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Review

# Anogenital psoriasis: clinical picture and therapy

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ABSTRACT

Psoriasis presenting with anogenital lesions is an important medical and social problem that is not sufficiently covered in the literature.

The genitals and perianal area are involved in severe plaque and inverse psoriasis. Occasionally, the disease can be localized only in the anogenital zone. Diagnosis of psoriasis with localization on the genitals and/or perianal area is difficult, which is associated with the anatomical and physiological characteristics of the affected area. The manifestations of psoriasis become exudative, infiltration of papules and plaques is expressed little, the borders of rashes lose clarity, peeling on the skin is expressed weakly, in the depth of the folds due to maceration and friction is absent. Subjectively significant localization of the process, its prolonged course, pruritus lead to significant violations of the quality of life of patients and serve as prerequisites for the formation of anxiety-depressive disorders and sexual dysfunction

Diagnosis and treatment of anogenital psoriasis presents significant challenges. Clinical guidelines tend to emphasize external therapy with topical corticosteroids and calcineurin inhibitors; in recent years, the efficacy of genetically engineered biological agents, including interleukin-17 inhibitors and phosphodiesterase-4 inhibitors, has been considered.

The presented review systematizes information about anogenital psoriasis, peculiarities of its epidemiology, clinical picture, diagnosis and approaches to therapy.

**Keywords:** psoriasis; anogenital region; clinical picture; diagnosis; topical therapy; systemic therapy.

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Научный обзор

# Псориаз аногенитальной области: клиническая картина и принципы терапии

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АННОТАЦИЯ

Псориаз, протекающий с поражением аногенитальной области, представляет собой важную медико-социальную проблему, которая недостаточно освещена в литературе.

Гениталии и перианальная область вовлекаются в процесс при тяжёлом течении дерматоза и при инверсном псориазе. Изредка заболевание может быть локализовано только в аногенитальной области. Диагностика псориаза с изолированной или преимущественной локализацией на гениталиях и/или в перианальной области затруднена, что связано с анатомо-физиологическими характеристиками поражённой области. Проявления псориаза приобретают экссудативный характер, инфильтрация папул и бляшек выражена мало, границы высыпаний теряют чёткость; шелушение на коже выражено слабо, а в глубине складки вследствие мацерации и трения — отсутствует. Субъективно значимая локализация процесса, его длительное течение, зуд приводят к существенным нарушениям качества жизни пациентов и служат предпосылкой для формирования тревожно-депрессивных расстройств и сексуальной дисфункции.

Диагностика и лечение псориаза аногенитальной области представляет существенные трудности. В клинических рекомендациях акцент, как правило, делается на наружную терапию топическими кортикостероидами и ингибиторами кальциневрина; в последние годы рассматривается эффективность генно-инженерных биологических препаратов, в том числе ингибиторов интерлейкина-17, а также ингибиторов фосфодиэстеразы-4.

В представленном обзоре систематизированы сведения о псориазе аногенитальной области, особенностях его эпидемиологии, клинической картины и диагностики, а также подходах к терапии.

**Ключевые слова:** псориаз; аногенитальная область; клиническая картина; диагностика; топическая терапия; системная терапия.

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## ABSTRACT

Psoriasis is a systemic immune-associated disease of multifactorial origin, affecting between 0.51% and 11.43% of the population and ranking among the most prevalent skin diseases [1, 2]. Psoriasis may occur in different age groups and is associated with several comorbidities, including depression, psoriatic arthritis, and cardiometabolic syndrome [2].

The most prevalent form of the disease is chronic plaque psoriasis or psoriasis vulgaris [3], which develops in individuals with a genetic predisposition, primarily in carriers of the *HLA-C*06:02* allele, under the influence of environmental factors, including streptococcal infection, stress, smoking, obesity, and alcohol consumption. The rash manifests on the scalp, sacral skin, and extensor surfaces of the extremities. In approximately 20% of cases, the nail plates are affected.

The anogenital area is typically involved in cases of severe dermatosis and inverse psoriasis. According to Meeuwis et al. [4], up to 60% of patients with widespread psoriasis vulgaris have had a genital rash at least once in their lives. Similarly, Wang et al. [5] reported that the frequency of anogenital lesions in patients with the inverse form of the disease reaches 75%.

The diagnosis of genital and/or perianal psoriasis is challenging [6]. This complexity arises from the unique clinical pattern of the dermatosis, which is influenced by the anatomical and physiological characteristics of the affected region. They include varying degrees of keratinization of the epithelium, adequate vascularization, occlusion and maceration by sebum, sweat, and vaginal secretions, as well as connection with the excretory system, the high skin pH, resulting from the breakdown of uric acid by bacterial ureases to form ammonia, as well as friction and pressure [7]. The manifestations of anogenital psoriasis exhibit exudative characteristics, with a paucity of papules and plaques, indistinct boundaries of the rash, and minimal skin exfoliation. In the deeper folds, exfoliation is absent due to maceration and friction [8]. Subjectively, patients experience pruritus of varying intensity.

The treatment of anogenital psoriasis presents significant challenges. Clinical guidelines typically emphasize topical therapy with topical corticosteroids and calcineurin inhibitors. In recent years, the efficacy of genetically engineered biological agents, including interleukin (IL)-17 inhibitors and phosphodiesterase-4 inhibitors, has been considered [9].

Subjectively, significant localization of the process, its prolonged course, pruritus, and resistance to treatment lead to significant disturbances in the patients' quality of life and serve as a prerequisite for anxiety-depressive disorders and sexual dysfunction [10].

Therefore, anogenital psoriasis is an important medical and social problem that is not adequately addressed in the literature. The aim of this review was to systematize the knowledge about anogenital psoriasis, its epidemiology, clinical pattern, diagnosis, and therapeutic approaches.

