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Dermatology and Pruritus Ani

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Key Concepts

- Pruritus ani is a dermatologic condition characterized by itching or burning at the perianal area.
- Pruritus ani can be either primary (idiopathic) or secondary.
- Primary pruritus ani is the most common form of pruritus ani. The most common causes of secondary pruritus ani are local irritants and common anorectal conditions.
- All chronic perianal dermatoses require a detailed history and physical exam, including all past diagnostic tests and forms of treatment.
- The single most valuable diagnostic test in patients with recurrent or ongoing pruritus ani is skin biopsy.
- Treatment options for pruritus ani are numerous. Management should focus on the underlying or suspected etiology, following an evidenced-based stepwise diagnostic and treatment algorithm.

Introduction

Dermatologic diseases of the anus are a group of inflammatory, infectious, and neoplastic conditions that are difficult to diagnose and challenging to manage. While patients often do not openly discuss the associated symptoms with medical professionals, these conditions can often have a significant impact on their quality of life. Patients presenting with anal dermatologic disease are often seen by a diverse group of providers, including general practitioners, gastroenterologists, dermatologists, and colorectal surgeons. Some providers such as primary care physicians may encounter these conditions less commonly, thus making efficient and evidence-based treatment strategies highly important.

In 1660, Samuel Hafenreffer defined "itch" as "an unpleasant sensation that elicits the desire or reflex to scratch" [1]. More specifically, pruritus ani is defined as a dermatologic condition characterized by persistent and unpleasant itching or burning sensation in the perianal region [2]. The incidence of pruritus ani is estimated to range from 1 to 5 % in the general population, with men being affected more than women in a 4:1 ratio and most commonly diagnosed in the fourth–sixth decades of life [3–5].

Pruritus ani can be classified into primary or idiopathic (accounting for 50–90 % of cases) and secondary [6]. It may be caused by a wide spectrum of conditions, among which perianal eczema is probably the most common. Because pruritus ani often has a multifactorial etiology and high chronicity, most patients have symptoms for many years, as well as a long list of prescribed or over-the-counter treatments. Appropriate management can be difficult and requires a detailed evaluation in search for its etiology.

Pathophysiology of Perianal Signs and Symptoms

The sensation of itch is elicited as a surface phenomenon mediated by nonmyelinated C-fibers in the epidermis and subdermis and can be also classified as pruritoceptive (C-fiber mediated), neuropathic (i.e., after herpes zoster infection), and central or neurogenic. Itch has long been considered as a sub-modality of pain. The intensity hypothesis postulates that neurons are activated by both painful and pruritogenic stimuli, but weaker activation of nociceptive receptors can also result in itch [7]. Recent evidence suggests that the overall neurophysiology of itch is much more complex than initially thought. For example, when algogens are applied topically in lower concentrations, they typically result in low-intensity pain and not pruritus [8].

Microneurography experiments conducted by Schmelz et al. [9] identified afferent C-nerve fibers that were histamine sensitive but insensitive to mechanical stimuli. These findings support the labeled line theory of pruritus, which hypothesizes that discrete and mutually exclusive afferent

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fibers are able to detect either itch or pain [10]. The stimulation of these histamine-sensitive C-nerve fibers demonstrates a central response in a subset of spinothalamic tract neurons [11]. In contrast, subdermally injected histamine-induced pruritus has been shown to activate multiple sites in the brain, overall indicating that itch is a multidimensional sensation, and there is not a single neurologic itch center [12].

Biochemically, histamine, kallikrein, bradykinin, papain, and trypsin can experimentally and individually produce itching. This may explain the lack of effectiveness of antihistamine medications against itching. While multiple itch mediators have been identified, the antagonism of these mediators produces varied clinical results (Table 18-1). This strongly suggests that specific neuronal pathways are involved at both peripheral and central levels in mediating itch.

Scratching is thought to produce inadequate feedback to inhibit further itching. Persistent scratching causes skin trauma, which is an additional stimulus for itching and additional scratching; therefore, this can lead to a chronic vicious cycle. Substituting scratching for other stimuli such as heat, cold, pain, or stinging by applying alcohol or pepper extract (capsaicin) may cause inhibitory feedback and then can decrease the urge to scratch.

Table 18-1. Itch mediators and corresponding antipruritic agents

Itch mediator	Antipruritic agent
Histamine	Antihistamines
Acetylcholine	Doxepin (mainly antihistaminic mechanism)
Serotonin	Paroxetine, fluoxetine (SSRIs)
	Mirtazapine (serotonin inverse agonist)
	Ondansetron (5HT3 antagonist)
Opioids	Naloxone, naltrexone (μ-receptor antagonists)
	Nalfurafine, butorphanol (kappa-receptor agonists)
Leukotrienes	Zafirlukast, zileuton
Prostaglandins	NSAIDs
Substance P	Aprepitant
TRPV1	Capsaicin
TRPM8	Menthol
TNF-alpha	Thalidomide
GABA	Gabapentin, pregabalin

SSRI selective serotonin reuptake inhibitor, *TRPV1* transient receptor potential vanilloid 1, *TRPM8* transient receptor potential melastatin 8, *TNF* tumor necrosis factor, *GABA* gamma-aminobutyric acid, *NSAIDs* nonsteroidal anti-inflammatory drugs, *5HT* 5-hydroxytryptamine

Itching associated with healing is also common after the inflammatory response caused by common anorectal conditions (i.e., fissure and hemorrhoids), as well as after anorectal operations and trauma. The release of histamine and various kinins and prostaglandins is a contributing factor in this situation; therefore, antihistamines, topical anti-inflammatory agents (steroids), and topical anesthetics have shown beneficial effects in these patients [13].

The complexity of the neurophysiological mechanisms causing pruritus as well as the extensive range of peripheral as well as central mediators of pruritus suggests that an effective antipruritic strategy would require a diverse approach.

Etiology and Contributing Factors

Although the overall differential diagnosis of anal dermatoses includes a long list of inflammatory, infectious, sexually transmitted, and neoplastic diseases, in this section, we will focus on the most common primary and secondary etiologies. Proposed etiologies of primary or idiopathic pruritus ani include a variety of associated factors, including anatomic, dietary, hygienic, psychogenic, local irritants and medications (Table 18-2). In many cases, both primary and secondary etiologies coincide, but a careful history and full physical examination will help elucidate the most significant contributing factor. For example, a patient with pruritus ani may present with irritable bowel syndrome, diarrhea, and fecal incontinence. Both primary and secondary etiologies in this patient may include fecal contamination, anal leakage, anxiety, dietary, and hygiene; and some of these may be directly related to one another. One must therefore individualize each case and focus on the most significant contributing factor for that patient taking into consideration the overlap of different etiologies. The causes of secondary pruritus ani can be divided into several broad categories: infectious, dermatologic, systemic disease and anorectal causes (Table 18-3) [3, 4].

In the absence of a primary cutaneous disorder, pruritus ani is thought to have two probable causes: (1) irritation from mucus, fecal material, or other perineal moisture (such as urine in an elderly patient with urinary incontinence) and (2) nerve impingement in the sacral region that causes a neuropathic itch or notalgia paresthetica. While there is good

Table 18-2. Proposed etiologies of primary or idiopathic pruritus ani

Anatomic factors	Obesity, deep clefts, hirsutism, tight clothing
Diet	Coffee (including decaffeinated), chocolate, spicy and heavily condimented foods, citrus fruits, tomatoes, beer, dairy products, vitamin A and D deficiencies, fat substitutes, consumption of large volumes of liquids
Personal hygiene	Poor cleansing habits, excessive perianal hygiene causing trauma
Local irritants	Fecal contamination, moisture, soaps, perfumes, topical medications, toilet paper, wet wipes, alcohol, witch hazel
Drugs	Quinidine, colchicine, IV steroids
Psychogenic	Anxiety, neurosis, psychosis, neurodermatitis, neuropathy, "itch syndromes"

Modified from Stamos MJ, Hicks TC, Pruritus ani: diagnosis and treatment. In: Perspectives in Colon and Rectal Surgery, 1998;11(1):1–20. Thieme Medical Publishers [17]

