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Pruritus Ani: the neglected stepchild of coloproctology

State of the Art and Management

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ABSTRACT

Pruritus ani (PA) is a chronic unpleasant itching and/or burning sensation in the perianal region that affects up to 5% of the population. It can be secondary or idiopathic, and it can dramatically affect the quality of life of the patient. A substantial number of patients do not respond adequately to the majority of treatments available and the pathophysiology of PA has not yet been completely elucidated.

A multidisciplinary approach aimed at detecting and addressing any possible causes is paramount in secondary PA. In chronic indeterminate PA in patients more than 50 years of age, a colonoscopy may be indicated to rule out a tumour.

In mild-moderate idiopathic PA, self-care measures, including administration of a short cycle of a topical steroid and an attempt to exclude causative items from the diet with the goal of breaking the vicious cycle (itching-scratching-itching), may be effective. In cases of severe unresponsiveness PA, intradermal injection of methylene blue in the perianal area represents a reasonable option with a high rate of success in the short term and with an acceptable number of complications.

Unfortunately, no international guidelines or consensus conference exists, and most of the literature available on this topic is anecdotal or based on small case series or on a few small randomized trials.

INTRODUCTION

Pruritus ani (PA) is a relatively common condition characterized by *a chronic unpleasant itching* and/or *burning sensation in the perianal region*. It can affect up to 5% of the population and has a 4:1 male predominance. PA most commonly presents between 40 and 60 years of age and can result in significant discomfort and a worse quality of life for the patient.

Because most individuals do not consult a doctor and large population-based studies are rare, the true prevalence of PA is probably underreported and the disorder is likely undertreated. In a recent survey of general practitioners in France [1] regarding the prevalence of proctological symptoms in their patients, PA was the third most common symptom reported (22%) after bleeding and pain.

PA can be either **secondary** or **idiopathic** (primary). Idiopathic PA accounts for 25% to 90% of cases and often represents a clinical challenge due to the lack of a long-lasting effective therapy along with a high rate of recurrence after seemingly successful treatment.

Our understanding of the pathological features and management of the disorder is based on case reports/case series, a few randomized trials on a small number of patients and some excellent reviews that have attempted to unify the literature. Currently, no international guidelines or multidisciplinary consensus conferences are available.

For these reasons, PA has been defined as “the least researched everyday symptom from which humans suffer” [2] or as a “condition that eludes all attempts at cure” [3]. More than 100 causes of PA have been reported in the literature.

In 1966, Caplan [4] reported that perianal skin is more prone to develop itching than other body areas. Different factors (such as soiling, inflammation, and infection) may stimulate below the pain threshold specific superficial unmyelinated C-fibres in the perianal area, producing an itching sensation. The feedback from scratching can cause excoriation and inflammation leading to a vicious cycle. Recognizing and avoiding all irritating factors, along with breaking this cycle, is the key to successful treatment.

DIAGNOSIS

SECONDARY FORMS

A step-by-step approach to obtain a broad differential diagnosis is crucial to discover an underlying pathology and properly treat it (**Figure 1**). An incomplete diagnostic assessment could overrate the idiopathic forms (reported to be up to 90% by some authors) and increase the treatment failure rate. For children, a shorter diagnostic approach is reasonable, with the aim of identifying one of the two most common causes of PA in this group: infections and atopic dermatitis.