## EPIDEMIOLOGY OF ANOGENITAL PSORIASIS

Precise data concerning anogenital lesions in psoriasis are lacking. This may be because the genital and perianal areas are often not examined by specialists in patients with widespread rashes, and patients may not report skin lesions in such intimate areas [11]. In general, anogenital lesions may be diagnosed in 29%–40% of patients with psoriasis vulgaris [12]. According to Mahajan et al. [13], no correlation has been identified between the severity of skin lesions (Psoriasis Area Severity Index [PASI] score, $p = 0.86$), body mass index ($p = 0.62$), and clinical patterns of widespread psoriasis ($p = 0.13$). This suggests that genitalia may be affected in patients with a limited skin process. The risk factors for genital lesions in psoriasis are male sex (odds ratio [OR]: 21; 95% confidence interval [CI]: 15–30), age over 60 years (OR: 36; 95% CI: 17–77), inverse psoriasis (OR: 44; 95% CI: 22–89), scalp psoriasis (RR: 19; 95% CI: 13–26), nail psoriasis (RR: 19; 95% CI: 13–28), external auditory canal psoriasis (RR: 18; 95% CI: 11–28), and severe psoriasis (RR: 20; 95% CI: 14–30) [11]. In 4% of patients, genital and/or anal lesions may be the first symptom of the disease [13, 14].

Isolated lesions of the anogenital area are rarely observed, with prevalence rates of no more than 2%–5% among patients, with a slight predominance of men [15, 16]. Some authors hypothesize that the perception of more frequent genital lesions in men may be due to two factors. First, men may be more likely to consult specialists because of the possibility of observing their own genital lesions. Second, the formation of a rash similar to Koebner phenomenon may occur due to traumatization of the penile skin as a result of sexual activity [13]. According to Marcos-Pinto [17] et al., psoriasis is responsible for approximately 11% of all cases of non-venereal balanitis. Furthermore, psoriatic lesions of the glans penis occupy the third place in the structure of dermatoses, following plasma cell balanitis and lichen sclerosus et atrophicus.

The prevalence of genital and anal lesions in psoriasis among women is not well documented. Women comprise up to 17% of all cases of vulvar pruritus (excluding cases of diaper dermatitis) among girls [18] and 5% among adults [19]. Psoriasis is thought to be the third most common etiology of anogenital dermatoses in girls, after lichen sclerosus et atrophicus and allergic dermatitis [18]. Notably, unlike atopic dermatitis, psoriasis has the potential to manifest under diapers in early childhood due to irritation from urine, feces, and heat [18, 20].

## CLINICAL PATTERN OF ANOGENITAL PSORIASIS

The clinical manifestations of anogenital psoriasis generally do not differ from those in other localizations. However, different morphophysiological features of the affected area lead to changes in the clinical pattern of the dermatosis [7]. Genital rashes are less well demarcated, poorly infiltrated but more vividly hyperemic, often with an exudative component [8] (Fig. 1, images *1–15*). Exfoliation is typically minimal and may be undetectable within the folds.

The preferred localization of the process in men is the glans penis and penile shaft, with less frequent involvement of the scrotum and inguinofemoral folds. In women, the process is most commonly localized on the labia majora, with occasional involvement of the labia minora. In many cases, the process involves the skin of both labia symmetrically; however, it may also be unilateral [21]. According to our unpublished data, when assessing the sexual features of the localization of the anogenital process, the perineum and perianal area are found to be significantly more frequently affected in women. In combination with the lesion of the labia majora, this results in the formation of rashes resembling the number eight. Conversely, such involvement of the anogenital area is atypical of men. The aforementioned features of skin lesions in psoriasis in women are similar to those in lichen sclerosus et atrophicus and may be due to anatomical differences between men and women [7].

Anogenital psoriasis is characterized by isomorphic Koebner reaction and complication of the process by irritant dermatitis associated with urinary incontinence in genitourinary menopausal syndrome, use of daily pads, lubricants, and synthetic underwear, including irrational therapy or excessive hygiene [22] (Fig. 1, images *7–11*). The use of topical corticosteroids, especially in patients with excessive body weight, insulin resistance, or diabetes mellitus, may cause vulvovaginal candidiasis or