Table 18-3. Causes of secondary pruritus ani

Infectious
Bacterial
Fungal/yeast
Viral
Parasitic
Dermatologic
Psoriasis
Lichen planus, lichen simplex chronicus
Lichen sclerosus
Contact dermatitis
Atopic dermatitis
Local malignancy (squamous cell carcinoma, Paget's and Bowen's disease)
Systemic disease
Diabetes mellitus
Leukemia, lymphoma, polycythemia vera
Liver disease (jaundice)
Chronic renal failure
Thyroid disorders
Colorectal and anal causes
Hemorrhoids (internal and external)
Rectal prolapse (mucosal and full thickness)
Fissure
Fistula-in-ano
Diarrhea (infectious, inflammatory bowel disease, irritable bowel syndrome)
Secreting villous tumors
Other
Radiation dermatitis
Fecal incontinence and anal leakage
Gynecologic conditions (pruritus vulvae, vaginosis, vaginal discharge)

evidence supporting fecal contamination as a cause of anal pruritus, this seems to produce more of an irritant effect rather than an allergic effect [14]. The perianal skin also seems to be more susceptible to fecal contamination as a cause of perianal skin irritation compared to other sites of the body [14]. Anal leakage alone is frequently associated with anal pruritus, and this has been correlated with a pronounced anal inhibitory reflex in patients with pruritus ani [15]. Anxiety, stress, and fatigue, as well as personality, coping skills, and obsessive-compulsive disorders, probably play a role in the exacerbation of pruritus ani [16].

Irritants

Pruritus ani can result from several products including lanolin, neomycin, parabens, topical anesthetics from the "caine" family, and certain toilet papers [18]. Bowyer and McColl [19] studied 200 consecutive patients with pruritus ani and found that topical local anesthetics were the most commonly found causative factor. The enzymes responsible for perianal skin irritation from fecal contamination include lipase, elastase, and chymotrypsin [20]. Further skin irritation is often exacerbated by multiple and diverse treatment attempts and excessive hygiene measures. This allows for sensitization of the perianal area, which may then be followed by allergic contact dermatitis or perianal eczema.

There are six common foods that often are associated with and thought to cause perianal irritation and pruritus: coffee, tea, cola, beer, chocolate, and tomato (ketchup). In some cases, total elimination will result in remission of itching in 2 weeks [21]. After a 2-week elimination period, foods may be reintroduced to determine the association and potentially the threshold exposure with the appearance of symptoms.

Steroid-Inducing Itching

Although anogenital itching has been reported with both topical and systemic steroids, it commonly occurs as a rebound phenomenon after withdrawal of steroids [22, 23]. Application of topical steroids for as little as 2 weeks can produce acute dermatitis resembling that seen with a blister that has been unroofed and exposed to air [24]. Steroids should only be used to achieve specific effects to the anogenital area. The potency and dosing of steroids should be tapered in a planned fashion with the goal of eliminating steroids altogether from a maintenance regimen. Allergic contact dermatitis to topically applied steroids has been well documented and is class specific. Switching to desoximetasone (a less commonly used agent in steroid class) may be a solution, but the ideal solution would be elimination of all steroids. Calcineurin inhibitors (tacrolimus and pimecrolimus) offer excellent anti-inflammatory effect without many of these steroidal side effects.

Infectious

Perianal infections associated with pruritus can be bacterial, viral, fungal, or parasitic in origin. Overall, infections have been commonly described as rare causes of pruritus ani [25]. However, emerging data demonstrates that fungal infections may be more prevalent in patients with pruritus ani than once thought [26].

Common bacterial causes include beta-hemolytic *streptococci*, *Staphylococcus aureus*, and *Corynebacterium minutissimum* [27], with beta-hemolytic *streptococcus* being the leading cause of perianal dermatitis in children [28]. *Staphylococcus aureus* perianal infections are more commonly reported in the adult population and typically present as a refractory and prolong dermatitis [29]. Erythrasma, a superficial infection of the intertriginous skin caused by *Corynebacterium minutissimum*, has been reported to cause up to 18 % of cases of pruritus ani in warm climates [27].

Fungal infections may account for 10–43 % of secondary infectious pruritus ani cases [4, 26, 27]. *Candida albicans* is the most common fungi identified in patients with pruritus ani [26, 30]. *Candida*, however, often colonizes the skin and

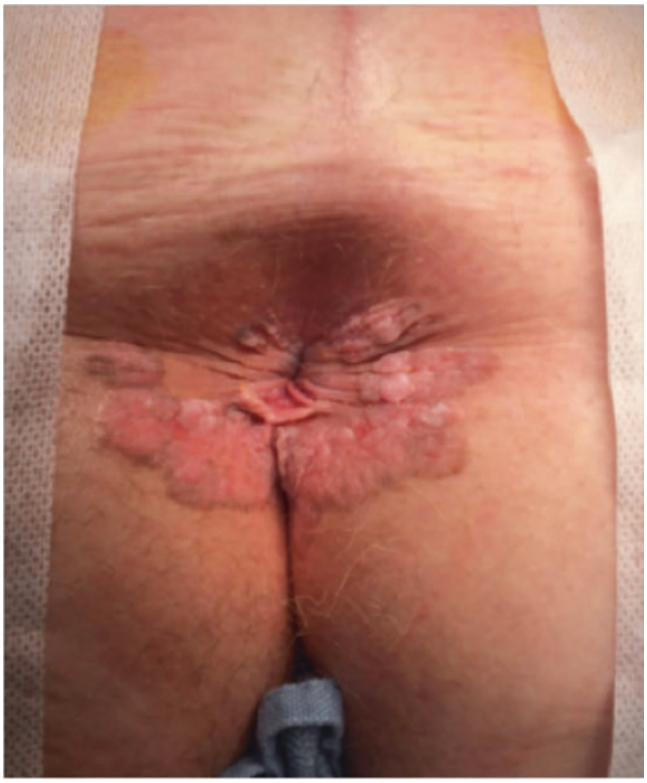

FIGURE 18-1. Patient with external anal condyloma acuminata and perianal fungal infection that presented with anal pruritus. Condyloma fulguration and antifungal treatment were effective at resolving pruritus.

can also be cultured from the perianal skin in normal subjects. *Dermatophytes* can cause pruritus ani less frequently but should be considered pathogenic and treated appropriately when found in patients with pruritus ani [27].

Several viral and sexually transmitted diseases (STD) can present as pruritus ani. These include herpes syndromes, syphilis, gonorrhea, molluscum contagiosum, and condyloma accuminata. Condyloma accuminata, which is associated with human papillomavirus infection (see section of "Neoplasm"), is a common cause of itching (Figure. 18-1). The diagnosis of condyloma accuminata is easy to recognize and should not be confused with primary or idiopathic causes. Herpes syndromes are typically characterized by pain and burning with red macules that progress to vesicles that rupture, ulcerate, and may become secondarily infected. Although parasite infections are a rare infectious cause of pruritus ani, they should be considered when clinically appropriate. Common perianal parasites include *Enterobius vermicularis* (pinworms), *Sarcoptes scabiei*, and pediculosis pubis [3]. Pinworms, in particular, are a common cause of nocturnal and post-defecation pruritus ani, especially in children.

Dermatologic

Several dermatologic conditions may present as pruritus ani. These conditions include psoriasis, seborrheic dermatitis, atopic dermatitis, contact dermatitis, lichen planus, lichen sclerosus, lichen simplex chronicus, and local malignancies. Accurate diagnosis largely depends on a thorough history and physical examination of the perianal skin as well as the skin of the entire body [18].

Anal eczema, probably the most common dermatologic cause of pruritus ani, is generally considered to primarily represent contact dermatitis to chemicals and medications that are applied to the anal area. These substances are used by up to 57 % of patients with anogenital complaints and include popular hemorrhoid ointments that contain potent sensitizers (local anesthetics, *Myroxylon pereirae*, bufexamac), dyes, and perfumes used in scented toilet paper and soaps, feminine hygiene sprays and deodorants, and medicated talcum powders and skin cleansers [31–33]. Patients with anal eczema are also more likely to have asthma and hay fever. Most studies evaluating the role of specific allergens causing anal eczema have identified local anesthetics, aminoglycoside antibiotics, and thimerosal as the most common causative agents [26, 31, 34]. It is also important to test the patients' own products, as some studies have found these to be common and clinically relevant allergens. Although the role of dry, moist, or recycled toilet paper has been looked at, well-designed studies have not shown toxic effects of its components [33, 35, 36].