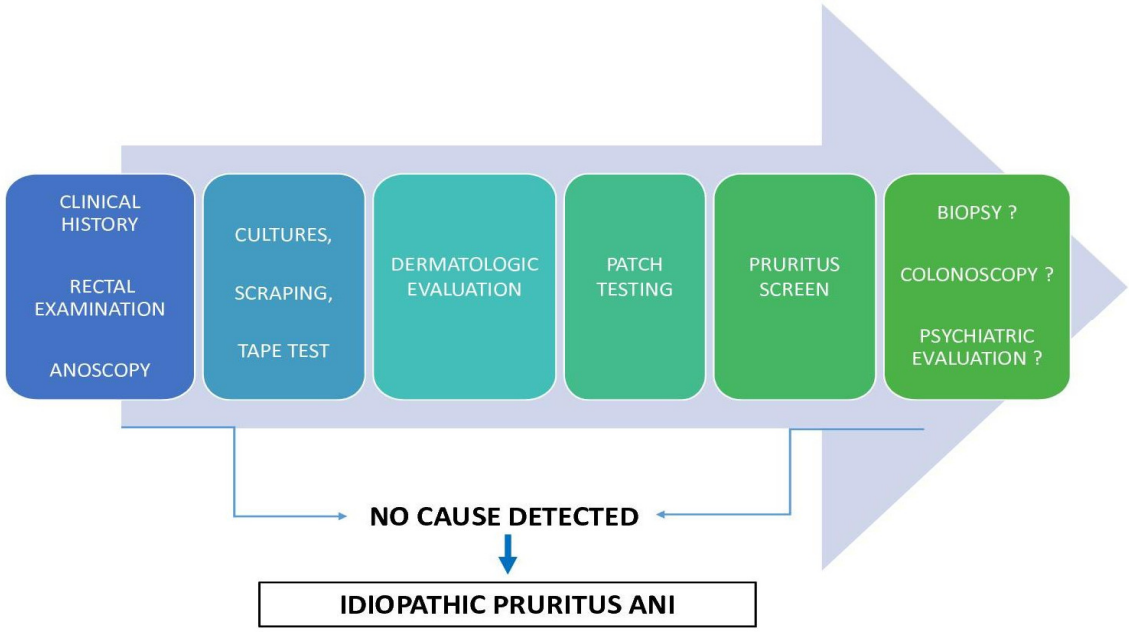

Figure 1. Diagnostic approach in pruritus ani.

1. Anorectal Pathology

Anorectal disease accounts for more the 50% of all causes of PA [5]. High-grade haemorrhoids, anal fissure, anal fistula, and rectal prolapse can cause perianal moisture that can lead to PA. Ileoanal or coloanal anastomosis and restorative proctocolectomy weaken the anal sphincters and lead to removal of the rectum with frequent stools.

A thorough history and a physical examination including digital rectal examination (DRE) and anoscopy are sufficient for a diagnosis in most cases.

Anorectal conditions can lead to PA by faecal contamination, inadequate cleanliness and/or occult seepage in the perianal region. Any suspected area should be biopsied to rule out an anal neoplasm, such as squamous cell carcinoma and Paget's or Bowen's disease, which are associated with PA in half of the cases.

2. Infections

Bacterial, viral and fungal infections are well-known causes of PA, although in "everyday practice", the role of infections, especially in adults, appears to be less important than what is stated in the literature.

Pinworm infestation (Enterobius vermicularis) *is the most frequent cause of PA in children* [6] . The eggs laid on the perianal skin by the adult parasites emerging from the anal canal at night produce an inflammatory reaction. A "tape test" administered when the child wakes on three consecutive mornings is the key to the diagnosis. *B-haemolytic Streptococcus* infection may result in

perianal streptococcal dermatitis (PSD) most frequently in children [7], but it can be diagnosed at all ages [8].

While dermatophytes are always pathogenic and should be treated, the role of *Candida albicans* is still controversial. Some authors [9] reported that *Candida albicans* accounts for up to 15% of cases of PA, while others [10] failed to demonstrate a relationship between *Candida albicans* and PA when cultures of affected patients were compared with asymptomatic controls. A positive culture for *Candida* should only be treated in patients with diabetes, undergoing steroid therapy or taking systemic antibiotics.

Perianal warts, herpes infections, gonorrhoea, *Chlamydia trachomatis*, scabies and *Molluscum contagiosum* may occur in association with PA. Erythrasma caused by *Corynebacterium minutissimum* can easily be detected using a Wood's lamp upon referral to a dermatologist, which is the third reasonable step once the previous causes have been excluded.

A stool test, a swab of the ulcerated lesion, a scraping and, in some cases, a skin biopsy may be indicated for a diagnosis. The swabs must be taken before DRE because of the potential bactericidal activity of water-soluble lubricants [5].

3. Dermatologic Disease and Contact Dermatitis

A consultation with a dermatologist serves two purposes: diagnosis of dermatologic skin conditions (including undiagnosed infections) and investigation of possible contact dermatitis.

Psoriasis is the most common dermatologic cause of PA. It may occur as an isolated lesion in the perianal area and can have a nontypical appearance due to maceration. Lichen sclerosis, lichen planus, and seborrheic dermatitis are other possible causes [11, 12].

