2022 European guideline for the management of balanoposthitis

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Abstract

Balanoposthitis describes inflammation of the glans penis and prepuce and is caused by a range of disparate conditions including infection, dermatoses and premalignancy. The main objectives of this guideline are to aid recognition of the symptoms and signs and complications of penile skin conditions and to offer recommendations on the diagnostic tests and treatment for a selected group of these conditions.

What is new in the 2022 guideline

- Amended management for infective balanitis to provide clear guidance for Group A streptococcal infections
- Management of ongoing Lichen sclerosus to include circumcision and supportive management to reduce the recurrence of genital herpes and warts
- Additional regimens for Zoonoid change
- Use of calcineurin inhibitors in management and risk of premalignancy
- Change of nomenclature from Premalignant conditions to Penile Intraepithelial neoplasia (PeIN)

Introduction

The main objective of this guideline is to aid recognition of the symptoms and signs and complications of penile skin conditions that may present to a variety of clinical specialties in Europe, including dermatology, sexual health and urology[1] and provide recommendations on therapeutic treatment and management. It is not intended as a comprehensive review of the treatment of all forms of balanoposthitis. In view of the breadth of the topic, this guideline concentrates on the following selected group of conditions, which were identified as being either common or significant[1] and which may be managed by clinicians primarily practising in dermato-venereology (or sexual health) clinics, either alone or in conjunction with other specialists or primary care.

- Candidal balanoposthitis
- Anaerobic infection
- Aerobic infection
- Lichen sclerosus
- Lichen Planus Zoon's (plasma cell) balanitis
- Psoriasis and circinate balanitis
- Seborrheic dermatitis
- Irritant /Allergic eczema
- Fixed drug eruptions
- Pre malignancy or suspected malignancy

It is not intended as a comprehensive review of the treatment of all forms of balanoposthitis. It is aimed primarily at managing penile conditions in people aged 16 years or older.

Aetiologies

Balanitis describes inflammation of the glans penis, and posthitis is inflammation of the prepuce. In practice both areas are often affected and the term balanoposthitis is then used. It is a collection of disparate conditions with a similar clinical presentation and varying aetiologies affecting this particular anatomical site (see table 1). Balanitis is uncommon after circumcision[2] and in many cases preputial dysfunction is a causal or contributing factor.

Table 1 Conditions affecting the glans and prepuce[3,4,5]

Infectious	Inflammatory Dermatoses	Premalignant Penile intraepithelial neoplasia (PeIN) (Clinical appearances)
Candida albicans	Lichen sclerosus	Bowen's disease
Group A Streptococci	Lichen planus	Bowenoid papulosis
Anaerobes	Psoriasis and circinate balanitis	Erythroplasia of Queyrat
Trichomonas vaginalis	Zoon's balanitis	
Herpes simplex virus	Eczema (including irritant, allergic and seborrheic)	
Human papillomavirus	Allergic reactions (including fixed drug eruption and Stevens Johnson Syndrome)	
Syphilis		

Other, rarer dermatoses can cause balanoposthitis but are not included in this table. Infections, especially with candida, may often be secondary to primary inflammatory dermatoses.

General Management of the Patient with Balanoposthitis[4,6,7]

Clinical Features

Symptoms and signs vary according to aetiology and specific conditions are covered in more detail individually. Descriptions of the typical appearances of specific conditions are given separately in the management section.

Diagnosis

- Balanitis and balanoposthitis are descriptive terms covering a variety of unrelated conditions, the appearances of which may be suggestive but should never be thought to be pathognomonic. Biopsy[8] is sometimes needed to exclude pre-malignant disease.
- The following investigations are intended to aid diagnosis in cases of uncertainty[9] 2,D
    - Sexual history taken with specific questioning on sexual risk taking
    - Full routine screening for other sexually transmitted infections (STIs) including HIV as indicated by sexual history and presentation and in line with guidelines[10] – for example:
        - HSV nucleic acid amplification test (NAAT) - if ulceration present.
        - *Treponema pallidum* (TP) NAAT (or alternative test as per local availability) if an ulcer is present. Alternatively check syphilis serology and repeat after 3 months.
        - Screening for *Chlamydia trachomatis* infection / non-specific urethritis if a circinate-type balanitis is present
    - Sub-preputial swab for *Candida spp* and bacterial culture - may be useful to exclude an infective cause or superinfection of a skin lesion or dermatosis
    - Urinalysis for glucose - appropriate in some cases but especially if candidal infection is suspected.