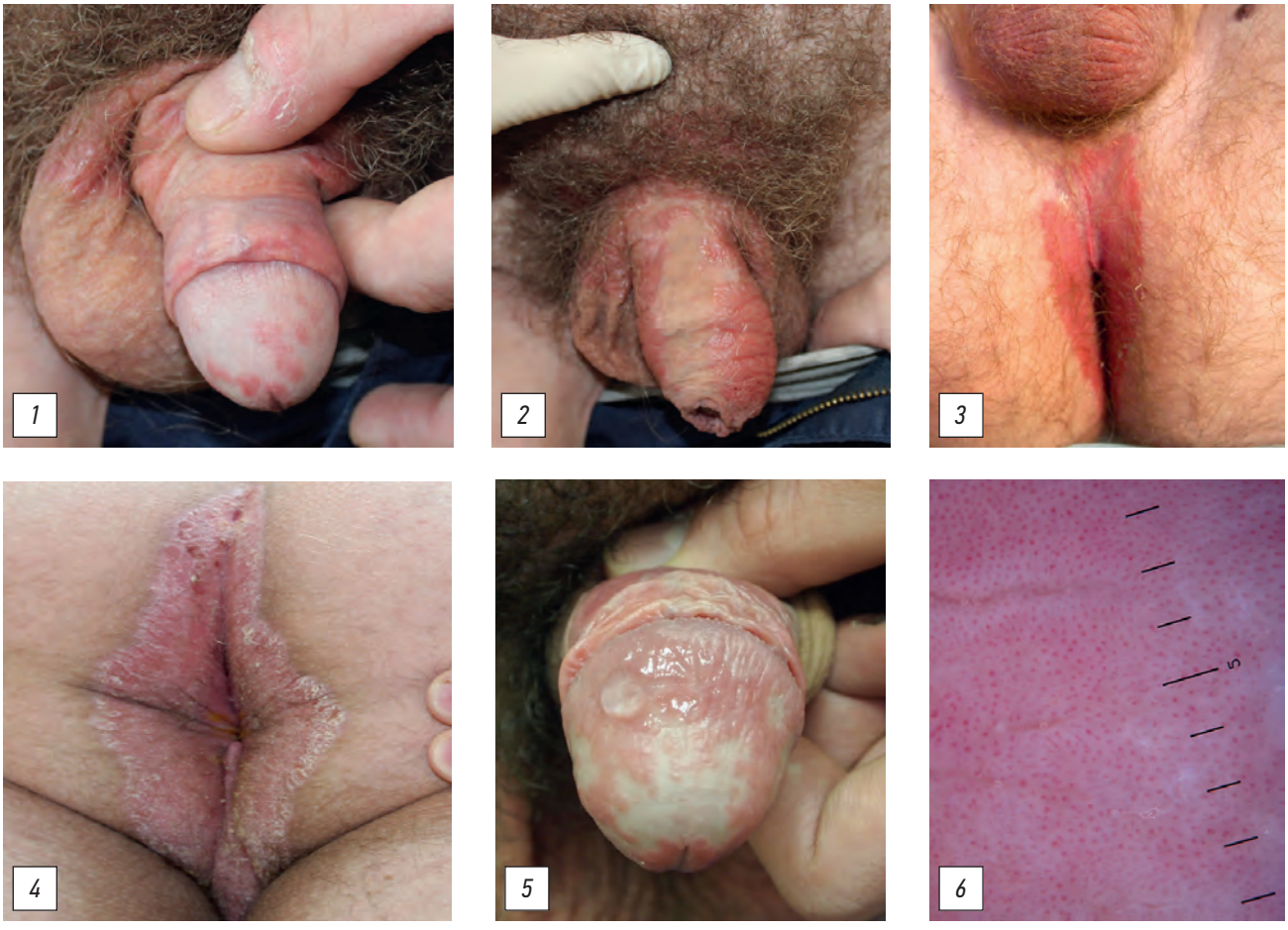


**Fig. 1.** Clinical manifestations of psoriasis of the anogenital area: psoriatic balanitis (*1*); vivid rashes with weakly expressed desquamation involving the skin of the trunk, pubis and scrotum (*2*), perineum (*3*), perianal area (*4*); clinical and dermatoscopic picture of psoriatic balanitis with evenly distributed pitting vessels (*5*, *6*); symmetrical and predominantly unilateral lesion of the labia majora (*7*, *8*); process with irritation dermatitis on the background of menopausal genitourinary syndrome with urinary incontinence (*9*) and involvement of the labia majora, labia minora, perineum and perianal area with Kebner's phenomenon on the background of using daily pads (*10*, *11*); pustular psoriasis on the background of long-term uncontrolled use of topical corticosteroids: clinical (*12*, *13*), dermatoscopic (*14*) and histological (*15*) picture with formation of massive crusts on the surface of papules, acanthosis of irregular character, exocytosis of neutrophilic granulocytes into the epithelium and formation of large Munro microabscesses.

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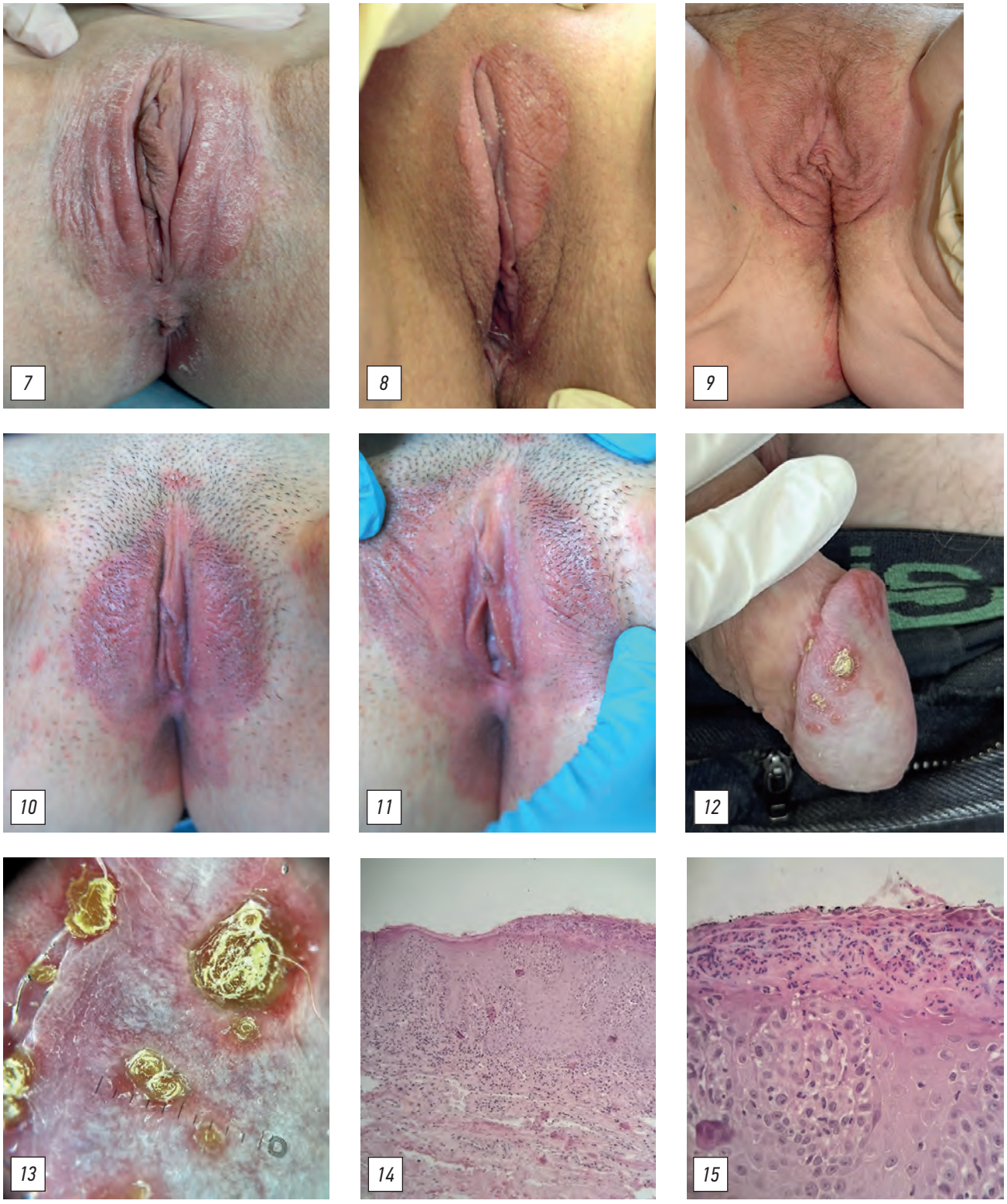