For example, Kranke et al. [26] prospectively studied 126 patients with a presumptive diagnosis of anal eczema over a 4-year period. All patients followed a diagnostic algorithm that involved medical history, physical examination, biochemical and microbiology testing, patch tests, proctoscopy, and biopsy if appropriate. The majority of patients had symptoms for over 1 year. Fifty-eight patients (46 %) were confirmed to have contact eczema, and the leading noneczematous etiology was intertrigo dermatitis with *Candida* spp. in 54 patients (43 %). The most common positive contact allergen identified was thimerosal.

Atopic dermatitis may be the most common hereditary cause of pruritus ani, with a frequency of 15–20 % of the population. Atopic dermatitis is caused by disruption of the epidermal barrier function. Filaggrin, the cement of the epidermis, is defective or absent in patients with atopic dermatitis because of mutations of the filaggrin gene [37]. Complete loss of the filaggrin gene is seen in ichthyosis vulgaris, a common keratinizing disorder frequently associated with atopic dermatitis and seen at the buttocks and perianal skin [38]. Psoriasis affects 1–3 % of the general population and is an important etiology of secondary pruritus ani, with reports varying from 5.5 to 55 % [19, 39–41].

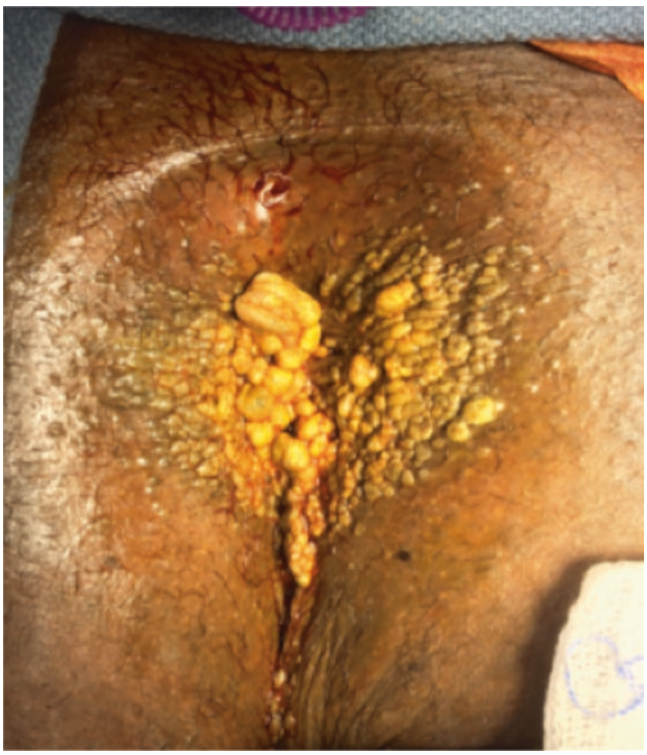

Figure 18-2. External anal condylomata acuminata presenting with perianal pruritus. Condyloma fulguration was effective at resolving pruritus.

Other less common dermatologic causes of pruritus ani include seborrheic dermatitis, lichen planus, lichen sclerosus, and lichen simplex chronicus. Seborrheic dermatitis is an uncommon cause of pruritus ani, characterized by extensive, moist erythema in the perineum [4]. Lichen planus is a relatively common inflammatory disease that affects the skin and mucous membranes and is thought to be caused by an altered, cell-mediated immune response. It is commonly seen in patients with other disease processes, such as ulcerative colitis, primary biliary cirrhosis, hepatitis C infection, and myasthenia gravis [42]. It is typically self-limited, resolving after 8–12 months.

Lichen sclerosus is a disease of unknown cause, seen more frequently in women, and involves the vulva extending posteriorly to the perianal region [4, 18, 43]. When it occurs on the penis, it is termed balanitis xerotica obliterans. Lichen simplex chronicus, also known as neurodermatitis, is a secondary skin manifestation that develops in an area of repetitive trauma from scratching or rubbing. A primary etiology may not be found in many cases, and the pruritus is typically intermittent and worsens at night or when a patient is quiet or still [44].

Neoplasms

Although uncommon, pruritus ani can be a presenting symptom of dermatologic neoplasms, such as condylomata, Paget's disease, and Bowen's disease. Condyloma acuminata with anal intraepithelial neoplasia is the sequel to human papillomavirus infection and refers to premalignant changes in the area of the dentate line and anal transitional zone. Although pruritus has not been well studied in large studies evaluating patients with AIN [45, 46], it is commonly identified in patients with a history of anal warts (Figure 18-2). Extra-mammary Paget's disease (cutaneous adenocarcinoma in situ) is rare and occurs more often during the sixth decade of life, in white patients, and in women compared to men (3–4:1 ratio) [47]. The perianal region is the most commonly involved extra-mammary site, and pruritus is a common presenting symptom [48]. When diagnosed, it may be indicative of and associated with an underlying apocrine or eccrine carcinoma. In particular, the rate of anorectal malignancy associated with perianal Paget's disease ranges from 33 to 86 % [48, 49]. Therefore, investigations of the gastrointestinal, urinary, and gynecologic systems should be performed for a potential associated malignancy. Intraepithelial squamous cell carcinoma in situ, also known as Bowen's disease, of the anus is also rare but frequently presents with pruritus as the main symptom [50].

Anorectal Conditions

Hemorrhoidal disease, skin tags, and chronic anal fissure in ano are commonly seen pathologies in patients with pruritus ani [51, 52]. These conditions alone can cause pruritus but also are often associated with varying degrees of leakage, prolapse, and soiling. Correcting these disorders in patients with pruritus ani is typically warranted. However, the response to treatment and the impact of correcting these conditions on pruritus ani symptoms are unclear and have only been reported in small retrospective studies [39, 40, 52]. Treatment modalities have included both office-based and operative strategies with varying degrees of success.

For example, Murie et al. [52] found that pruritus was more common in 82 patients with hemorrhoids than in age- and sex-matched controls without hemorrhoids and that correction (with banding or hemorrhoidectomy) usually eliminated itching. Bowyer and McColl [19] reported that hemorrhoids were the sole cause of itching in 16 of 200 patients and contributory in 27 others. Correction of fissure was required in five patients before symptoms were relieved. Five others had skin tags which when removed, eliminated symptoms. In general it is difficult to know whether anorectal conditions are the cause or a contributing factor of pruritus ani. Operative management that avoids further scaring or corrects fecal incontinence or leakage should be offered to pruritus patients in most cases.

Systemic Diseases

Several systemic diseases have been associated with pruritus ani; however, the precise causative factors remain unknown. Diabetes mellitus is the most commonly reported systemic

disease. Other frequently reported associated conditions include liver disease, lymphoma, leukemia, pellagra, vitamin A and D deficiencies, renal failure, iron-deficiency anemia, and hyperthyroidism [3, 4, 27].

Diagnoses of Perianal Disease

Establishing an exact diagnosis may be difficult mainly because the clinical presentation is frequently nonspecific. This often results in dissatisfied patients, who may be seen multiple times and by several doctors in different specialties. Consequently patients can have symptoms for many years, as well as a long list of prescribed and over-the-counter medications [53].

To pinpoint the cause of dermatologic diseases of the anus, it is recommended that patients be asked about their current diet, current and previous medications, personal history of atopy, information about bowel habits, and perianal hygiene regimen, including how they routinely clean the anal area after a bowel movement. A review of the patient's medical history, including any history of anorectal conditions or operations, is essential. Other pertinent history includes previous skin infections, especially mycotic infections of the genitalia, STDs, anal seepage, and symptoms of fecal and urinary incontinence.

A diagnostic algorithm, including a full history and physical examination, biochemical and microbiology testing, proctoscopy, and patch tests (including the patient's own products), is strongly recommended (Figure 18-3).

Physical Examination

The morphology of a lesion is a starting point for diagnosis, but may not be specific, and some diseases may present with a number of different appearances. Physical examination should also include evaluation of other related sites of skin manifestations including the groins, axillae, buttock cleft, and other intertriginous areas or skin folds. Response to treatment at these areas should also be documented at follow-up examinations. Washington Hospital classifies pruritus ani based on physical exam findings: stage 0 is normal skin, stage 1 is red and inflamed skin, stage 2 has lichenified skin, and stage 3 has lichenified skin, coarse ridges, and ulcerations [18]. This classification system is practical and useful for communicating with other providers.