- Dermatology opinion for dermatoses and suspected allergy
- Biopsy - if the diagnosis is uncertain and the condition is persistent[7,8]

Management

The aims of management are to minimise sexual dysfunction, to minimise urinary dysfunction, to exclude penile cancer, to treat pre-malignant disease, and to diagnose and treat sexually transmitted diseases. Predisposing factors for balanoposthitis include poor hygiene, over-washing, non-retraction of the foreskin, and some medical conditions such as diabetes mellitus. Many cases of balanoposthitis seen in practice are a simple 'intertrigo' i.e. inflammation between two skin surfaces with bacterial or fungal overgrowth. Good personal hygiene, washing daily, avoiding irritants (such as soap), and keeping the foreskin retracted until the glans penis is dry (while advising the patient about the risk of paraphimosis especially if the prepuce is tight) can be effective, but compliance may be challenging.

General Advice (2,D)

- Avoid soaps while inflammation is present[6,11]
- Advise about risks of condom failure if creams are being applied to the glans or foreskin
- Patients should be given a detailed explanation of their condition with particular emphasis on any implications for their health (and that of their partner where a sexually transmissible agent is found[12]).

Management of specific conditions

Infective balanoposthitis

A range of infective agents have been isolated more frequently in patients presenting with balanoposthitis and may not be easily differentiated by clinical findings[13]. These include viral infections such as Human papillomavirus (HPV)[14] and Herpes simplex virus (HSV), fungal infections including a variety of *Candida spp,* and bacterial infections such as *Staphylococcus spp[15], Streptococcus spp*[15, 16, 17]. Asymptomatic carriage of organisms may also be associated with subclinical inflammation and a greater risk of Human Immunodeficiency Virus (HIV) infection[18]. Other sexually transmitted infections have been reported as causing balanoposthitis, particularly Syphilis[19], and Chlamydia trachomatis (see Circinate balanitis), and there are case reports linking *Trichomonas vaginalis* [20].

Candidal balanoposthitis (less than 20% of cases)

Clinical Features

- Symptoms: erythematous rash with soreness and/or itch
- Appearance: blotchy erythema with small papules which may be eroded, or dry dull red areas with a glazed appearance.

Older age and diabetes have been identified as risk factors[21]

Diagnosis

- Sub-preputial culture - although isolation of candida on culture does not prove causality, as it may represent opportunistic infection of other underlying dermatoses
- Consider urinalysis for glucose
- Investigation for other causes e.g. HIV or other causes of immunosuppression if balanitis is severe or persistent
- Many dermatologists believe that this primary diagnosis is very rare even in HIV infection (apart from in diabetes mellitus) and that candida is almost always an opportunistic pathogen, signifying an underlying dermatosis.

Management

Recommended regimens[22]

- Clotrimazole cream 1%[21,23](1,C) Apply twice daily for 7-14 days.
- Fluconazole 150mg orally[23] (1,C) - if symptoms severe

Alternative regimens

- Miconazole cream 2%[22,24](2,B)
- Nystatin cream[24] 100 000units/gm - if resistance suspected, or allergy to imidazoles (2,B)
- Topical imidazole with 1% hydrocortisone - if marked inflammation is present[22] (2, D)
- Although there has been an increase in reports of drug resistance in serious candidal infection, there is no new evidence pertaining to treatment of candidal balanoposthitis.

Sexual partners

Routine treatment is not required.

Follow up

Not required unless symptoms and signs are particularly severe or an underlying problem is suspected.

Anaerobic infection[18, 25]

Clinical Features

- Symptoms: foul smelling sub preputial inflammation and discharge, in severe cases associated with swelling and inflamed inguinal lymph nodes
- Appearance: preputial oedema, superficial erosions; milder forms also occur.

Diagnosis[8]

- Diagnosis can be made on the clinical presentation; subpreputial culture can be considered to exclude other bacterial infection
- Subpreputial NAAT for *Trichomonas vaginalis*
- Herpes simplex virus NAAT from subpreputial swab if ulceration present

Management

- Advice about genital hygiene.
- Circumcision may be required in recurrent cases or if phimosis is present

Recommended regimen

- Metronidazole 400 - 500mg twice daily x 1 week (1,D)

Alternative regimen (2,D).