**Fig. 1.** The End.

balanoposthitis, changes in the clinical pattern of psoriasis, and fissure formation. In some cases, pustular psoriasis may develop (Fig. 1, images *12–15*).

The predominant subjective symptom associated with anogenital lesions is pruritus, which is variable in intensity [9]. In genital lesions, pruritus is more common in women (65% vs. 45% in men) [8, 19, 23], whereas in men the process may proceed without significant subjective symptoms. While the intensity of pruritus is often reported as moderate or low, the presence of this symptom, especially over a long period of time, has been associated with depressive disorders in both sexes [19]. Notably, more than 50% of women with vulvar discomfort in psoriasis do not consult a dermatologist. Pruritus may be intolerable when the perianal area is

involved [24]. In addition, pain, burning, and scratching may occur when the anogenital process is complicated by candida or streptococcal flora [25] and fissures. In some cases, these symptoms are associated with rashes in patients without infectious complications [21, 23].

These characteristics of anogenital lesions are the reason for poor recognition of psoriasis, especially when patients are referred to other specialists [26]. For example, Kapila et al. [6] analyzed data of 114 patients with vulvar psoriasis and found that only 12.3% of patients were referred to a dermatologist with a presumptive diagnosis of psoriasis. The remaining patients were followed and treated with other diagnoses. The situation was further exacerbated by the fact that patients used topical corticosteroids for the treatment of rashes on their own or on the recommendation of various specialists. This was accompanied by a pathomorphosis of the clinical manifestations of the dermatosis [7]. In fact, approximately 50% of patients receive topical corticosteroids and/or antifungals for anogenital lesions without an established clinical diagnosis [6].

In many cases, skin rashes on the trunk or extremities may be a crucial element in the diagnostics in patients exhibiting genital and perianal lesions. However, there is limited data concerning the prevalence of skin, nail plate, and joint involvement in these patients. According to Mahajan et al. [26], among men diagnosed with psoriatic balanitis, concurrent lesions of folds were identified in 22% of patients, while nail plates and joints were affected in 30% and 25% of patients, respectively.

## ANOGENITAL PSORIASIS: DISEASE BURDEN

Anogenital psoriasis is a significant medical and social problem. Subjectively, the disease is characterized by its localization, the duration, and the presence of pruritus and discomfort of varying degrees of severity. These factors result in impaired quality of life in patients and serve as a prerequisite for anxiety and depressive disorders [10, 27].

Reduced quality of life is characteristic of anogenital psoriasis in all age groups, with the greatest impairment reported in younger patients [10]. Psoriatic lesions make them more vulnerable, especially when transitioning to independent living or finding a job. Additionally, these patients are more likely to be dissatisfied with treatment, have difficulties in discussing treatment with healthcare professionals, and have poor compliance.

The quality of life of patients with anogenital psoriasis is affected in several areas, including sexual function [28]. These patients frequently report feelings of guilt and low self-esteem, and they are less likely to engage in long-term relationships [10, 26]. In 36% of cases, they avoid sexual intercourse due to both unpleasant subjective sensations (e.g., pain during or after intercourse) and the high stigma and fear of rejection by the partner [10]. These patients have a lower perception of their own nakedness and are less likely to engage in dating activities when compared with patients whose psoriasis affects other body parts [29].

## COMORBIDITIES IN ANOGENITAL PSORIASIS

Psoriasis is known to be associated with various comorbidities, including arthritis, metabolic disorders, depression, and others [2, 7]. Predicting comorbidities and disease progression enables personalized patient care. According to Wilson et al. [30], anogenital psoriasis, specifically psoriasis accompanied by perianal involvement, has been identified as a predictor of psoriatic arthritis (OR: 2.35, 95% CI: 1.32–4.19), with this risk increasing in proportion to the duration of the underlying disease. However, not all researchers agree. For example, Patrizi et al. [31] suggest that involvement of the gluteal region and perianal fold, as opposed to nail plate lesions, does not correlate with psoriatic arthritis.

In recent years, there has been an increased focus on the study of sexual dysfunction in patients with dermatoses. For example, research has indicated that men with psoriasis, irrespective of its localization, demonstrate an elevated prevalence of erectile dysfunction [32, 33]. The probability of erectile dysfunction is positively associated with the duration of the disease, dyslipidemia, hypertension, diabetes, obesity, metabolic syndrome, depression, and a sedentary lifestyle. However, psoriasis itself is an independent risk factor for erectile dysfunction [34]. Anogenital psoriasis has a significant impact on patients' sexual activity. In turn, sexual contact has been shown to exacerbate the skin process in at least one-third of patients, thereby worsening existing sexual dysfunction [35].

Some authors claim that psoriatic genital lesions do not inherently affect sexual function in women. However, they argue that these lesions are often accompanied by significant sexual distress, characterized by dyspareunia and, in some cases, more profound sexual dysfunction, including anorgasmia [36].

