2014 UK National Guideline on the Management of Vulval Conditions

Clinical Effectiveness Group British Association for Sexual Health and HIV

Date of writing: Feb 2014
Date review due: 2018

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New in the 2014 Guidelines

- General advice for the management of vulval disorders
- Onward referral guidelines
- Vulval lichen simplex
- Vulval psoriasis
- Use of calcineurin inhibitors

Introduction and Methodology

Objectives

This guideline offers recommendation on the management of a range of vulval disorders who may present to Genitourinary Medicine clinics. Vulval disorders represent a disparate group of conditions with a variety of causes, affecting a particular anatomical site and may affect women of any age.
These guidelines concentrate on a selected group of conditions, which may be managed by Genitourinary Physicians, either alone or in conjunction with other specialists, dependant on local expertise. Guidance for onward referral is also included. It is not intended as a comprehensive review of the treatment of all vulval disease. The main categories of non-infective vulval diseases are dermatoses, pain syndromes and pre-malignant conditions.
This guideline offers recommendations on the diagnostic tests and treatment regimens needed for the effective management of the following vulval conditions:

- Vulval lichen sclerosus
- Vulval lichen planus
- Vulval eczema
- Vulval lichen simplex
- Vulval psoriasis
- Vulval intraepithelial neoplasia
- Vulval pain syndromes

It is aimed primarily at people aged 16 years or older presenting to Genitourinary Medicine clinics.

Search Strategy.
This document was produced in accordance with the guidance set out in the CEG's document 'Framework for guideline development and assessment' at http:/www.bashh.org/guidelines.

Four reference sources were used to provide a comprehensive basis for the guideline:

1. Medline and Embase Search up to March 2012
   The search strategy comprised the following terms in the title or abstract:
   - Vulval lichen sclerosus
   - Vulval lichen planus
   - Vulval eczema
   - Vulval lichen simplex
   - Vulval psoriasis
   - Vulval intraepithelial neoplasia
   - Vulval pain syndromes/vulvodynia
2. Green-top Guideline 58 The Management of Vulval Skin Disorders. 2011 http://www.rcog.org.uk/files/rcog-corp/GTG58Vulval22022011.pdf
3. British Association of Dermatology Guidelines
4. Cochrane Collaboration Databases (www.cochrane.org)

Methods
Article titles and abstracts were reviewed and if relevant the full text article obtained. Priority was given to randomised controlled trial and systematic review evidence, and recommendations made and graded on the basis of best available evidence. (Appendix 1)

Piloting and Feedback
The guidelines have been reviewed and approved by an expert patient, and also by the BASHH patient and public engagement panel.

Management
General advice for delivery of vulval care

Vulval conditions may present to Genitourinary Medicine Physicians, Dermatologists and Gynaecologists and treatment modalities also span across this spectrum. Care of patients with vulval conditions is therefore best managed by a multidisciplinary approach[1]. This includes clear working arrangements between disciplines or access to a specialist multidisciplinary vulval service. The service should also have access to clinicopathological discussion and review of histology results.

General Advice for all vulval conditions

- Avoid contact with soap, shampoo and bubble bath. Simple emollients can be used as a soap substitute and general moisturiser
- Avoid tight fitting garments which may irritate the area
- Avoid use of spermicidally lubricated condoms
- Patients should be given a detailed explanation of their condition with particular emphasis on any long-term implications for the health of themselves and their partner(s). This should be reinforced by giving them clear and accurate written information. (The British Society for the Study of Vulval Disease produces some patient information leaflets

www.bssvd.org/leaflets.asp, also include BAD leaflets, ISSVD, Vulval Pain Society and NZ Dermnet)
- The patient's GP should be informed.
- STI screening should be considered in all patients and vulvovaginal candidiasis excluded if the patient presents with vulval itch.
- All patients should be assessed for sexual dysfunction

Sexual partners
- Partner tracing is not required unless screening detects a sexually transmitted infection.

Vulval lichen sclerosus [2]

These guidelines relate to the management of lichen sclerosus in adult females. Additional guidelines have been produced by the Royal College of Obstetricians and Gynaecologists[1] and the British Association of Dermatologists[3].