- Amoxicillin + clavulanic acid 250/125mg three times daily x 1 week

Aerobic infection.

Streptococcus spp (B and D) and Staphylococcus aureus have been isolated from men with balanitis[15, 16,17]but may be commensals or superinfection and their presence does not imply causality. Group A Streptococci have been reported as causing balanitis[17] and are potentially sexually transmissible (either via the vaginal or oral route).

Clinical Features

- Variable inflammatory changes including erythema +/- oedema

Diagnosis

- Clinical appearance
- Subpreputial culture - *Streptococcus spp (A, B and D) and Staphylococcus aureus* have been isolated from men with balanitis[15, 16, 17]. Other organisms may also be involved.

Management

- Treatment can be topical for mild symptoms
- Severe cases may require systemic antibiotics.

Recommended regimens

Severe cases may require systemic antibiotics while awaiting culture results[23]

- If symptoms are severe treat with 10 days of penicillin to cover for Group A Streptococci (1, D)

Alternative regimens (2,D)

- Oral antibiotics dependent on the sensitivities of the organism isolated.

- Mupirocin ointment 2-3 times per day for 7-10 days
- Clobetasone butyrate with Nystatin and Oxytetracycline cream once or twice daily for 7-10 days

Sexual Partners
- Case reports suggest Group A streptococci may be transmitted by fellatio[17]

Sexually Transmitted Infections (STIs)
Cases of balanoposthitis have been described with:
- Syphilis[19]
- Human papillomavirus[14]
- Herpes simplex virus[26]
- *Trichomonas vaginalis*[20]

Management is as per specific guidelines[9]

Lichen sclerosus [4,6, 27,28,29,30,31]

Aetiology

An inflammatory scarring skin condition: although an autoimmune pathogenesis has been postulated, it may be due to chronic occluded contact with urine in the uncircumcised[32]. The condition occurs in all ages. It is probably responsible for many cases of phimosis in childhood[6]. Obesity, congenital and acquired anatomical abnormalities (hypospadias), piercing and urological surgery are predisposing factors.

Clinical Features[6, 27, 28, 29, 30, 31]

Symptoms
- Itching, soreness, splitting, haemorrhagic blisters, dyspareunia, problems with urination including post micturition micro-incontinence or dribbling.
- May be asymptomatic.

Signs
- Typical appearance: lichenoid (lilac) balanoposthitis with white patches on the glans, often with involvement of the prepuce. There may be subtle or florid Zoonoid inflammation and also haemorrhagic vesicles, purpura and rarely blisters and ulceration. Architectural changes include blunting of the coronal sulcus, destruction of the frenulum, phimosis or 'waisting' of the prepuce (constrictive posthitis), and meatal thickening and narrowing.

Complications
- Phimosis and paraphimosis
- Urethral stenosis
- Penile intraepithelial neoplasia (PeIN) and malignant transformation to squamous cell carcinoma. The published risk ranges from 0-12.5%[6, 29, 30, 33]. In established penile cancer the association with lichen sclerosus is thought to be about 50% (the other 50% being associated with HPV)[34]
- Extra-genital disease can occur.
- In contrast with females, perianal disease is uncommon.

Diagnosis
- Typical clinical features
- Biopsy: this initially shows a thickened epidermis which then becomes atrophic with follicular hyperkeratosis. This overlies a band of dermal hyalinisation with loss of the elastin fibres, with an underlying perivascular lymphocytic infiltrate. A negative biopsy does not exclude lichen sclerosus, and a positive biopsy does not exclude squamous cell carcinoma or PeIN elsewhere. The choice of the area biopsied is important both in terms of the risks and in getting an adequately representative sample from any

persistent areas of hyperkeratosis, erosion or erythema, or new warty or papular lesions. Several mapping biopsies may be required if there is extensive abnormality[27]. Histological interpretation can be difficult and needs clinico-pathological correlation.