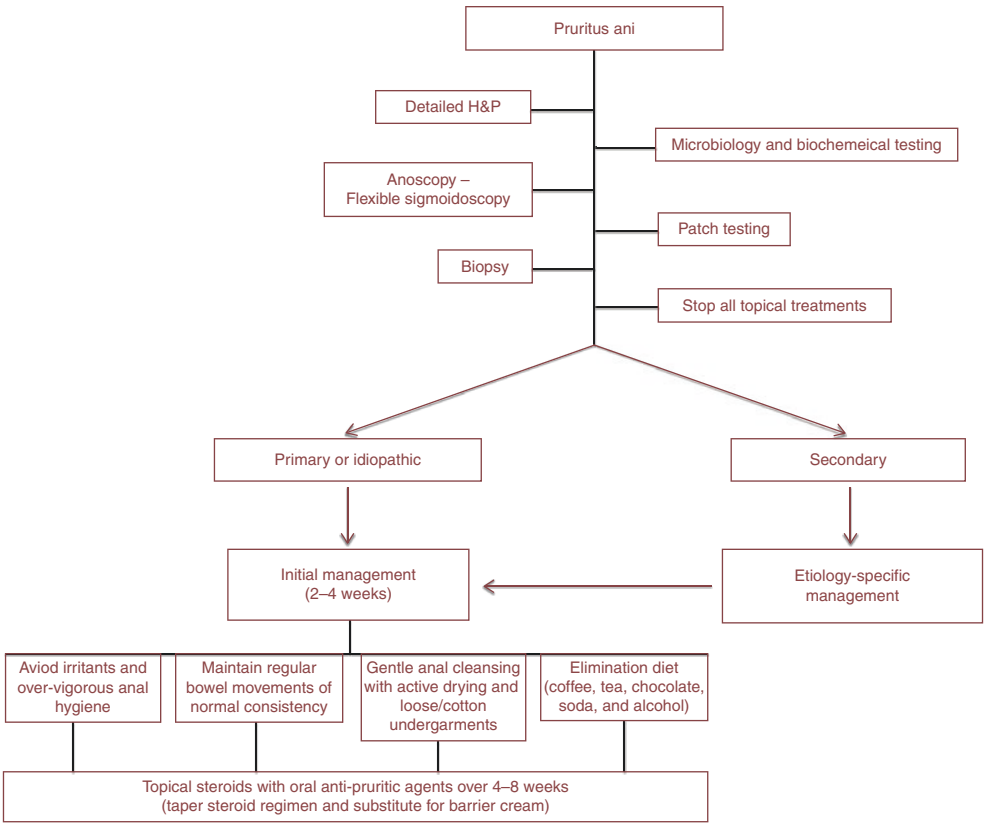

FIGURE 18-3. Diagnostic and treatment algorithm for patients presenting with pruritus ani.

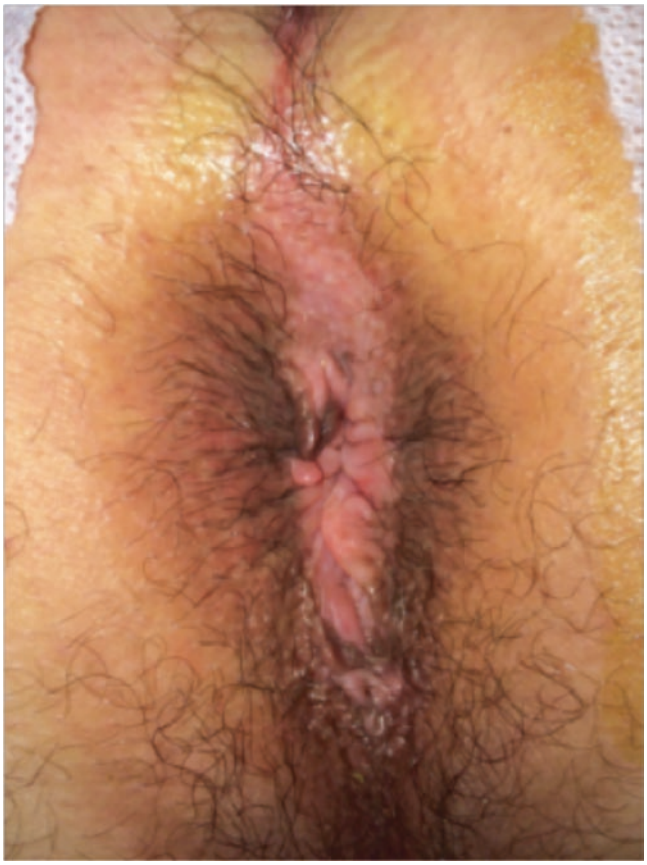

FIGURE 18-4. Hyperpigmentation and perianal skin lichenification seen in a patient with erythrasma.

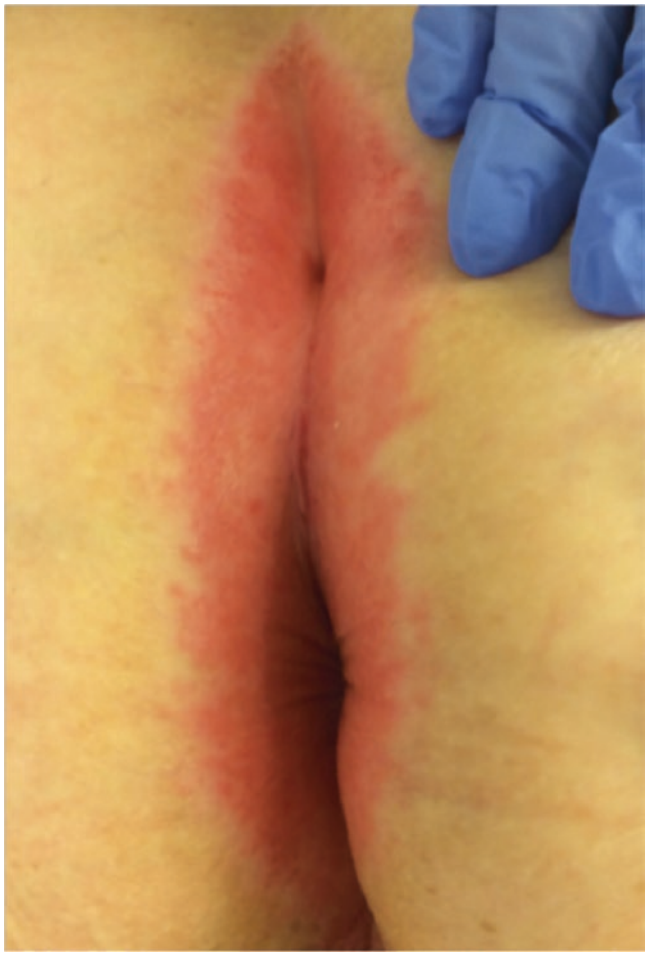

FIGURE 18.5. Perianal fungal infection in a patient with anal seepage and fecal incontinence. This infection is characterized by a bright red rash at the perianal area and intergluteal fold in a "butterfly" distribution.

Infectious

In the setting of bacterial perianal dermatitis, the perianal skin typically shows a moist, bright, and erythematous eruption with distinct borders and no satellite lesions. Patients usually do not have upper respiratory symptoms [28]. Chronic infected discharge from the anus may lead to hyperpigmentation of the anorectal cleft. This finding is commonly seen in patients with long-standing anorectal conditions, including pilonidal disease, anorectal fistulas, and hidradenitis suppurativa. Erythrasma is often associated with scaly, well-defined patches of initially reddish and then brownish-colored lesions at other intertriginous areas (Figure 18-4) [54, 55]. When caused by *Corynebacterium minutissimum*, these lesions show a characteristic coral-red fluorescence when examined with a Wood's lamp. *C. minutissimum* is commonly present and pathogenic at other body folds (axillae, groin, inframammary) and toe webs [54].