Aetiology
Lichen sclerosus (LS) is an inflammatory dermatosis of unknown aetiology. There is evidence to suggest that auto-immune factors may be involved in its pathogenesis and recent evidence has shown autoantibodies to extracellular matrix protein 1[4]. There is an increased frequency of other autoimmune disorders in females with lichen sclerosus[5]

Clinical Features

Symptoms
- Itch
- Soreness
- Dyspareunia if introital narrowing
- Urinary symptoms
- Other symptoms, e.g. constipation, can occur if there is peri-anal involvement
- Can be asymptomatic, but this is rare

Signs
- Pale, white atrophic areas affecting the vulva
- Purpura (ecchymosis) is common
- Fissuring
- Erosions, but blistering is very rare
- Hyperkeratosis can occur
- Changes may be localised or in a 'figure of eight' distribution including the perianal area
- Loss of architecture may be manifest as loss of the labia minora and/or midline fusion. The clitoral hood may be sealed over the clitoris so that it is buried

Complications
- Development of squamous cell carcinoma (actual risk <5%[6])
- Development of clitoral pseudo cyst
- Sexual dysfunction

- Dysaesthesia

Diagnosis

- Characteristic clinical appearance
- Histology of vulval biopsy: thinned epidermis with sub-epidermal hyalinization and deeper inflammatory infiltrate. In early disease histology can be difficult.[7]

Management

Further investigation

- Biopsy: is mandatory if the diagnosis is uncertain, there are atypical features or coexistent vulval intraepithelial neoplasia (VIN) / squamous cell carcinoma (SCC) is suspected
- Investigation for autoimmune disease if clinically indicated, especially thyroid dysfunction (i.e. T4 and TSH) as it is often asymptomatic and has been found be associated (IV,C)[5]
- Skin swab: only useful to exclude co-existing infection if there are symptoms or signs suggestive of this
- Patch testing: rarely required and only if secondary medicament allergy suspected. The advice of a dermatologist should be sought.

Treatment

General Advice

- Patients should be informed about the condition and given written information. Patients should be made aware of the small risk of neoplastic change. They should be advised to contact the doctor if they notice a change in appearance or texture (e.g. lump or hardening of skin), or if there is a major change in symptoms.

Recommended Regimen

- Ultra-potent topical steroids[8] e.g. Clobetasol proprionate (I A). Various regimens are used one of the most common being daily use for one month, alternate days for one month, twice weekly for one month with review at 3 months. It can then be used as needed depending on symptoms. There is no evidence on the optimal regimen.
- 30gm of an ultra-potent steroid should last at least 3 months
- Ointment bases are much better to use on the ano-genital skin because of the reduced need for preservatives in an ointment base, and hence less risk of a secondary contact allergy.

Alternative regimens

- An ultra-potent topical steroid with antibacterial and antifungal e.g. Dermovate NN® or generic equivalent (Clobetasol with neomycin and nystatin) or an alternative preparation that combats secondary infection (such as Fucibet® cream) may be appropriate if secondary infection is a concern. These should only be used for a short period of time to clear infection (IV, C).

Research findings and unlicensed treatments

- Topical calcineurin inhibitors. This is not a licensed indication and long-term safety and efficacy is not established.
  Tacrolimus 0.1% has been shown to be effective when used for 16 to 24 weeks (IIb B) [9]. This study, which included males and females and genital and extra genital lichen sclerosus, showed that 77% of evaluable patients responded to treatment with 43% showing a complete response (absence of symptoms and skin findings excepting induration and atrophy) at 24 weeks. The follow up period was 18 months and whilst no patient was shown to have skin malignancy or dysplastic change the long-term risks need to be studied in view of concerns about the possibility of topical immunosuppression increasing susceptibility of malignancy. A study of the related agent, pimecrolimus, showed that 42% of patients were in 'complete remission' after 6 months application[10]. (IIb B) Local irritancy was the most common side effect with both tacrolimus and pimecrolimus but usually improved after the initial period of use. Cases of malignancy have been reported[11,12] and it is recommended that these agents should not be used first line.
- Oral retinoids, e.g. acitretin[13] – these may be effective in severe recalcitrant disease (Ib A) but should only be given by a dermatologist, experienced in the use of these agents. They are severely teratogenic and pregnancy must be avoided for 2 years after finishing treatment.
- UVA1 phototherapy has been reported as successful in a small number of cases.[14] (III,B)