Management [27, 28, 29, 30, 35]

Recommended regimens

- Soap free washing, avoidance of contact with urine e.g by application of barrier preparations such as petroleum jelly, weight loss, removal of genital jewellery (1D) [29, 30, 31, 35, 36]
- Ultrapotent topical steroids[27, 28, 29, 30, 31, 37, 38] (e.g. clobetasol proprionate) applied twice daily for a month then ceased and replaced with a barrier preparation. 50-60% of patients are treated successfully in this way[27, 30, 31]. Intermittent use of potent steroid creams to maintain remission is not encouraged as circumcision is indicated. A double-blind study in children showed response to topical mometasone furoate particularly in early cases without scarring[39]. (1,A)
- Patients with a history of genital warts should be warned about the risk of a relapse associated with the use of potent steroid creams (adjunctive HPV vaccination can be considered[40]). Consider prophylactic aciclovir or in patients with recurrent genital herpes simplex infection (2,D).
- Secondary bacterial or candidal infection should be treated

Alternative regimens

- Although topical calcineurin inhibitors have been claimed to be efficacious[37, 41] (pimecrolimus applied twice daily, 2,A). Stinging after initial application may occur and can be minimised by use of emollients. There is concern about the development of malignancy[42] in case of continuous long-term use, although there have been no systematic reviews assessing the risk in lichen sclerosus[36].
- Circumcision is indicated for a) failed topical medical treatment or b) persistent requirement for daily topical treatment (2,D).[27, 29, 30]
- Surgery may be indicated to address symptoms secondary to persistent phimosis or meatal stenosis, and urethral disease (2,B) This may include circumcision, meatotomy, glans resurfacing, urethroplasty and bariatric surgery. [4, 27, 28, 29, 30, 31, 35, 43, 44]

Follow up (2,D) [27, 29, 30, 35]

- Patients deemed to be cured by medical or surgical treatment can be discharged with the caveat that although the risk of recurrence is low (especially after circumcision), urethral disease and neoplastic change can occur so they should keep an attentive watch on their genitalia and report any changes promptly to their GP.
- Patients should be reviewed if further symptoms or signs develop (especially if the patient gains weight or develops a neo-foreskin).

Lichen planus[7]

Aetiology

Lichen planus is an inflammatory disorder with manifestations on the skin, genital and oral mucous membranes. More rarely it affects the conjunctiva and oesophagus. It is an inflammatory condition of unknown pathogenesis, but it is thought to have an immunological basis. An association with hepatitis C is controversial[45]. Certain drugs, most frequently Angiotensin Converting Enzyme-inhibitors, beta blockers, non-steroidal anti-inflammatory drugs (NSAIDs), thiazide diuretics, and biologics may cause lichen planus like eruptions[4, 46, 47].

Clinical Features

- Symptoms: Change in appearance, rarely associated with itch and soreness / dyspareunia. It may also be asymptomatic.
- Clinical appearance: Purplish well demarcated plaques (can be on glans and prepuce and on the shaft of the penis), or alternatively erosive or annular lesions on the mucosal surfaces.
- Natural history: Mucosal lichen planus is often a chronic condition with remissions and exacerbations, in contrast to cutaneous lichen planus which tends to resolve spontaneously after 12-18 months.

Diagnosis

- Clinical features of purplish lesions, or supporting evidence of lichen planus lesions elsewhere on the body (e.g. Wickham's striae on the oral mucosa). This particularly includes the mouth in cases of erosive (penogingival) disease.
- Biopsy: irregular saw-toothed acanthosis, increased granular layer and basal cell liquefaction. Band-like dermal infiltrate (mainly lymphocytic). The condition may very rarely be associated with pre-cancerous change[7, 48]

Management[7, 49, 50, 51]

General advice

- Avoidance of irritants like soaps and shower gels
- The use of lubricants may be helpful in case of dyspareunia

Recommended regimen

- Moderate to ultrapotent topical steroids (e.g. clobetasol proprionate ointment), depending on severity (for both mucosal and cutaneous disease) [49, 50, 51]. (1,B)

Alternative regimens

- Topical calcineurin inhibitors can be efficacious[49, 50,51,52](pimecrolimus or tacrolimus applied twice daily (1, B). Stinging after initial application may occur and can be minimised by use of emollients. There is still concern about the risk of malignancy in case of continuous long-term use[42, 53, 54,55]
- Topical and oral ciclosporin can be used for erosive disease [50, 56, 57](2,C)
- In severe cases oral prednisolone or acitretin may be necessary (2, D)[58].
- Circumcision: May be the treatment of choice for some cases of erosive lichen planus[59] (2,D)

