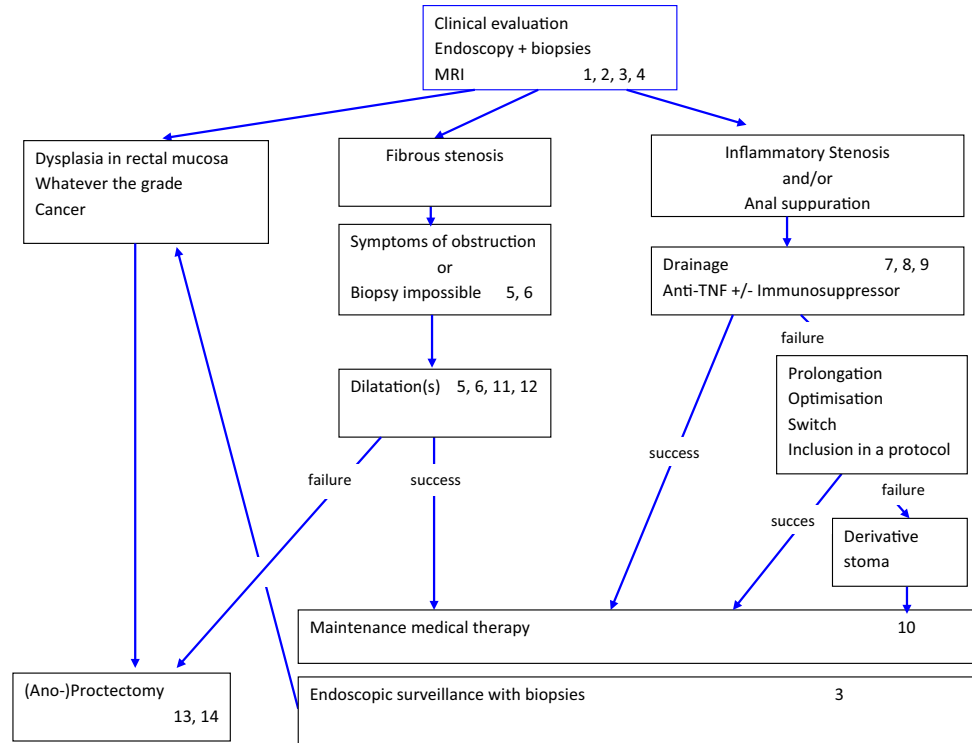
It is recommended to obtain sufficient dilatation, even in the absence of functional signs, to allow monitoring by endoscopic examination so as to detect any dysplasia. EA

The risk associated with the dilatation of an anal or rectal stenosis is the appearance or aggravation of continence disorders. EA

**Fig. 1** Management of anal ulcers associated with Crohn’s disease



**Fig. 2** Management of anorectal stenosis associated with Crohn’s disease



In the case of suppuration associated with anal or rectal stenosis, the treatment of the suppuration must be given priority. Grade C

If a stenosis is associated with fistulising perineal lesions, it is recommended to first treat the suppuration medically and/or surgically, with or without dilatation [29]. This intervention should be guided by the MRI data. In case of complex and recurrent suppuration, it may be necessary to propose a temporary derivative stoma.

The first line treatment of an inflammatory anal or rectal stenosis should be medical. PA

Type 1 inflammatory anorectal stenosis (Cardiff classification) should be treated medically in the same way as luminal CD [2].

The recommended first line treatment of an isolated fibrous stenosis is dilatation of the stenosis. PA

Cardiff type 2 stenosis [2] should be treated using a simple minimally invasive procedure [29]. The dilatation consists of increasing the diameter of the anus or rectum, by a mechanical release of the fibrosis. It should be performed in an operating room under general or locoregional anesthesia, following a thorough anorectal and perineal examination. It may be necessary to repeat the dilatation to obtain a sufficiently large passage.

The diameter must be adapted to the risk of continence disorders, signs of obstruction or occlusion and be sufficient to perform an endoscopy with biopsies at and above the stenosis.

In the event of failure of conservative treatments of a stenosis that is tight, symptomatic and/or impedes any endoscopic exploration, an anoproctectomy with resection of the mesorectum may be proposed. EA

In case of low rectal stenosis, in the presence of dysplastic lesions (whatever the stage) of the colonic mucosa, it is necessary to consider an anoproctectomy with excision of the mesorectum (due to concerns about carcinogenesis).

## Conclusions

Literature about treatment of anal ulceration and anorectal stenosis associated with CD is scarce. These recommendations add expert and professional agreement to available demonstrated data and, therefore, can help specialists to discuss optimal treatment for these difficult patients.

The only medical treatment of AUCs that has proven effectiveness is based on anti-TNF+/- and an immunosuppressor. Medical treatment with anti-TNF that induces remission must be continued as maintenance therapy.

In case of anal or rectal stenosis, thorough assessment is necessary, including a clinical examination, possibly under general anesthesia, MRI and endoscopy with biopsies of the stenosis and upstream, possibly following dilation due to the risk of degeneration. The first-line treatment of an inflammatory anal or rectal stenosis should be medical. The recommended first-line treatment of an isolated fibrous stenosis is dilatation of the stenosis.

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## Compliance with ethical standards

**Conflict of interest** Bouchard D: Abbvie, Takeda (consultant and lecture fees), Pigot F: Abbvie (lecture fees), Abramowitz L: Abbvie, Takeda (research fees), Faucheron JL: AMI, Medtronic (consultant, research fees), Laharie D: Abbvie, Janssen, MSD, Takeda (board, lectures fees), Siproudhis L: Abbvie, Ferring, MSD, Takeda (teaching sessions, consultant, research fees). The authors declare that they have no conflict of interest.

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