## DIAGNOSTIC PRINCIPLES

The diagnosis of anogenital psoriasis is challenging, and recognition of the dermatosis may be delayed in isolated genital or perianal lesions [6]. Skin rashes, even if limited in area, may facilitate the timely diagnosis of genital and/or perianal psoriasis, which requires a comprehensive examination of the entire skin, including the dermal appendages, in patients presenting with anogenital rashes [7]. In some cases, histologic examination is used [6]. The histological pattern of anogenital psoriasis is not always indicative of the disease on smooth skin, with the formation of typical interpapillary acanthosis [6]. In such cases,

histological examination is imperative to exclude genital squamous cell neoplasms of a high degree of malignancy, which may sometimes mimic dermatoses, particularly psoriasis. Furthermore, it is essential for the differential diagnosis of other dermatoses of the anogenital region, such as localized neurodermatitis [7, 37].

Dermatoscopy is used as an additional diagnostic tool [38]. The most characteristic dermatoscopic signs of psoriasis, irrespective of localization and genitalia, are vascular symptoms [39]. These signs most often manifest as round or punctate vessels, which exhibit a diffuse and uniform arrangement within the examined rashes [38]. The morphological basis of this phenomenon is the dilatation of vessels within the elongated papillae of the dermis.

## ASSESSMENT OF THE SEVERITY OF ANOGENITAL PSORIASIS

Scales are actively being developed to assess the severity of anogenital psoriasis. One of these, the Static Physician's Global Assessment of Genitalia (sPGA-G), is a six-point numerical scale for assessing erythema, infiltration, and exfoliation in the anogenital area [40]. Symptoms are assessed on the clitoral hood, labia majora, labia minora, and perineum in females and on the penis, scrotum, and perineum in males, excluding rashes on the pubic skin, inguinal folds, perianal area, and gluteal fold.

The Genital Psoriasis Symptoms Scale (GPSS) is a tool designed to assess the symptoms of psoriasis from the patient's perspective [41]. This scale is frequently used in conjunction with the GenPs-SFQ (Genital Psoriasis Sexual Frequency Questionnaire), which is designed to evaluate sexual limitations associated with anogenital psoriasis [42].

## THERAPEUTIC PRINCIPLES

The therapeutic principles for anogenital psoriasis remain underdeveloped, with recent systematic reviews addressing treatment methods for both anogenital psoriasis [43] and inverse psoriasis [44]. Conventional treatment for this condition involves topical corticosteroids, calcineurin inhibitors, and calcipotriol preparations. Recently, the efficacy of phosphodiesterase-4 inhibitors and genetically engineered biological agents, including IL-17 inhibitors, has been discussed [9].

Topical corticosteroids are considered first-line treatment for genital and inverse psoriasis (B and C grades of recommendations, respectively) [45]. For example, the use of 0.005% fluticasone propionate, a medium-potency corticosteroid, twice daily for two weeks is associated with at least a 50% improvement in the rash of intertriginous psoriasis [46]. The achieved therapeutic effect was maintained with further use of the product in an intermittent regimen, administered once a day, two days a week. In general, the authors recommend low or medium-potency corticosteroids for anogenital psoriasis [9, 47]. However, in cases of treatment resistance, the use of high-potency medications is permissible.

In a double-blind, randomized, controlled study, the use of 0.1% betamethasone valerate once daily for 28 days was associated with a greater reduction in psoriasis area and severity scores (modified PASI) compared with 0.005% calcipotriol and 1% pimecrolimus (86.4% vs. 62.4% and 39.7%, respectively) [48].

Given the thin skin and numerous pilosebaceous follicles in the genital area, it is recommended that corticosteroids be used for not more than four weeks [9] and the treatment be continued with other medications, such as topical calcineurin inhibitors or calcipotriol preparations, to prevent adverse effects such as atrophy, telangiectasias, and striae.

Atopic dermatitis is the indication for the prescription of topical calcineurin inhibitors (tacrolimus and pimecrolimus). However, these medications also play an important role in the treatment of psoriasis in specific anatomical areas (anogenital and facial regions) and inverse psoriasis (grade B recommendation) [9, 49, 50]. The efficacy of these agents in anogenital psoriasis has been confirmed by several studies and systematic reviews [50]. Thus, the use of tacrolimus (0.1% ointment twice daily) in inverse psoriasis allows achieving a clinically significant effect after eight days of treatment. Additionally, a substantial improvement has been observed according to the Physician Global Assessment (PGA) after eight weeks of therapy [51]. Additionally, the drug has been shown to have a significant effect after four weeks of use in patients with psoriatic balanitis and lesions of the penile shaft and scrotum [52]. The use of pimecrolimus (1% cream twice daily) resulted in a significant improvement of the skin process in 71% of patients after eight weeks of therapy [53] (Fig. 2). Once disease control is achieved, topical calcineurin inhibitors are recommended for use as proactive therapy in an intermittent regimen (once a week) [49].

Importantly, the effects of this group of medications are associated with the suppression of T-lymphocyte activity and the secretion of cytokines, including IL-2 and IFN-γ [55]. These medications demonstrate no effect on collagen synthesis, and there is no risk of skin atrophy [54]. Mild pruritus and burning are reported as adverse events. Topical calcineurin inhibitors are generally considered to be an effective and safe treatment for anogenital psoriasis. They may be used alone, sequentially, or in combination with topical corticosteroids and as supporting therapy [50].