Follow up

- Atypical or persistent disease should be referred for a specialist dermatology opinion including biopsy
- Patients should be advised to contact their physician if the appearances change. (1,D)

Zoon's (plasma cell) balanitis[7]

Aetiology

Zoon's balanitis is a disease of the uncircumcised penis in patients aged 40 years or older. It is thought to be due to irritation, partially caused by urine, in the context of a 'dysfunctional prepuce'. It is generally regarded as a benign condition. Zoonoid inflammation (clinically and histologically) very frequently complicates other dermatoses, including precancer and cancer, but especially lichen sclerosus; this may be so common that it has been suggested that true Zoon's balanitis may actually be rare or not even exist at all[60].

Clinical Features

- Symptoms: Change in appearance. Rarely bloodstained discharge. Rarely dyspareunia

- Clinical appearance: Includes well-circumscribed orange-red glazed areas on the glans and the inside of the foreskin, with multiple pinpoint redder spots - "cayenne pepper spots". These are in a symmetrical distribution.

Diagnosis

- Clinical features of symmetrical, well demarcated, shiny erythema of the glans and foreskin; however, clinical distinction from other inflammatory and pre-malignant conditions is difficult and a high index of suspicion is recommended.
- Biopsy: early cases show epidermal thickening but this is followed by epidermal atrophy, at times with erosions. There is epidermal oedema (often mild) and a predominantly plasma cell infiltrate in the dermis with haemosiderin deposition and extravasated red blood cells[61]. Caveat: Zoonoid inflammation complicates other dermatoses and 'positive' biopsy findings do not confirm the diagnosis or exclude neoplasia. Penile biopsy should be performed if features are atypical or do not resolve with treatment. There are cases where even biopsies failed to identify pre-malignant disease. In case of doubt, repeated biopsies might therefore be useful.[61]

Management[7]

. Recommended regimens

- Hygiene measures
- Management of underlying dermatoses[60]
- Circumcision - this has been reported to lead to the resolution of lesions[62] (1, C)
- Topical steroid preparations - with or without added antibacterial agents e.g. Clobetasone butyrate with Nystatin and Oxytetracycline cream, applied once or twice daily.[63] (2,D)
- Antibacterial creams like mupirocin 2% ointment applied twice daily [64, 65, 66] (2, D)
- Topical calcineurin inhibitors[67, 68] (2,D) can be efficacious (pimecrolimus applied twice daily,). There is still concern about the risk of malignancy[55] in case of continuous long-term use. Stinging after initial application may occur and can be minimised by use of emollients.

Alternative treatments

- Laser ablation - this has been used to treat individual lesions[70, 71]. (2,D)

Follow up

Follow up is required for persistent disease to assess the use of steroids and review the diagnosis

Psoriasis[6],[72,73]

Clinical Features

- Symptoms: Change in appearance, soreness or itching.
- Appearance: Psoriasis on the glans in the circumcised male is similar to the appearance of the condition elsewhere, with red scaly plaques. Scaling is lost on the uncircumcised penis and the patches appear red and glazed.

Diagnosis

- Is supported by evidence of psoriasis elsewhere.
- Biopsy may be necessary, particularly in the case of a glazed appearance which can look similar to pre-malignant conditions such as Bowen's disease, extramammary Paget's disease and other inflammatory conditions. The typical histological appearances include parakeratosis and acanthosis with elongation of rete ridges. There are collections of neutrophils in the epidermis. Maceration and secondary infection can modify appearances.

Management [72,73,74]

Although the number of studies assessing treatment efficacy have increased in the last decade, there is still a paucity of high-quality evidence concerning the efficacy and safety of topical and systemic treatments for psoriasis affecting the groins and anogenital area (also known as inverse psoriasis). [74]

Recommended regimen

- Moderate potency topical steroids once or twice daily until resolved[73,74] (with or without antibiotic and antifungal) (1,C) Emollients

Alternative regimens

- Topical Vitamin D preparations (calcipotriol or calcitriol applied twice daily)[75] (2,C)
- Intermittent topical use of moderate to potent steroids with or without calcipotriol. Potent steroids may not be indicated[46] due to the risk of skin atrophy and bacterial superinfection (2,C).
- Topical calcineurin inhibitors have been used in small studies[73,74,76] but should not be used as first line therapy (2,D), and with caution in the uncircumcised..