A large number of sensitizing agents can cause contact dermatitis and associated PA[13,14].These include local anaesthetics, topical antibiotics, antiseptics, nickel and products such as parabens and methyldibromoglutaronitrile, which are often included in over-the-counter products (such as creams, soaps, wet wipes, and sanitary towels) used by patients to relieve their itch.

In the most recent study published about the role of patch testing in PA [15], methylchloroisothiazoline/methylisothiazoline, which is often included in wet wipes and sanitary towels, was found to be the most common positive allergen.

Patch testing is paramount to detecting a specific allergen to be avoided by the patient.

4. Exclusion of Mental Disorders

Although some case reports [16, 17, 18] anecdotally describe the resolution of PA after psychiatric therapy (drugs or hypnosis), most patients complaining of PA do not exhibit psychiatric features. Smith et al. [19] in a study of 25 patients affected by PA did not find any deviation on the clinical scale using the MMPI (Minnesota Multiphasic Personality Inventory). Similarly, Laurent et al. [20] did not find any significant differences in the psychological profiles of 17 patients affected by idiopathic PA compared with a control group of 28 patients with secondary PA. Obsessive-compulsive disorder, stress, and fatigue can exacerbate the symptoms and should not be ignored. Therefore, psychiatric evaluation and the use of related therapy

should be considered on an individual basis.

5. Consideration of Systemic Diseases as possible causes

Systemic diseases, such as iron deficiency, uraemia, hepatic/biliary disease, and malignancy (e.g., lymphoma and myeloma), can cause generalized itch, sometimes mainly expressed in the perianal region. A "**pruritus screen**" including blood tests and chest radiographs (**Table 1**) represents the last diagnostic step in the case of long-lasting symptoms or an earlier step if the itch occurs in other areas of the body.

PRURITUS SCREEN
BLOOD TESTS
FBC (Full Blood Count)
Ferritin / serum Fe / % sat / TIBC
U&E (Urea and electrolytes)
ESR
LFT (Liver Functional Tests)
TFT (Thyroid Function Tests)
Glucose
Calcium
Serum electrophoresis
CHEST X-RAYS

Table 1. Pruritus screen to detect systemic diseases as underlying causes of PA.

6. Some caveats

In the case of a long history of "idiopathic" PA *in patients aged >50 years*, a **colonoscopy** is mandatory: villous adenomas/colorectal cancer can cause overt seepage, and PA can present as an initial symptom [21].

In woman, vaginal discharge or urinary incontinence can also produce itching in the perianal area; the presence of concomitant pruritus vulvae and/or urogynecological problems should be investigated during the patient interview.

IDIOPATHIC PRURITUS ANI

The pathogenesis of idiopathic PA is multifactorial and not yet fully understood. Faecal soiling, food irritants and excessive cleaning are thought to be the major contributing factors.

Occult faecal leakage onto the perianal skin can cause irritation and itching. Patients with idiopathic PA show a greater and prolonged rectoanal inhibitory reflex and exhibit reduced anal pressure during rectal balloon distension [22]. After a saline infusion test, leakage (600 ml) occurred earlier in the idiopathic PA group than in the control group (1300 ml) [23].

Potentially implicated **foods** are listed in **Table 2**. Coffee consumption lowers the resting anal pressure and may increase the chance of leakage [24]. There is no definitive evidence regarding the exact mechanisms by which the other foods affect PA. However, changes in the diet in an attempt to exclude these foods have proven successful for minimizing symptoms.

DIETARY FACTORS IN PA
Coffee (caffeinated and decaffeinated) and tea
Chocolate
Milk and dairy products
Tomatoes
Carbonated drinks
Citrus fruits
Alcohol (beer and wine)
Peanuts
Popcorn
Grapes
Prunes
Figs

Table 2. Dietary factors implicated in PA.

Excessive cleaning may damage the skin, increase the chance of local irritation and contribute to the "itch-scratch" cycle. Perianal skin is more responsive to irritants than are other skin areas, as Caplan et al. [4] showed in the classic faecal patch test study.

Finally, obesity, hirsutism, excessive sweating and tight clothes, particularly those made of synthetic material, increase the moisture in the perianal region and worsen the symptoms.