Pregnancy and Breast-feeding

- Topical steroids are safe to use while pregnant or breast-feeding
- Topical calcineurin inhibitors are contra-indicated whilst pregnant or breast-feeding.
- Retinoids are absolutely contra-indicated during pregnancy and for at least 2 years before. They should be used with caution in females of child-bearing age.

Onward referral criteria

- Those with active disease which has not responded adequately to treatment should be referred to a specialised Vulval Clinic
- Any patient who develops differentiated or undifferentiated VIN or an SCC on a background of LS should be seen and follow-up in a specialised Vulval Clinic. Surgery[15] – should only be used for the treatment of coexistent VIN / SCC or fusion. Disease tends to recur around the scar. (III, B).

Follow-up

- After 3 months to assess response to treatment
- Stable disease should be reviewed annually and this can be done by the General Practitioner in those with well controlled disease. This must be communicated to the patient and GP by the clinic.

- Patients should be informed that if they notice the development of a lump, sore area, change in symptoms or change in appearance they should prompt medical review.

Auditable outcome measures

- Biopsy should be performed in patients not responding to an initial course of steroid treatment and if raised lesions develop Target 100%
- Written information should be given to all patients Target 100%

Vulval Lichen Planus

Aetiology

Lichen planus is an inflammatory disorder with manifestations on the skin, genital and oral mucous membranes. More rarely it affects the lacrimal duct, oesophagus and external auditory meatus. It is an inflammatory condition of unknown pathogenesis but it is probably an immunological response by T cells activated by, as yet, unidentified antigens. Weak circulating basement membrane zone antibodies have been shown to be present in 61% of patients with erosive lichen planus of the vulva[16]. In some cases there is overlap between lichen sclerosus and lichen planus.

Clinical Features

Symptoms

- Itch / irritation
- Soreness
- Dyspareunia
- Urinary symptoms
- Vaginal discharge
- Can be asymptomatic

Signs

The anogenital lesions of lichen planus may be divided into three main groups according to their clinical presentation:

1. Classical: typical papules will be found on the keratinised anogenital skin, with or without striae on the inner aspect of the vulva. Hyperpigmentation frequently follows their resolution, particularly those with dark-skin. This type of lichen planus may be asymptomatic. Vulval lesions were found in 19 out of 37 women with cutaneous lichen planus, with four of the 19 having had no symptoms[17]
2. Hypertrophic: these lesions are relatively rare and can be difficult to diagnose. They particularly affect the perineum and perianal area, presenting as thickened warty plaques which may become ulcerated, infected and painful. Because of these features, they can mimic malignancy. They do not appear to be accompanied by vaginal lesions.
3. Erosive: the most common subtype to cause vulval symptoms. The mucosal surfaces are eroded. At the edges of the erosions the epithelium is mauve and a pale network (Wickham's striae) is sometimes seen. The vaginal lesions in erosive lichen planus are important to recognise early and start treatment as they can lead to scarring and complete stenosis. The lesions consist of friable

telangiectasia with patchy erythema which are responsible for the common symptoms of postcoital bleeding, dyspareunia and a variable discharge which is often serosanguinous. As erosions heal synaechiae and scarring can develop.[18] This type is also seen in the oral mucosa although synaechia are uncommon. The term vulvo-vaginal gingival syndrome is used when erosive disease occurs in these three sites. The presenting symptom is usually of pain and soreness.