Calcipotriol preparations are regarded as a long-term therapy for anogenital psoriasis and inverse psoriasis (grade C recommendation). Their long-term use, including in proactive therapy, is possible. However, the risk of adverse events associated with calcipotriol is slightly higher than that associated with topical calcineurin inhibitors [56]. Consequently, calcipotriol is often used as part of combination products, such as fixed combinations with betamethasone

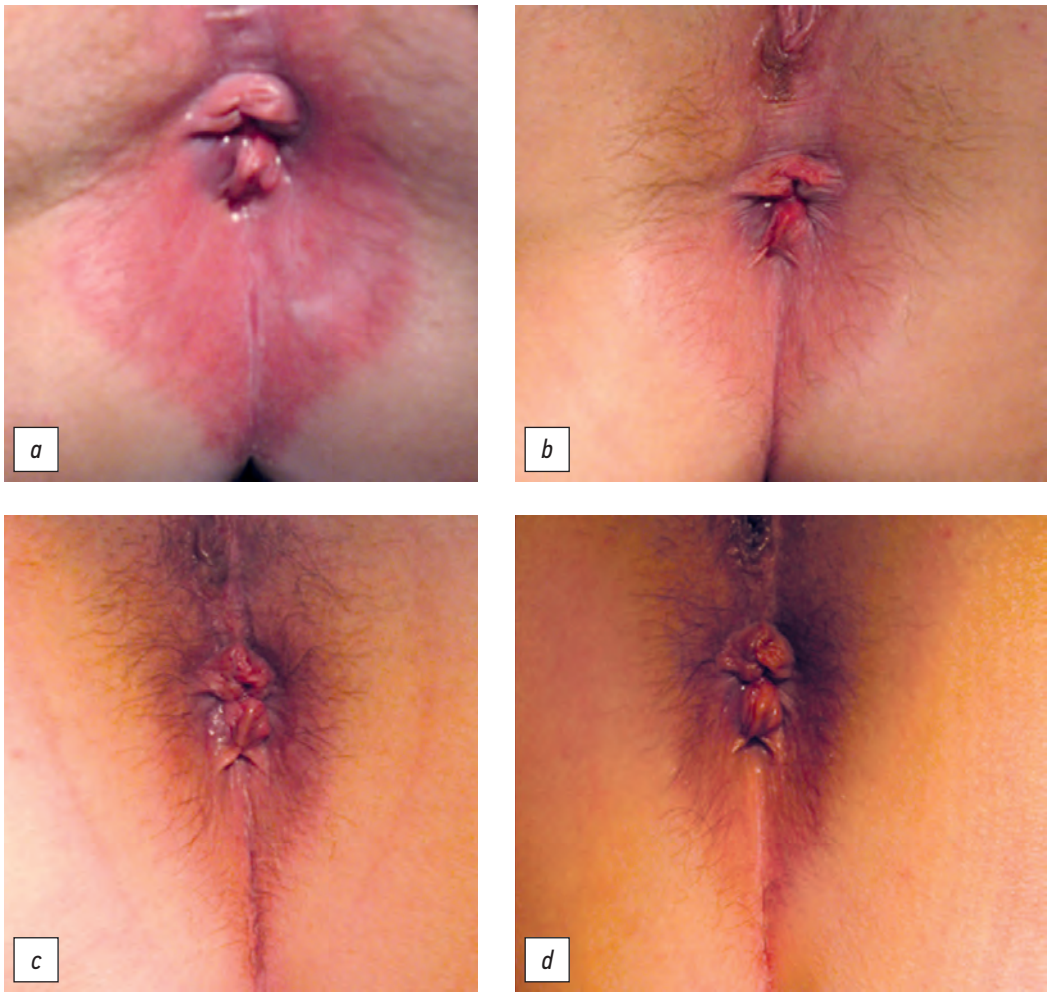


**Fig. 2.** Isolated psoriatic lesion of the perianal region. Features of clinical picture with a bright slightly infiltrated plaque (*a*) and dynamics of the process against the background of consecutive application of topical corticosteroids of medium potency for 3 weeks (*b*), calcineurin inhibitors for 4 weeks daily (*c*) and further in an intermittent mode (*d*).

dipropionate [57]. This combination allows for the synergy of the effects of the active ingredients and ensures a higher efficacy of the therapy with a reduced risk of adverse events [58, 59] (Fig. 3).

Data from clinical studies suggest that phosphodiesterase-4 inhibitors may be a safe and effective alternative to topical corticosteroids and calcineurin inhibitors for the treatment of mild to moderate atopic dermatitis and psoriasis (grade C recommendation) [60, 61]. The effects of crisaborole are mediated by increasing intracellular levels of cyclic adenosine monophosphate and suppressing the secretion of proinflammatory cytokines, including tumor necrosis factor alpha (TNF-α), IFN-γ, IL-1β, IL-2, IL-5, and IL-6 [62]. A randomized, double-blind, placebo-controlled study showed that treatment with 2% crisaborole ointment (applied twice daily) for four weeks in patients with psoriasis of specific anatomic areas, including the anogenital area, resulted in a 66% improvement (compared with 9% in the placebo group) [63]. The positive changes were sustained during the subsequent four weeks of treatment, with 81% of patients demonstrating significant improvement and 71% experiencing rash resolution. No adverse events were reported during treatment. The efficacy and safety of crisaborole treatment were further substantiated in another clinical study [64].

When prescribing systemic agents such as methotrexate, cyclosporine, and genetically engineered biological agents for the treatment of patients with limited inverse psoriasis or anogenital psoriasis, the risk-benefit ratio of such therapy should be evaluated [43]. Traditionally, the so-called rule of ten (psoriasis-affected body surface area [BSA] ⩾10%, PASI ⩾10, or dermatologic quality of life index [DLQI] ⩾10 [65] or a combination of PASI and DLQI ranges [66]) has been used to determine the prescription of systemic medications and to assess the disease severity. The 2019 Delphi consensus discussed approaches to assessing psoriasis severity, with three criteria proposed as indications for prescribing systemic therapy, each with independent significance. These criteria include BSA >10%, lesions of specific anatomical areas (scalp, genitalia, palms, soles, or nails, as well as visible areas), and the ineffectiveness of topical therapy [67]. In addition, several national clinical guidelines for the