Molluscum contagiosum has a distinct presentation with clusters of small, palpable, flesh-colored papules with central umbilication. In general, human immunodeficiency virus (HIV)-associated lesions rarely present with itching except for secondary fungal infections. Perianal fungal infections are characterized by a bright red rash without the cheesy exudate sometimes seen in other parts of the body (Figure. 18-5). These infections may present following treatment with systemic antibiotics and topical or systemic steroids [56]. *Candida* is commonly found in patients with pruritus secondary to common anorectal conditions (i.e., hemorrhoids, fissure) and is typically eliminated with adequate treatment of the underlying condition [57]. Infections where *dermatophytes* are cultured almost always present with pruritus and are considered pathogenic, as compared to infections caused by *C. albicans* [30]. Topical steroids may render direct scrapings negative for hyphae but frequently facilitate *dermatophyte* growth.

Dermatologic

Anal eczema or contact dermatitis is characterized by erythema, scaling, and vesicles. Similar findings may be located on the face, neck, dorsum of the hands, as well as popliteal and antecubital fossas. Atopic dermatitis presents as nonspecific and diffuse erythema, often seen with signs of

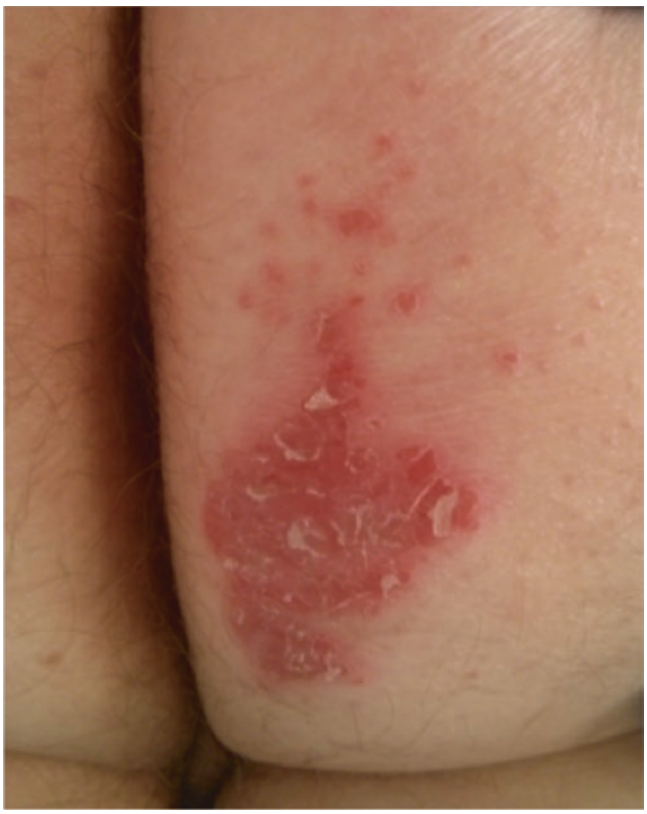

FIGURE 18-6. Perianal psoriasis or psoriasis inversa showing a well-demarcated, scaly, bright red, plaque-like lesion.

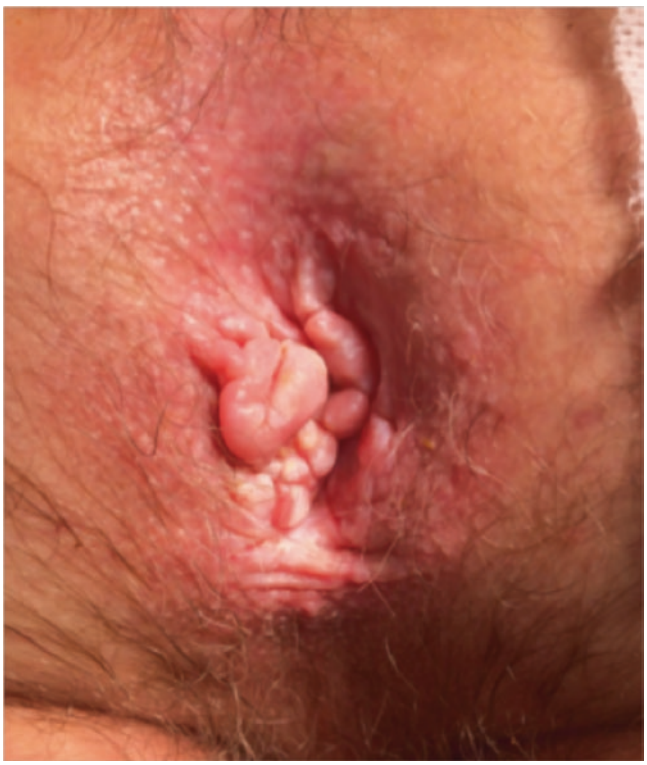

FIGURE 18-7. Lichen sclerosus of the anus with chronic healing showing replacement by chronic inflammation, sclerosis, and atrophy of the affected area.

skin excoriation. Associated findings include: keratosis pilaris (rough sandpaper-like texture over the posterior biceps and thighs), Morgan's folds or Morgan–Dennie lines (redundant creases beneath the eyes), "sniffers" lines (a subtle transverse crease across mid-nose), urticaria, and white dermatographism. With the loss of an adequate epidermal barrier, secondary infections and irritation by contact agents are common in patients with atopic dermatitis.

Psoriasis typically appears as well-demarcated, scaly, plaque-like lesions that are bright red in color (Figure 18-6). Typical lesions are commonly found on the scalp, elbows, knees, knuckles, and penis [18], but perianal psoriasis may also present as an isolated lesion. In the perianal region, lesions tend to be poorly demarcated, pale, and non-scaling because of persistent maceration, hence the term inverse psoriasis [4, 18]. With seborrheic dermatitis, excessive perianal moisture is the common denominator, and special attention should be directed to the scalp, chest, ears, beard, and suprapubic areas since these regions are commonly affected as well.

Lichen planus presents as shiny, flat-topped papules that are darker than the surrounding skin and begin on the volar aspects of the wrists and forearms. Genital and mucous membrane involvement are common [18]. Wickham striae are intersecting gray lines that can be seen if mineral oil is applied to the plaques and help to establish the diagnosis. Lichen sclerosus mainly involves the vulva but typically extends posteriorly toward the perianal region. The first phase of this condition begins as ivory-colored, atrophic papules that break down and expose underlying erythematous raw tissue. This process is severely pruritic and painful. As this heals, the area is replaced by chronic inflammation, sclerosis, and atrophy of the affected area (Figure 18-7). The classical finding is white patches around the vulva and anus [4, 18]. Histologically, these lesions are consistent with a chronic scar, lacking a lymphocytic interface (Figure 18-8) [41, 58–61]. Because of a reported 4–6 % risk of developing squamous cell carcinoma, all nonresponders or those with recurrent sclerosis should have a skin biopsy to rule out malignancy [27, 62]. Treatment of the disease does not appear to modify this risk [63].

Lichenification is the characteristic finding seen in patients with lichen simplex chronicus or neurodermatitis. The perianal skin appears thickened and is commonly described as cracking and scaling. Patients frequently have a history of an anorectal operation that involved a chronic wound or delayed healing.

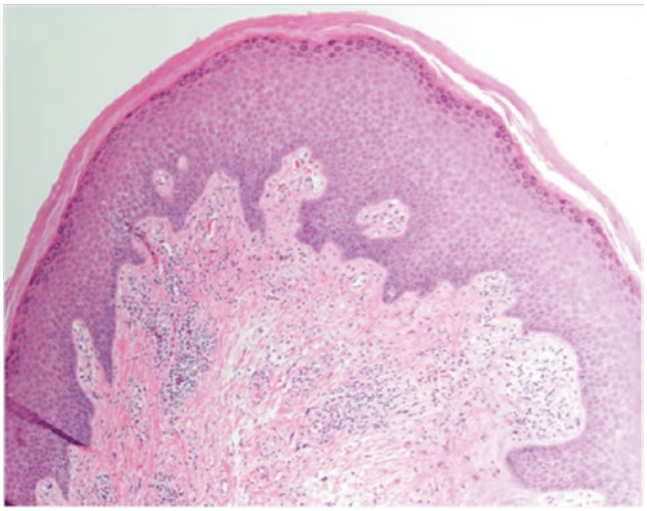

FIGURE 18-8. Photomicrograph of lichen sclerosus showing signs of chronic scaring and lack of lymphocytic interface dermatitis.