MANAGEMENT

PA is a distressing condition. Treatment should be individualized and based on the aetiology, severity of symptoms and impact on the quality of life of the patient.

In **secondary PA**, *any underlying cause should be treated*. Surgery may be necessary for anorectal conditions, such as prolapsing haemorrhoids, anal fissure, anal fistula, and rectal prolapse. Skin tags can trap faecal residue and prevent adequate cleaning in the perianal area. Although some authors [25] consider skin tag excision effective in the treatment of PA, the only randomized trial comparing excision versus expectant management failed to demonstrate any benefit from surgery [26]. Therefore, the surgical removal of skin tags should be considered on an individual basis, and the patient should be informed about the chance that they might continue to have symptoms.

Any causative infections or dermatologic conditions must be treated. In the case of contact dermatitis, avoiding the inciting agent can dramatically resolve the symptoms. Silvestri et al.[27] reported the case of a patient who consumed peanut butter daily and, after a patch testing positive for nickel sulphate, definitively resolved prolonged PA by dietary nickel restriction. In another case, Dasan et al. [28] described complete resolution of PA in a patient with positive patch testing to an ingredient in the patient's wife's shampoo. All symptoms disappeared after cessation of its use in the shared bathtub.

In **idiopathic PA**, the *reassurance of the patient* regarding the absence of malignancy and the offer to view the therapy as a long-term course instead of a single treatment are paramount.

Any excessive cleaning habits must be discouraged. The patient should use a warm sitz bath or bidet without any soap or detergent, avoid scented toilet tissue and preferably gently dry the skin with a cotton towel or hair dryer. *Loose cotton underwear* aids in transpiration and prevents moisture accumulation. A *barrier cream*, such as zinc oxide, Calmoseptine ® (menthol + zinc oxide) or vitamin E ointment (VEA Olio ®), can provide some relief in the case of excoriated skin.

For loose stools and diarrhoea, a *bulking agent* and *loperamide* can reduce soiling and decrease itching in the perianal area. *Oral antihistamines* (e.g., hydroxyzine) *at bedtime* may be required to reduce nocturnal scratching (**Figure 2**).