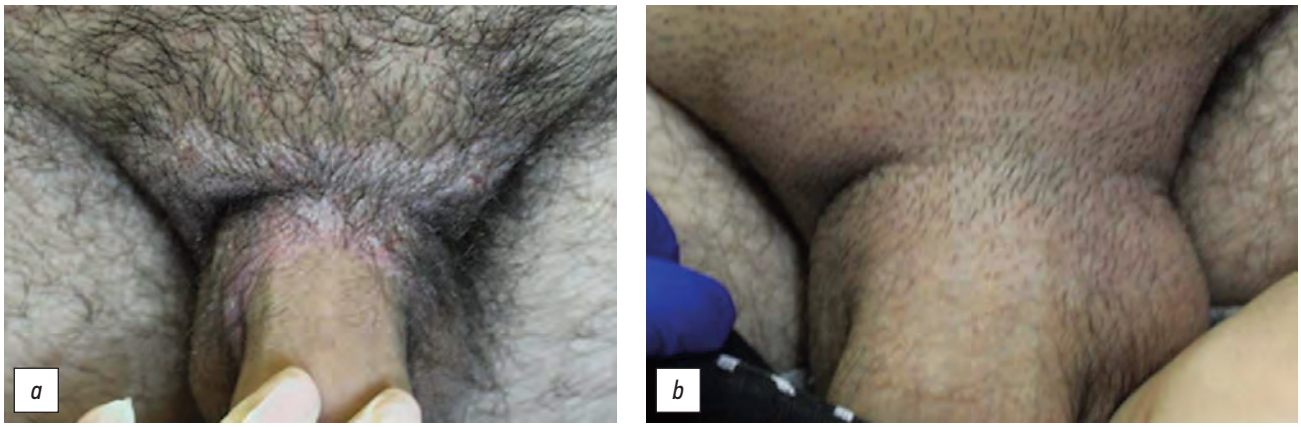


**Fig. 3.** Psoriatic lesion of the pubis and penis. Features of the clinical picture with weakly expressed desquamation (*a*) and the dynamics of the process against the background of treatment with the combined preparation of calciptoriol and betamethasone for 4 weeks (*b*).

treatment of psoriasis emphasize the assessment of lesions in specific anatomical areas, along with their functional or psychosocial impact, even in cases of relatively limited skin lesions, in determining disease severity [68].

There are no large-scale clinical studies of the efficacy and safety of traditional systemic drugs for the treatment of anogenital psoriasis. There are only isolated reports on the efficacy of methotrexate, mycophenolate mofetil, and dapsone [6, 9, 65, 69], which provide no indication of the priority of a particular type of treatment [70]. Furthermore, there are reports on the use of antifungals, antibacterials, antipsychotics, and antihistamines [43].

Tofacitinib, a potent selective inhibitor of Janus kinases (JAK), namely JAK1, JAK2 and JAK3, and to a lesser extent tyrosine kinase 2 (TYK2), has anti-inflammatory and immunomodulatory effects by inhibiting the signaling of IL-2, IL -4, IL -6, IL -7, IL -15, and IL -21, as well as INF-α and INF-γ [71]. The product is indicated for the treatment of rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis [72]. It was used at a dose of 5 mg twice daily in combination with narrowband ultraviolet phototherapy three times a week to treat a patient with a combination of inverse psoriasis, alopecia areata, and vitiligo [73]. This combination therapy was supported by studies showing that JAK inhibitors may be more effective with phototherapy [74, 75]. Adverse events included several episodes of headache and flu-like symptoms, which led the patient to discontinue tofacitinib after one month.

In recent years, the potential of genetically engineered biological agents in the treatment of genital and perianal psoriasis and their impact on quality of life and sexual function has been widely discussed [76, 77]. There are reports on the use of the IL-17 inhibitors (ixekizumab and secukinumab) [77, 78], the TNF-α inhibitors (adalimumab, certolizumab, and etanercept), and the IL-12/23 inhibitors (uxekinumab) [76] in patients with anogenital psoriasis.

Research has demonstrated the efficacy of ixekizumab and secukinumab in the treatment of moderate and severe anogenital psoriasis [77]. The treatment has been shown to result in the resolution of rashes, a reduction in pruritus intensity, and improvements in sexual health and quality of life [78–82].

A comparison of ixekizumab (80 mg every two weeks after an initial dose of 160 mg) and secukinumab (300 mg subcutaneously at weeks 0, 1, 2, 3, and 4, followed by every four weeks) in patients with severe or moderate anogenital psoriasis demonstrated their similar efficacy with rapid improvement of the skin process (25% and 23% of patients, respectively) within two weeks, complete clearance of genital skin by week 24 of therapy (68% and 65% of patients, respectively), and normalization of sexual life [77].

Tildrakizumab, an IL-23 inhibitor, is recommended for the treatment of moderate to severe plaque psoriasis. A retrospective analysis was performed of the efficacy of the drug in seven patients with anogenital psoriasis in specific anatomical areas [83]. The drug was administered at a dose of 100 mg on day 0, followed by four weeks of treatment and then every 12 weeks. This resulted in a significant decrease in sPGA-G, from 3.3 to 0.2, by week 28 of therapy. Other authors have also expressed optimism regarding the drug's potential for treating psoriasis with genital and perianal lesions [84]. Risankizumab, another agent in this group, is proposed to be used in isolated genital psoriasis [85].

Hong et al. [9] conducted an analysis of the efficacy of various therapeutic methods for anogenital psoriasis and proposed an algorithm for patient management. According to this algorithm, the treatment of patients with isolated anogenital lesions should be started with topical corticosteroids, followed by calcineurin inhibitors or calcipotriol preparations. In cases where these drugs prove ineffective, the prescription of phosphodiesterase-4 inhibitors is considered. In patients with widespread skin rashes and genital or perianal involvement, immediate initiation of systemic agent therapy is recommended, with individualized consideration of genetically engineered biological agents or methotrexate.