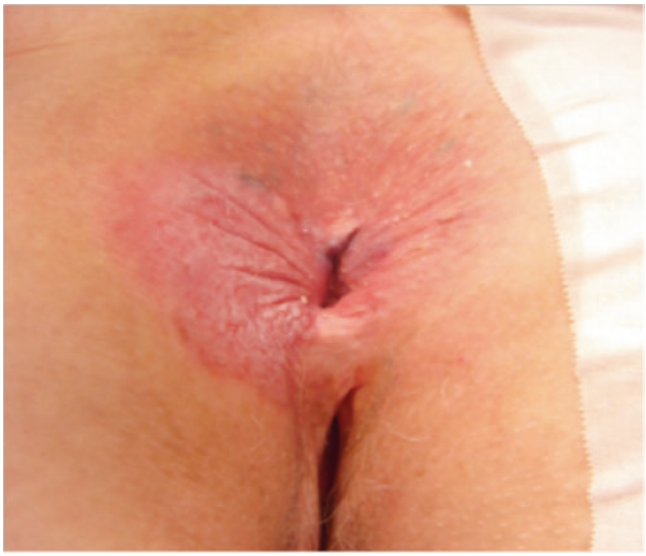

FIGURE 18-9. Perianal Paget's disease presenting with anal pruritus.

Neoplasms

The presentation of dermatologic malignancies, such as Paget's and Bowen's disease, may vary from a mild rash to a florid type of eczema at times associated with indurated skin. The classic presentation is an erythematous and eczematoid perianal plaque (Figure 18-9). Infiltrative processes may be less well defined in Paget's disease with the same caveat about margins. Pruritus and bleeding are the most common complaints [48]. Other symptoms include pain, mucous seepage, lump, and difficulty with defecation [64].

Biochemical Testing

After failed topical management and if systemic disease is suspected, biochemical testing is warranted. Common laboratory tests to rule out systemic and infectious causes include liver and kidney function tests, blood glucose level, white blood cell count with differential, C-reactive protein, and erythrocyte sedimentation rate. These tests are most useful in patients with decompensated chronic systemic disease like hepatic and renal failure and severe perianal infections.

Microbiology Testing

Cultures of perianal skin exudates and infectious material are simple and straightforward but can be misleading if not performed adequately. Infected material should be aspirated with a syringe and expelled into a sterile container. Alternatively, a swab may be used to collect a specimen but this is less than ideal. Culture specimens should be placed in appropriate media (anaerobic, bacterial, fungal, and viral) and refrigerated without delay. Viral cultures should be kept on ice. Fluid from vesicular lesions should be aspirated or taken with a swab from the base of an unroofed lesion and placed on a cell culture media or a microscopic slide for Tzanck smears if herpes zoster is suspected [65]. Swabs should be lubricated with saline if lubricated at all because conventional water-soluble lubricant is bactericidal for some organisms including *Neisseria gonorrhoeae*. Skin scrapings may be submitted for fungus culture. Scrapings can also be examined for hyphae with KOH prep, but this test is rarely available because of the lack of trained and experienced personnel. It is essential to have discussed the proper arrangements with the laboratory and nursing personnel (clinic and operating room) to assure adequate specimen handling and testing well before obtaining a specimen.

In patients with diarrhea, bacterial stool cultures as well as ova and parasites on three different stool samples can be useful. In patients with suspected or confirmed streptococcal or staphylococcal perianal infections, nasal or throat swabs rarely detect the offending bacteria and therefore are unnecessary [42]. If pinworms are suspected, a cellophane or scotch tape test in the early morning identifies adult worms and their eggs and confirms the diagnosis [4].

Patch Testing

Patients with an extensive list of allergies, both dietary and drug related, are good candidates for patch testing. This usually involves a dermatologic consultation, which can be very helpful when the staff has a particular interest in perianal dermatology. As part of a diagnostic algorithm in a prospective study of patients with clinical suspicion of anal eczema, Kranke and colleagues [26] found that patch testing was confirmatory in 33 of 58 patients (57 %), with at least one positive

Table 18-4. Patch test findings in 58 consecutive patients suspected of having allergic contact anal eczema [26]

Contact allergen	*N* (%)
Thimerosal	11 (19)
Patients own products	6 (10)
Balsam of Peru (*Myroxylon pereirae*)	5 (9)
Amerchol	3 (5)
Lanolin alcohol	3 (5)
Nickel sulfate	3 (5)
Fragrances/perfumes	3 (5)
Lidocaine, benzocaine	2 (3)
Propolis	1 (2)
Neomycin	1 (2)

allergic reaction (Table 18-4). It is important to also test the patient's own products as these have been shown to be a significant etiology in pruritus ani [1, 26].

Endoscopic Evaluation

All patients with pruritus ani should undergo anoscopy and flexible sigmoidoscopy. These exams are especially useful in patients with anorectal pathology and inflammatory bowel disease. Full colonoscopy is indicated for patients who are age-appropriate for colorectal cancer screening and those with hematochezia, iron-deficiency anemia, and positive family history of colorectal cancer.

Biopsy

Skin lesions not responding to treatment or suspicious for malignancy require biopsy. This is the single most valuable test in patients with primary pruritus ani and should include an area of the lesion with adjacent normal skin. Specific query should be made to a pathologist with expertise in dermatologic pathology with clinically suspected diagnoses. Biopsy may conveniently be done with either an 11 blade or skin punch blades (Keyes dermal punches) that come in numerous sizes in separate sterile packages. Bleeding is readily controlled with silver nitrate or topical thrombin-based hemostatic agents.

Evidence-Based Management

The management of dermatologic diseases of the anus in practice is particularly challenging for several reasons. These conditions are hidden on a part of the body often associated with embarrassment, and therefore patients may have advanced disease before they present to a doctor for help. Additionally, there is limited class A data regarding the management of pruritus ani.

Aims of Treatment

The aims of treatment for any form of anal dermatitis are rapid relief of symptoms, healing of dermatitis, and prevention of recurrence. Long-term recurrence can be prevented in many patients by avoiding contact with allergens and irritants, as well as curing the underlying anorectal disease or condition. The choice of treatment must take into account the different causative factors: irritation from contact, allergic contact, infection, primary inflammatory disease, and neoplasia. Treatment of underlying anorectal conditions (hemorrhoids, fistula, incontinence, etc.) should be initiated from the first patient visit.

Primary Pruritus Ani

Because primary or idiopathic pruritus ani is more common, a therapeutic trial of generic management is recommended. This will be effective in more than 90 % of patients [6]. This management strategy focuses on reestablishing ideal anal hygiene and providing reassurance that there is no underlying condition causing the symptoms. Treatment begins with avoiding known irritants such as soaps, lotions, creams, perfumed powders, medicated baby wipes, and any product with witch hazel. The patient must also know to avoid further trauma to the perianal skin, which may be caused by scratching, dry toilet paper, and vigorous scrubbing with bathing. Gently blotting the skin clean with moist toilet paper, a cotton ball, or a soft, unscented, and non-medicated baby wipe is recommended. Generally, baby wipes of all types should be avoided, especially when contact and atopic dermatitis is suspected. An important part of the initial management of primary pruritus ani is to avoid moisture and keep the perianal area dry. Patients should avoid tight-fitting, synthetic undergarments and may also use a small piece of cotton or makeup removal pad to help soak up any excess moisture. The brief use of a hair dryer with cool air is an excellent way to keep the perianal skin dry after cleansing. Unscented Dove® (Unilever, London, UK) is free of conventional soap and is the preferred bathing agent. It is also important for patients to maintain regular bowel movements of normal consistency. This is especially useful to avoid seepage and fecal contamination of the perianal skin. A high-fiber diet without excessive fluid intake and the judicious use of loperamide or cholestyramine is recommended, as needed. As mentioned earlier in this chapter, an elimination diet excluding "high-risk" dietary components such as coffee, tea, chocolate, soda, and alcohol for 2 weeks can be strongly considered in most patients with primary pruritus ani. Smith et al. [39] showed that an elimination diet gave partial or complete relief in 27 of 56 (48 %) of their patients.