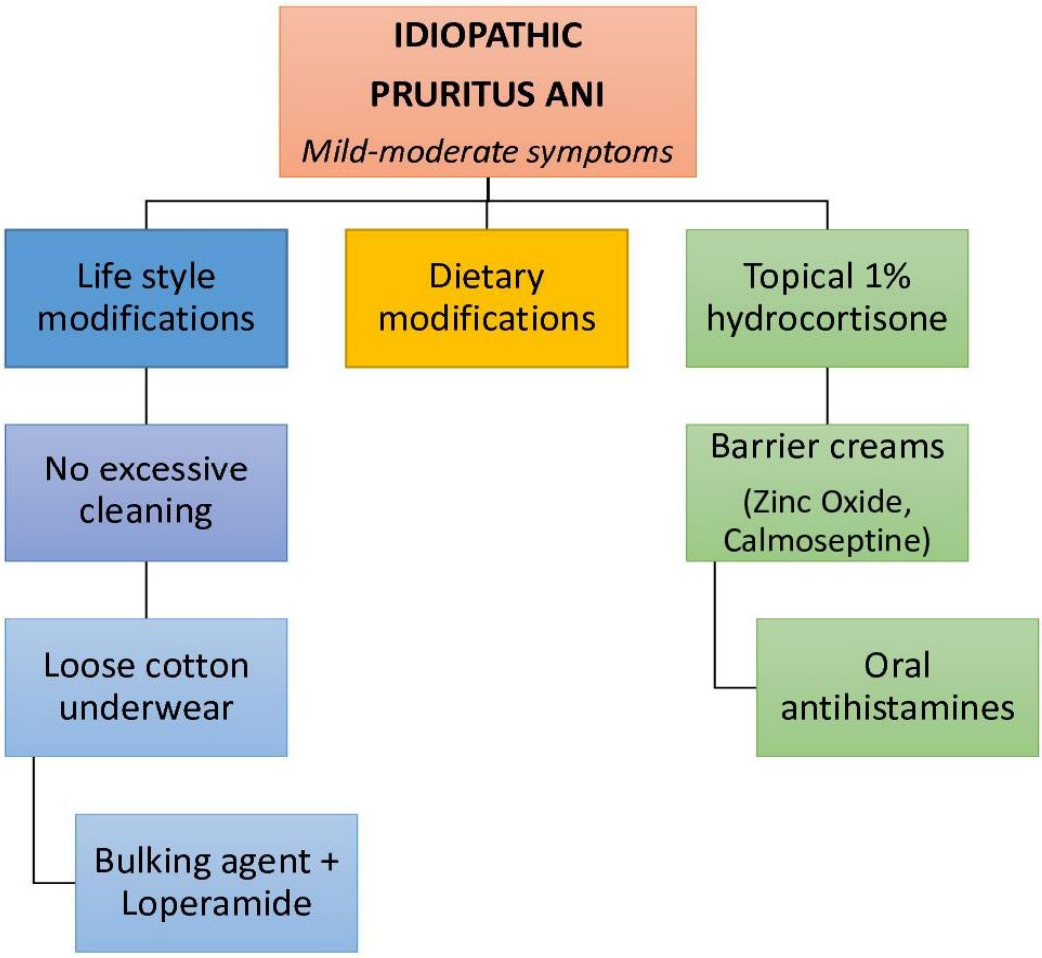

Figure 2. Treatment of mild-moderate idiopathic pruritus ani.

These measures are also useful for treating secondary PA during the time between diagnosis and definitive treatment.

The next step is to *completely exclude from the diet* for 2-3 weeks *potential dietary factors* contributing to PA to determine whether there is any associated symptomatic relief [29]. Any suspected food should be gradually reintroduced to determine the threshold above which the symptoms recur.

In mild-moderate cases not respondent to previous treatment, a *short course of a low-potency topical steroid* (1% hydrocortisone) twice daily is usually effective. There is no consensus on the exact duration of treatment, but most authors [5, 11, 30, 31] recommend a maximum of 8-12 weeks to avoid the risk of atrophic skin and superinfection. Ointments are better than creams because they have fewer preservatives and because they make the skin less prone to atrophy [32].

Some patients have intractable perianal itch despite maximum medical therapy; this is defined as **severe PA**. *Sedatives and gloves worn at night* should be suggested to avoid nocturnal scratching.

In a nerve conduction study of 18 patients with idiopathic PA, Cohen et al. [33] found that 80% (16/18) had a lumbosacral radiculopathy. These patients showed significant improvements in itch scores when treated with paravertebral injections of steroid and lignocaine. The authors therefore recommended that all patients with idiopathic PA be screened for radiculopathy. These data should be considered mainly in older patients with chronic back pain and unsatisfactory therapeutic responses, although the inadequate sample size and absence of other studies with similar results renders these conclusions not generalizable.

Capsaicin, tacrolimus and methylene blue injection are the last options available (**Figure 3**).