Follow up

Review is required if the patient is not responding to treatment.

Circinate balanitis[6]

Aetiology

This characteristic presentation may occur in isolation or be seen in Reactive Arthritis – a post-infective syndrome, triggered by urethritis or enteritis in genetically predisposed individuals. The clinical picture consists of skin problems, joint problems and ocular problems, with other systems affected more rarely. There is overlap with psoriasis in some cases. Circinate balanitis has been reported in association with HIV infection.

Clinical Features

Signs

- Typical appearance: greyish white areas on the glans which coalesce to form "geographical" areas with an irregular white margin. It may be associated with other features of Reactive arthritis but can occur without.

Diagnosis

- On clinical appearance in association with other features of reactive arthritis
- Biopsy: spongiform pustules in the upper epidermis, similar to pustular psoriasis.

Management

Further Investigation

- Screening for STIs[9]. Syphilis can also give rise to similar features[77].
- Consider testing for HLAB27. A positive test can help confirm a diagnosis and provide important information about the risk of associated disease, such as urethritis, gastrointestinal disease and arthritis.

Recommended regimen

- See under 'Psoriasis' (1,C)
- Treatment of any underlying infection (1,C)

Sexual partners

- If an STI is diagnosed, the partner(s) should be managed according to the appropriate IUSTI guideline.

Follow up

- Only required for persistent symptomatic lesions.
- Associated STIs should be followed up as per appropriate guidelines[9].

Eczema[6]

Irritant / allergic balanitis-balanoposthitis[78,79]

Aetiology

Symptoms can be associated with irritants, such as more frequent genital washing with soap, a history of atopy, or exposure to topical agents suggesting delayed hypersensitivity. In a small number of cases a history of a precipitant may be obtained, and common allergens are often found in intimate hygiene products e.g. preservatives and fragrances.[80]

It may arise as a primary condition but is regularly encountered as a secondary phenomenon in the presence of a pre-existing genital dermatosis.

Clinical Features

- Appearance: ranges from mild non- specific erythema to widespread oedema of the penis.

Diagnosis

- Patch tests: referral to a dermatologist is useful if allergy is suspected.
- Biopsy: eczematous with spongiosis and non-specific inflammation.
- Culture: to exclude superinfection

Management[81]

General Advice (1, D)

- Avoidance of precipitants - especially soaps.[11]
- Use of low-allergy products
- Emollients - applied as required and used as a soap substitute.[11]

Recommended Regimen

- Hydrocortisone 1% applied once or twice daily until resolution of symptoms. (1, C)

Alternative Regimen

- In more florid cases more potent topical steroids may be required and may need to be combined with antifungals and/or antibiotics (2,C)
- Calcineurin inhibitors (tacrolimus/pimecrolimus)[82] (2,C)

Follow up

Not required, although recurrent problems are common and the patient needs to be informed of this.

Seborrheic dermatitis

Aetiology

Hypersensitivity to *Malassezia furfur (Pityrosporum ovale)*

Clinical features

Mild itch or redness - scaling is less likely at this site.

Diagnosis

Supported by classical findings at other sites (nasolabial folds, scalp, ears, eyebrows)

Management

There is a paucity of evidence specifically for balanitis, and low-quality evidence for other sites[83,84]

Recommended regimen

- Antifungal cream with a mild to moderate steroid(1,C).

Alternative regimens[6]

- Oral terbinafine may be effective[85](1,A)
- Oral azole e.g. itraconazole (2,C)
- Oral tetracycline (2,D)

Non- specific balanoposthitis [6]

Aetiology: Unknown

Clinical features: Non-specific erythema and irritation in the absence of an identified cause. Chronic symptomatic presentation with relapses and remissions or persistence. No unifying diagnosis and poor response to a range of topical and oral treatments.