In those patients in whom the initial management strategy is not effective after 4–6 weeks, attention is directed toward excluding the multiple potential causes of secondary pruritus

Table 18-5. Marketed topical products most commonly prescribed for the treatment of perianal dermatitis [66]

Active ingredients	Brand name(s)
Single active agents	
Hydrocortisone	Procto-Kit, DermoPosterisan
Tribenoside	Borraza-G
Cinchocaine	Dolapostern
Glyceryl trinitrate	Rectogesic
Corticosteroids + local anesthetics	
Hydrocortisone + pramocaine or cinchocaine or lidocaine or benzocaine + amylocaine + esculin	Pramosone, Proctofoam, Proctocream-HC, Proctosedyl, Xyloproct
Prednisolone + cinchocaine or + desonide + lidocaine + heparin + vitamins A and E	Scheriproct, Cirkan
Diflucortolone + lidocaine	Neriproct
Fluocinonide + lidocaine	Jelliproct
Fluocortolone + lidocaine or cinchocaine	Doloproct, Ultraproct
Fluocinolone + lidocaine (+ menthol + bismuth)	Synalar Rectal
Corticosteroids + antimicrobials/antiseptics	
Hydrocortisone + benzyl benzoate + Peru balsam + bismuth + zinc with or without resorcinol	Anusol-HC
Corticosteroids + local anesthetics + antimicrobials/antiseptics	
Hydrocortisone + cinchocaine with neomycin + esculin or framycetin	Proctosedyl
Local anesthetics + antimicrobials/antiseptics	
Cinchocaine + policresulen	Faktu
Other combinations	
Trimebutine + ruscogenin	Proctolog
Peru balsam + bismuth + zinc	Anusol
Hydrocortisone + *Escherichia coli* suspension	Posterisan
Hydrocortisone + phenylephrine + paraffin oil + fish oil	Preparation H
Lidocaine + carraginates + zinc	Titanoreine

Products with >10,000 prescriptions in 2011 according to IMS data for Brazil, France, Germany, Japan, the UK, and the USA [66]

ani. If no secondary cause can be found, topical therapy is recommended (Table 18-5). After generic management and proper anal hygiene are assured, topical steroids are an effective and safe treatment option. First-line topical treatment includes preparations with a low-potency topical steroid such as 1 % hydrocortisone, which should not be given for more than 8 weeks. In a double-blinded, randomized trial, 11 patients with primary pruritus ani received 1 % hydrocortisone or placebo for 2 weeks followed by the opposite treatment for another 2 weeks [67]. There was a washout period of 2 weeks between treatments. Treatment with 1 % hydrocortisone resulted in a 68 % reduction of itch using a visual analogue score, and 75 % showed significant improvements in quality of life. Potent or extended use of topical steroids should be avoided as they can lead to skin atrophy, infections, and worsened pruritus ani (Figure 18-10) [18, 27]. Capsaicin has also been studied in a randomized fashion in 44 patients with primary pruritus ani [68]. This topical agent decreases levels of substance P, a neuropeptide that triggers itching and burning pain. Topical capsaicin (0.006 %) showed relief of symptoms in 70 % of patients as compared to 2 % patients who received placebo (1 % menthol).

The majority of patients with moderate symptoms and minimal skin changes will respond well to low-dose topical steroids or topical capsaicin. These preparations are applied at night and in the morning after bathing. If topical steroids are used, a tapering regimen should be set in place ending with substitution of a barrier cream such as Calmoseptine® (Calmoseptine, Inc., Huntington Beach, CA). Patients with chronic perianal skin changes should be managed with a medium- or high-potency steroid (Table 18-6). It is important to emphasize to patients that a high-potency steroid should be used for a limited period of time, generally 4–8 weeks. Once normalization of the skin has occurred, patients are switched to a mild steroid that can be further tapered down to bi-weekly applications until total elimination.

Non-irritating cleansers are highly recommended during the initial therapeutic trial, especially when patients do not have a bath or shower directly available. Dilute white vinegar (one tablespoon in an 8-oz glass of water) on a cotton ball is a cheap and effective non-soapy cleanser. It is our personal preference to use tea tree oil, a volatile oil with antibacterial and antifungal properties, in patients with moist perianal skin and pruritus. Patients who come to the office with acute moderate to severe changes of the perianal skin may be treated with Berwick's dye (crystal violet 1 % + brilliant green 1 % + 95 % ethanol 50 % + distilled H2O q.s.ad. 100 %), which is dried with a hair dryer, and subsequently covered with benzoin tincture as a barrier and dried similarly. This topical treatment will stay in place for several days if only water is used to cleanse, relieves symptoms rapidly, and allows for re-epithelialization of broken-down skin. Application of Berwick's dye to the perianal skin is especially useful for pruritus ani occurring after anorectal operations.

FIGURE 18-10. Chronic skin changes of atrophy and ulcerations secondary to pruritus ani with associated left buttock infection in a patient who had been taking steroids for 8 years.

Skin breakdown or maceration caused by scratching or over vigorous cleansing efforts must be avoided. A combination of topical and systemic medications has shown the best results compared to either alone. Doxepin (both topical and oral) and hydroxyzine are effective adjuncts to reduce or eliminate itching. Doxepin, a tricyclic antidepressant, possesses both anti-H1 and anti-H2 activity. Hydroxyzine, a potent H1 receptor inverse agonist, has shown to have equal antipruritic efficacy compared to oral doxepin but with higher sedation effects [70]. Although centrally acting agents such as gabapentin and paroxetine have shown to be effective antipruritic agents in uremic and cholestatic patients [71], their efficacy in patients with pruritus ani has not been studied. Our experience with gabapentin in severe refractory pruritus ani has been quite rewarding. Patients may not be aware of nocturnal scratching and this can be a serious contributing factor in many cases of primary pruritus ani. Patients who are awakened by the urge to scratch should gently cleanse the perianal skin and reapply their barrier ointment.

For intractable cases or primary pruritus ani, intradermal injection of methylene blue has been described with some efficacy (Figure 18-11) [27, 72]. The presumed mechanism of symptomatic improvement is through the destruction of nerve endings. This treatment modality was initially

TABLE 18-6. Relative potency of topical steroids

Group 1 (most potent)
Betamethasone dipropionate 0.05 % (Diprolene®)
Clobetasol propionate 0.05 % (Temovate®)
Group 2
Desoximetasone 0.25 % (Topicort®)
Fluocinonide 0.05 % (Lidex®)
Group 3
Betamethasone valerate ointment 0.1 % (Valisone®)
Triamcinolone acetonide 0.5 % (Aristocort®)
Group 4
Desoximetasone 0.05 % (Topicort LP®)
Flurandrenolide 0.05 % (Cordran®)
Group 5
Betamethasone valerate cream 0.1 % (Valisone®)
Hydrocortisone butyrate 0.1 % (Locoid®)
Triamcinolone acetonide 0.1 % (Kenalog®)
Group 6 (least potent)
Alclometasone dipropionate 0.05 % (Aclovate®)
Hydrocortisone 1 %

Finne CO, Fenyk JR, Dermatology and pruritus ani. In: Fleshman JW, Wolff BG, editors. The ASCRS textbook of colon and rectal surgery. New York: Springer; 2007. p. 277–294) [69]. © Springer

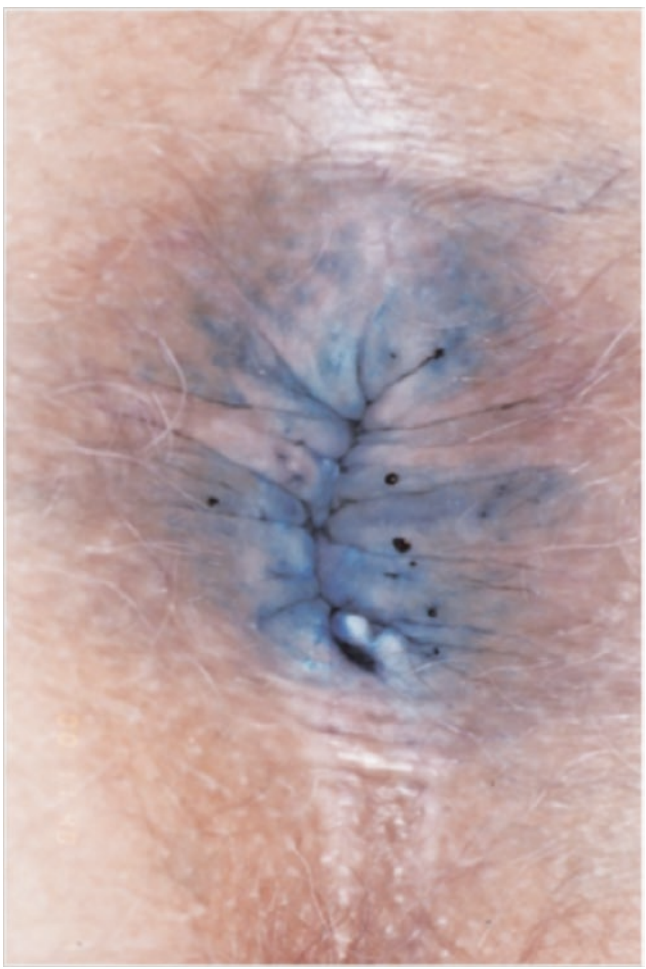

FIGURE 18-11. Tattooing with methylene blue for severe refractory idiopathic pruritus ani. Courtesy of C.O. Finne, St. Paul, MN.