In the treatment of patients with anogenital lesions in any dermatosis, including psoriasis, therapy aimed at

normalizing hygiene and reducing friction and pressure should be initiated to prevent the process exacerbation [7, 43]. Patients should use mild, neutral pH products suitable for cleansing the thin genital skin and avoid excessive hygiene. To cleanse the anogenital area, it is necessary to use products that restore the skin barrier. Syndet Xemose, which contains Uriage thermal water, Cerasterol 2F, ultra-soft soap-free and fragrance-free surfactants with a physiological pH may be used for this purpose. Emollients should be used in the anogenital area when there are indications, such as dry skin or exfoliation. However, oily, film-forming ointments may increase inflammation and pruritus. Furthermore, the use of agents comprising keratolytic components, such as urea, salicylic acid, lactic acid, or fruit α hydroxy acids, in the anogenital area appears to be incompatible with conventional basic therapy. Presently, the use of topical agents to modulate the secretion of antimicrobial peptides [86], which play a substantial role in the pathogenesis of dermatosis, is a viable option [87]. For example, cathelicidin peptide LL-37, which is secreted in the skin by keratinocytes, granulocytes, T cells, and mastocytes, induces neutrophil chemotaxis and enhances T helper type 17 activity. This process occurs through the signaling of Toll-like receptors and the secretion of cytokines, TNF-α, INF-γ, and IL-36 [87]. The URIAGE Dermatology Laboratory has developed and patented an AGHS plant extract designed to modulate the action of the cathelicidin peptide LL-37. An *in vitro* study showed that administration of the extract in the presence of LL-37 resulted in suppression of IL-17 and IL-23 production. LL-37, a cathelicidin modulator, is an active ingredient in Xemose PSO Soothing Concentrate Cream, which helps to restore the protective dermal barrier. In addition to the modulator LL-37, Xemose PSO contains Cerasterol 2F, which restores the skin barrier, Uriage thermal water, which has an anti-inflammatory effect, and shea butter, which has an anti-inflammatory and antipruritic effect. Xemose PSO has a creamy, light texture that allows for rapid absorption and use on thin and delicate skin areas. A clinical evaluation of the effects of Xemose PSO Cream in combination with systemic or topical treatments showed that patients experienced a significant reduction in exfoliation, infiltration and erythema. Importantly, this integrated treatment approach contributed to a 68% improvement in patients' quality of life, according to dermatologists.

The management of pruritus in patients with anogenital lesions, including psoriasis, is of equal significance. Chronic pruritus, even when only moderate, has been identified as the most distressing symptom of anogenital dermatoses and a risk factor for nosogenic anxiety and depressive disorders [10, 27, 88, 89]. Pruritus is perceived by cutaneous nerve fibers called pruriseptors, which are activated by histamine and other biological substances [89]. Long-lasting, persistent pruritus is believed to be non-histaminergic and is associated with the activation of G-protein coupled receptors, including protease-activated receptors (PARs) and ion channels, such as transient receptor potential receptors ankyrin, and vanilloid receptors [90].

The management of pruritus involves a variety of strategies. These include the treatment of psoriasis, the restoration of skin barrier function, and the use of products containing antipruritic components. If these approaches are ineffective, the use of topical corticosteroids, calcineurin inhibitors, antidepressants, gabapentin, and serotonin reuptake inhibitors may be considered [91]. Modulators of various PARs are actively being developed [92]. The Uriage Dermatology Laboratory offers a PAR-2 receptor modulator that is included in the Pruriced Gel and Cream for external use. The former is recommended for use in the folds and anogenital area. In addition to the PAR-2 receptor modulator, the gel contains 8% calamine, glycine, chamomile extract, and 30% Uriage thermal water. The combination of these agents provides a reduction in pruritus intensity and anti-inflammatory effects. Clinical observations have shown that the use of agents containing PAR-2 receptor modulators results in a rapid and significant reduction in pruritus intensity. *In vitro* studies have shown inhibition of cytokine secretion, including IL-1β and TNF-α, as well as matrix metalloproteinases 24 and 9.

## CONCLUSION

There are few publications evaluating the epidemiology, clinical manifestations, diagnostic approaches, and treatment of anogenital psoriasis. The literature review revealed that although the anogenital area is often involved in patients with severe and inverse psoriasis, data on the frequency of such lesions require clarification. With regard to predominant or isolated involvement of the genital and perianal areas, the data on such variants of dermatosis are extremely contradictory and limited. The pathomorphosis of anogenital psoriasis is attributable to anatomical and physiological characteristics of the affected area, as well as irrational topical therapy. This phenomenon contributes to diagnostic errors in psoriasis of this area. The results of histological examination are not always sufficient to address this issue, as the manifestation of psoriasis in this area does not always exhibit a characteristic pattern of the disease on smooth skin, accompanied by typical interpapillary acanthosis. Subjectively significant localization, a prolonged course of dermatosis, and pruritus are prerequisites for the anxiety and depressive nosogenic reactions and sexual dysfunction, especially in young patients. This emphasizes the medical and social importance of anogenital psoriasis.

Treatment options for patients with anogenital psoriasis are not well established. Conventional treatment for this condition involves topical corticosteroids, calcineurin inhibitors, and calcipotriol preparations. There are no large-scale clinical studies of the efficacy and safety of traditional

systemic drugs, such as methotrexate or cyclosporine, for the treatment of anogenital psoriasis. In recent years, the potential of genetically engineered biological agents in the treatment of genital and perianal psoriasis and their impact on quality of life and sexual function has been widely discussed. There are reports of high efficacy of IL-17 inhibitors (ixekizumab and secukinumab) and IL-23 inhibitors (tildrakizumab and risankizumab) in dermatosis of this localization. In addition, the experience with the phosphodiesterase-4 inhibitor (crisaborole) and the JAK inhibitor (tofacitinib) is being discussed.

Topical adjuvant therapy is of equal importance in the management of patients with anogenital lesions. This therapy is aimed at restoring the skin barrier, enhancing the anti-inflammatory effects of drugs, and controlling pruritus. The URIAGE Dermatology Laboratory has developed a series of active ingredients incorporated into medical cosmetics to achieve these objectives, including the cathelicidin modulator LL-37 and the PAR-2 receptor modulator.

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