Diagnosis:

- Failure to respond to maximal topical steroid and antifungal treatments (including potent steroids).
- Non-specific histology on biopsy.
- Non-specific histology at circumcision.
- No evidence of underlying infective cause (e.g. Chlamydia)

Management: Circumcision is curative (1,D)

Fixed drug eruption [86]

Aetiology

- An uncommon condition, but the penis is one of the more commonly affected areas of the body. Precipitants include non-steroidal anti-inflammatories, paracetamol and antibiotics[87]. Rarely a fixed drug eruption can occur when the sexual partner has taken the drug and it is assumed the toxic component of the drug is passed on through vaginal fluid[88.]

Clinical Features

Appearance: lesions are usually well demarcated and erythematous but can be bullous with subsequent ulceration. As the inflammation settles there may be post-inflammatory hyperpigmentation.

Diagnosis

- History: a drug history is essential.
- Re-challenge: This can confirm the diagnosis but can precipitate more severe reactions and should only be done in consultation with a dermatologist or allergy specialist and after adequate skin testing[89]
- Biopsy: Hydropic degeneration of the basal layer and epidermal detachment and necrosis with pigmentary incontinence.

Management

- Management is symptomatic and the lesions will settle without treatment when the precipitant is discontinued
- Topical steroids - e.g. mild to moderate strength twice daily until resolution.[86](1,C)
- Rarely systemic steroids may be required if the lesions are severe.

Follow up

- Not required after resolution
- Patients should be advised to avoid the precipitant.

Pre-malignant conditions

In 2016, the World Health Organisation proposed a new classification based on carcinogenesis pathway and histology (whether HPV related or non-HPV related), rather than clinical appearances[90] replacing the previous classification based on clinical features. They are strongly associated with human papillomavirus infection and/or lichen sclerosus. [4, 90, 91, 92, 93] The risk is increased if there is concomitant immune-incompetence such as in untreated HIV, in organ transplant patients or in those treated with small molecule (e.g. azathioprine, cyclosporin, methotrexate, leflunamide) or biologic immunosuppressants. Squamous cell carcinoma (SCC) presents as an asymmetrical, irregular tender or painful ulcer or nodule and may coexist with PeIN and lichen sclerosus.

Clinical Features[4, 6, 59, 92, 93]

Most lesions are located on the prepuce (45%), followed by the glans (38%) and shaft (3%).[92]
The terms Bowenoid papulosis, Bowen's disease of the penis and Erythroplasia of Queyrat remain useful. They describe different clinical appearances and reflect a differential risk of progression to

Squamous cell carcinoma (SCC) but are within a spectrum of clinical PeIN. All may progress to frank squamous cell carcinoma (SCC), but the risk is much less in Bowenoid papulosis (~1%) than Bowen's disease (~5%) and highest in Erythroplasia of Queyrat (10-40%).

PeIN of the balanopreputial epithelium (also known as Erythroplasia of Queyrat)

- Typical appearance: red, velvety, well-circumscribed area on the glans or visceral prepuce of the uncircumcised penis.

PeIN of keratinised, hair-bearing skin (also known as Bowen's disease of the penis)

- Typical appearance: scaly, discrete, erythematous patches or plaques

PeIN (also known as Bowenoid papulosis)

- Typical appearance: clinically very similar to genital warts. Lesions range from discrete papules to plaques that are often grouped and pigmented or erythematous. Patients are usually younger than those with Bowen's disease or Erythroplasia of Queyrat.

Diagnosis

- Biopsy: essential **–** histology shows penile intraepithelial neoplasia – differentiated type (lichen sclerosus-associated) or undifferentiated (HPV-associated)[92, 94]

Management [4,6, 59, 92, 95, 96, 97]

Patients with suspected penis cancer or pre-cancer are best managed jointly by specialists in dermatology and urology/andrology. A combined, sequential approach is often needed. The approach should reflect individual clinical circumstances (age, circumcision status, site/sites, comorbidities, concomitant immunosuppression) and the pathogenesis (HPV and/or lichen sclerosus) and histology (differentiated or undifferentiated type).