described by Eusebio and colleagues [72] and involved the intracutaneous and subcutaneous injection of 30 mL of 0.25 % bupivacaine with 1:200,000 epinephrine mixed with equal volumes of 0.5 % lidocaine at the anoderm and perianal areas, with the patient under deep sedation in the operating room. After this, 20–30 mL of 0.5 % methylene blue was injected at the same sites using a 25-G spinal needle. Twenty-one of 23 patients reported good short- and long-term results. However, the authors also reported full-thickness skin necrosis in three patients. Mentes et al. [73] used a slightly different technique in 30 patients with intractable primary pruritus ani. Patients underwent intradermal and subcutaneous injection of a mixture of 7–8 mL of 2 % methylene blue with equal volumes of 0.5 % lidocaine without previous local anesthesia or sedation. For patients who had a partial response at 1-month follow-up, a "rescue treatment" was offered. At 1 month, 80 % of patients were free of symptoms. Five patients underwent an additional "rescue" injection and four of five had complete relief of symptoms. No major complications or cases of skin necrosis were reported. The authors attributed this to a smaller injected volume.

Secondary Pruritus Ani

Infectious

Bacterial infections of the perianal region should be treated with systemic antibiotics. If a specific agent has not been identified, antibiotic coverage should include Gram-positive and Gram-negative cocci. Parenteral antibiotics have been reported to be especially useful with *Staphylococcus aureus* infections [74]. When refractory pruritus ani is associated with cultures that show growth of *Candida albicans*, antifungals should be given, especially in patients who are immunosuppressed, who are diabetic, or who were recently treated with systemic steroids or antibiotics [27]. We have seen good results with a combination of oral fluconazole and topical luliconazole 1 %, given for 2–3 weeks. Again, when *dermatophytes* are found in the setting of pruritus ani, this associated fungal infection should also be treated appropriately [27]. The treatment of erythrasma involves systemic antibiotics, typically erythromycin 250 mg *qid* for 10 days. Tetracycline may be used as a second alternative [54, 55]. Silver sulfadiazine is an effective topical adjunct in patients with bacterial perianal dermatitis, especially in patients with ulcerations and fissuring skin as it sooths and promotes re-epithelialization. It should be noted that when topical therapy is given with systemic antibiotics and antifungals, it should be for symptom relief but not as the primary antibacterial or antifungal agent.

Dermatologic

With regard to anal eczema, both the European and American Academy of Allergy, Asthma, and Immunology guidelines recommend starting treatment with basic skin care. Keys to success include avoiding allergens, irritants, and tight constricting undergarments, liberal use of warm sitz baths for comfort, and keeping the affected area dry at all other times. As mentioned above, gentle but thorough cleansing of the perianal area with soap substitutes (i.e., Dove) is recommended during bathing [75]. When these methods fail, mild-to-moderately potent topical corticosteroids for 2–3 weeks periods are recommended. The efficacy of topical steroids compared to placebo has been studied in a small, double-blinded, randomized controlled trial, favoring topical steroid treatment [66]. Topical calcineurin inhibitors such as tacrolimus and pimecrolimus are also effective for reducing inflammation and itch in patients with anal eczema and also avoid skin atrophy. Two randomized controlled trials comparing topical tacrolimus 0.1 % to placebo in a total of 53 patients with chronic idiopathic pruritus ani showed significant symptomatic improvement up to 6 weeks follow-up [76, 77]. One of these studies failed to show significant differences in quality of life as assessed by the Dermatology Life Quality Index questionnaire [77]. Although systemic gamma interferon and narrowband UVB therapy have shown promising results in patients with atopic dermatitis as well as cholestatic and uremic pruritus [78, 79], no evidence in patients with pruritus ani exists. Of importance, bacterial and fungal infections should be suspected after multiple or prolonged unsuccessful treatments.

Treatment of atopic dermatitis begins with providing a barrier such as Vaseline® (white petrolatum USP) or Calmoseptine® (Calmoseptine, Inc., Huntington Beach, CA), the use of anti-inflammatory agents (systemic and topical) and antipruritic agents. Psoriasis is not a curable condition, but symptoms can be well controlled with mild topical steroid preparations (i.e., 1 % hydrocortisone cream). Seborrheic dermatitis responds well to 2 % sulfur with 1 % hydrocortisone or miconazole lotion [80]. Keeping the perianal area clean and dry is essential for treatment success.

Lichen sclerosus is initially managed with topical steroids. Potent topical steroid creams, such as clobetasol 0.05 %, for a short course (4–6 weeks) followed by less potent hydrocortisone cream are the mainstay of treatment. Systemic steroids are given only for very severe cases [18, 42]. Topical calcineurin inhibitors are effective alternatives in the treatment of lichen sclerosus in patients who have failed therapy with potent corticosteroids or who have a contraindication for the use of corticosteroids [81]. Treatment with retinoid and testosterone creams may be useful in selective cases [28, 43]. Patients should be followed periodically for raised lesions or ulcers that fail to heal, and it is important to explain to patients that the appearance of the vulvar and perianal lesions may never change even if the symptoms are relieved [43]. The treatment of lichen simplex chronicus or neurodermatitis begins with topical steroids to decrease the inflammation and break the itch-scratch-itch cycle. Antihistamines, doxepin, or capsaicin creams are effective adjuncts to topical steroids. For patients who have a poor response to topical steroids, topical

acetylsalicylic acid/dichloromethane or immunomodulators, such as tacrolimus, have shown positive results [44].

Treatment of perianal Paget's disease requires wide local excision. Adequate microscopically clear margins and ruling out invasive disease are important to avoid clinical recurrence [82]. Positive skin margins are a common occurrence after excision; therefore, preoperative and intraoperative planning should involve a detailed discussion with an experienced pathologist regarding specimen location and orientation. Invasive disease is treated with abdominoperineal resection and delayed margin positivity requires re-excision. Soft-tissue and skin reconstruction frequently requires V–Y gluteal flaps or skin grafting, with the assistance of plastic surgery. It is important for the patient to be aware of the possibility of radical resection, delayed re-excision of margins, and stoma. Recurrence of disease is common and may occur up to a decade after initial excision [18]; therefore, regular and long-term follow-up is imperative.

Systemic Diseases

Effective treatment of pruritus ani in patients with poorly controlled or exacerbated systemic disease involves appropriate management of the underlying disease. Occasionally, pruritus will be the presenting symptom in patients with liver failure and diabetes mellitus. Appropriate skin cleansing, application of a topical barrier, and antipruritic agents are the mainstay of treatment. Cimetidine has been reported to eliminate itching induced by lymphoma and polycythemia vera. In our experience, doxepin and gabapentin are also effective antipruritic agents in patients with systemically induced pruritus ani. Chronic itching in these patients may also lead to lichenification and secondary infections. Appropriate systemic antibiotic or antifungal therapy is warranted.

In summary, perianal dermatologic conditions include a wide variety of diagnoses that require comprehensive and stepwise diagnostic and management algorithms. These conditions are likely to be much more common than estimated in the current literature, mainly because of the embarrassment associated with seeking medical attention as well as the relapsing and chronic nature of idiopathic etiologies. Patients with primary pruritus ani refractory to treatment should be aware of this chronicity and focus on symptom control instead of symptom eradication and also understand the potential need for treatment strategies for relapsing disease or flares.

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