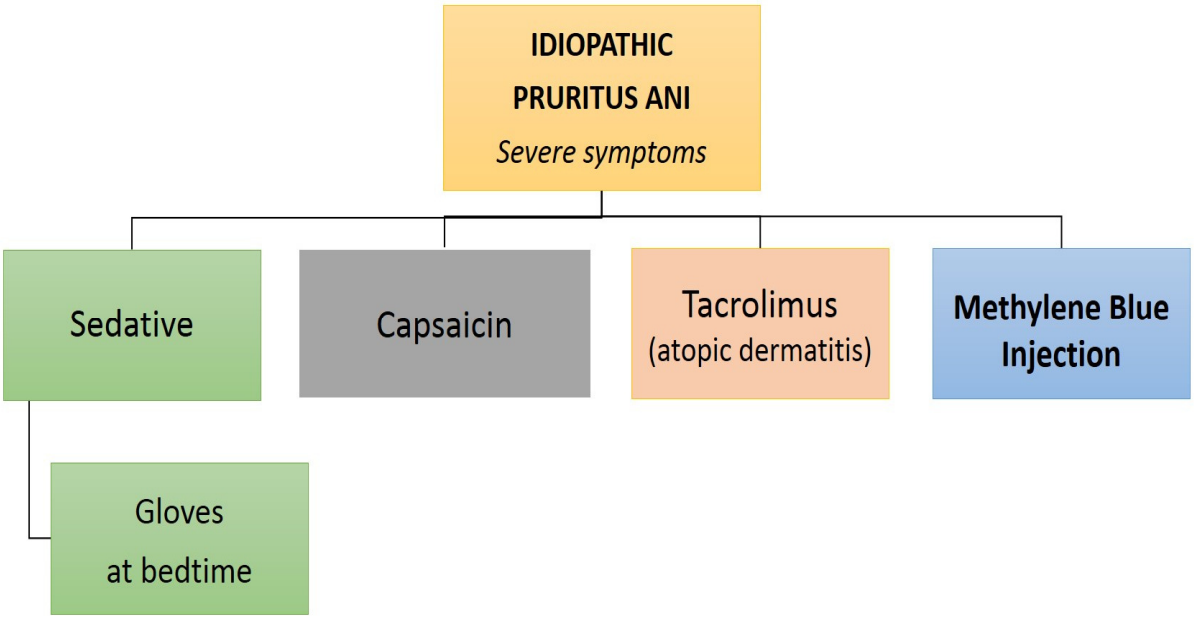

Figure 3. Treatment of severe idiopathic pruritus ani.

Lisey et al. [34] in a randomized, placebo-controlled crossover trial compared 0.006% *topical capsaicin* (an active ingredient in chili peppers) with placebo in a group of 44 patients with chronic PA. A total of 70% of patients (31) experienced symptom relief, 10% of patients (4) dropped out because of side effects and 93.5% of responders required application every day, on average, to maintain symptom relief. However, the small sample size, the occurrence of some methodological problems in the study and the poor results reported anecdotally in children suggest that these results should be interpreted with caution [35].

Tacrolimus, an immunomodulator, has been evaluated in two randomized trials. The underlying mechanisms of its ability to reduce PA are unclear and probably multifactorial. Suys et al. [36] reported symptom reduction in 68% of 21 patients with idiopathic PA after 2 weeks of treatment with tacrolimus 0.1% ointment compared with placebo. In another study [37] of 32 patients with PA and atopic dermatitis, a statistically significant decrease in all recorded scores was observed in patients treated with 0.03% tacrolimus ointment compared to those who received the placebo treatment. The treatment is usually well tolerated, and a recent meta-analysis [38] found no evidence to support the possible increased risk of malignancies or skin atrophy with prolonged use. A 4-week trial using patients with atopic dermatitis and severe symptoms should be considered.

Intradermal injection of methylene blue ("**anal tattooing**") is the most effective therapy for the treatment of chronic severe PA. Methylene blue temporarily destroys nerve endings in the perianal area [39], reducing the itching and breaking the "itch-scratch" cycle.

All studies [39, 40, 41, 42] report a high short-term success rate (65-100%), albeit only in small case series and in the absence of any randomized trial. The original technique has been modified [40] to avoid the risks of infection and skin necrosis that were reported in the first series. It now involves the intradermal injection of a 1% methylene blue solution, mixing 8-10 ml of 2% methylene blue with an equal volume of local anaesthetic (e.g., 2% lidocaine) or a 50/50 solution of local anaesthetic + saline. The perianal area is then infiltrated up to the dentate line using a 22-gauge needle.

Transient hypo-aesthesia and/or temporary faecal incontinence may occur, and the patient should be informed of this as well as of the risk of skin necrosis. The pigmentation of the skin usually disappears in 4-6 weeks after the procedure, and disappearance any sooner suggests that the technique used was incorrect. In most patients (up to 80%), symptoms recur after one year and are often less severe; conservative treatment or repeated injection can be considered on an individual basis.

CONCLUSION

PA can significantly affect a patient's quality of life. A multidisciplinary approach is necessary to identify and properly treat all secondary causes. Colonoscopy is mandatory in patients with chronic PA who are over 50 years of age. In idiopathic PA, patients should be informed about the absence of life-threatening risks and the effectiveness of self-care measures, including a short period of topical steroids, for treating mild-moderate symptoms. In patients with severe symptoms, capsaicin, tacrolimus or intradermal methylene blue injection should be considered.

Robust, well-designed studies as well as a multidisciplinary consensus conference would be useful to address the lack of evidence still present in this field.

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