Topical medical[98. 99]

- Imiquimod 5% (1,C)
- Fluorouracil cream 5% (2,C)
- Fluorouracil 0.5% / salicylic acid 10% combination (2,C)

Surgical/ablative (aims are tissue conservation) [100, 101]

- Surgical excision (local excision is usually adequate and effective).(1,B)
- Mohs' micrographic surgery (1,B)
- Cryotherapy (2,D)
- Photodynamic therapy (2,D)
- Laser (2,D)
- Mandatory circumcision for balanopreputial disease, especially for uncircumcised high-risk scenarios (eg HIV, transplant recipient etc) (1,D)
- Glans-resurfacing (generally, if topical treatments have failed) (2,D)

Adjunctive

- Polyvalent HPV vaccination[102] (2,D)
- Smoking cessation (2,D)

Follow up

- Usually mandatory because of the risks of field change and recurrence; up to one third of patients may harbour (micro) invasive disease. Optimum length of follow up is uncertain.
- Circumcised patients with Bowenoid papulosis or PeIN confined to the prepuce might be discharged. Circumcision is usually mandatory because of the risk of recurrence, although optimum length of follow up is uncertain. In one study ~20% recurred after 5 years.[101]
- Tuition in long-term self-examination if discharged.

- Bowenoid papulosis may remit spontaneously

Other skin conditions

A range of other skin conditions may affect the glans penis and genitalia. These include erythema multiforme and immuno-bullous disorders, including pemphigus, dermatitis artefacta and the very rare extramammary Paget's disease. [1, 4, 6]

A dermatologist's opinion should be sought for diagnosis and management of these conditions.

Table 2 Summary of recommendations

Summary of recommendations

Condition	Management	Alternative
Candidal balanoposthitis	• Clotrimazole cream 1% • Miconazole cream 2%	• Fluconazole 150mg stat orally if symptoms severe • Nystatin cream[13] 100000units/gm • Topical imidazole with 1% hydrocortisone - if marked inflammation is present
Anaerobic infection	• Metronidazole 400 twice daily x 1week	• Co-amoxiclav 375mg three times daily x 1 week
Aerobic infection	• Mupirocin ointment 2-3 times per day for 7-10 days • Topical steroid preparations added antibacterial agents once or twice daily for 7-10 days	• Severe cases may require systemic antibiotics while awaiting culture results ○ Oral flucloxacillin 500 mg four times a day for seven days. ○ Oral clarithromycin 250 mg twice daily for seven days
Lichen sclerosus	• Ultra-potent topical steroids (e.g. clobetasol propionate 0.05% ointment or cream) (1- 3/12 course) applied OD (or BD if a month's course is chosen) then reassess	• Referral for circumcision • Referral for alternative topical/intralesional therapies
Lichen Planus	• Moderate to ultrapotent topical steroids depending on severity eg Clobetasol propionate ointment or cream applied daily for 4 weeks then reducing in frequency over the next 8 weeks depending on response	• referral to specialist services is recommended for consideration of alternative medications
Zoon's (plasma cell) balanitis	• Referral for circumcision	• Topical steroid preparations with or without added antibacterial agents
Psoriasis and circinate balanitis	• Moderate potency topical steroids(+/- antibiotic and antifungal	• Topical Vitamin D preparations (calcipotriol or calcitriol applied twice daily)
Seborrheic dermatitis	• Antifungal cream with a mild to moderate steroid	• Oral azole

Irritant /Allergic eczema	• Hydrocortisone 1% applied once or twice daily until resolution of symptoms	• In more florid cases more potent topical steroids may be required and may need to be combined with antifungals and/or antibiotics
Fixed drug eruptions[115]	• Mild to moderate strength topical steroids may be required for symptomatic relief	• Oral steroids and antihistamines if severe (recommend referral to GP / specialist service)
Balanitis related to STIs	• Refer to relevant guidelines	
Balanitis related to systemic disease	• Onward referral to relevant specialists	
Pre malignancy or suspected malignancy	• Referral to Urology for multidisciplinary care	

Qualifying statement
The recommendations were made and graded on the basis of the best available evidence. However, high quality evidence specific to the management of penile disease is not available for all the conditions described above. Decisions to follow these recommendations must be based on professional clinical judgement, consideration of individual patient circumstances and available resources. All possible care has been undertaken to ensure publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing clinician to ensure the accuracy and appropriateness of the medication they prescribe.

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Composition of editorial board

Available at**:** https://iusti.org/wp-content/uploads/2019/12/Editorial_Board.pdf
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