Complications

- Scarring, including vaginal synechiae
- Development of squamous cell carcinoma. In one study the incidence was as high as 3%.[19]

Diagnosis

- Characteristic clinical appearance. Involvement of the vagina excludes lichen sclerosus. Skin changes elsewhere can be helpful but overlap between lichen planus and lichen sclerosus is described. Immunobullous disorders such as pemphigus can look clinically similar to erosive lichen planus.
- Histology of vulval biopsy: irregular saw-toothed acanthosis, increased granular layer and basal cell liquefaction. Band-like dermal infiltrate mainly lymphocytic.

Management

Further investigation

- Biopsy: is a necessity if the diagnosis is uncertain or coexistent vulval intraepithelial neoplasia (VIN) / squamous cell carcinoma (SCC) is suspected. Direct immunofluorescence should be performed if an immunobullous disease is considered in the differential diagnosis. Only 25% are classic on biopsy and clinicopathological discussion is important
- Investigation for autoimmune disease especially of the thyroid (i.e T4 and TSH if there is any suspicion of abnormality) (IV C)[5]
- Skin swab: to exclude secondary infection especially of excoriated lesions
- Patch testing: if secondary medicament allergy suspected
- Whilst a link with hepatitis C and sometimes B has been noted in some countries there is no evidence of increased incidence in the UK and routine screening is not thought necessary.[20]

Treatment

General Advice

- Patients should be informed about the condition and given written information. Patients should be made aware of the small risk of neoplastic change. They should be advised to contact the doctor if they notice a change in appearance or texture (e.g. lump or hardening of skin).

Recommended Regimen

- Ultrapotent topical steroids e.g. Clobetasol proprionate. (Iib,B) In a study of 114 patients in a vulval clinic, 89 used ultra potent topical steroids as first line treatment of whom 75% improved

and 54% were symptom free. However in only 9% was there resolution of signs of inflammation.[19] There is no evidence on the optimal regimen.

- Maintenance treatment may be required and can either be with weaker steroid preparations or less frequent use of potent steroids.
- Vaginal corticosteroids: Delivery of corticosteroids to the vagina is not easy. A proprietary preparation containing hydrocortisone (Colifoam), introduced with an applicator, is useful. Prednisolone suppositories may be used in more severe cases (IV,C).

Alternative regimens

- An ultra-potent topical steroid with antibacterial and antifungal e.g. Dermovate NN® or generic equivalent (Clobetasol with neomycin and nystatin) or an alternative preparation that combats secondary infection (such as Fucibet® cream) may be appropriate if secondary infection is a concern. These should only be used for a short period of time to clear infection (IV, C).

Pregnancy and Breast-feeding

- Topical steroids are safe to use while pregnant or breast-feeding.
- Topical calcineurin inhibitors are contra-indicated whilst pregnant or breast-feeding.
- Retinoids are absolutely contraindicated during pregnancy and for at least 2 years before. They should be used with caution in females of child-bearing age.

Onward referral

Referral to a multidisciplinary vulval clinic is recommended for erosive disease and any recalcitrant cases, or those in whom systemic therapy is considered.
Systemic treatments: There is no consensus and little evidence base for the use of systemic agents. In the vulvovaginal–gingival syndrome there is general agreement that azathioprine, dapsone, griseofulvin, chloroquine and minocycline, all tried empirically, are of little or no benefit;

- Oral ciclosporin may be considered.
- Retinoids can be very helpful in hypertrophic cases.
- Oral steroids are used, for example prednisolone 40 mg/day, tapered off over a few weeks; courses can be repeated as necessary for severe flares.
- The new biological agents have been used in oral and cutaneous disease. Basiliximab[21] has been found to be effective but its' use has not been evaluated in vulval disease. All these potentially toxic therapies need careful monitoring and are best supervised by a dermatologist in the context of a specialised clinic (IV, C).

Follow-up

- At 2-3 months to assess response to treatment
- Active disease should be assessed as clinically required. Erosive lichen planus needs long term specialised follow-up (IV, C).
- Stable disease should be reviewed annually except in well-counselled patients who control their symptoms well. If review is by the General

Practitioner this should be communicated to the patient and GP by the clinic.
- Patients should be informed that if they notice the development of a lump or change in appearance they should seek medical advice urgently.

Auditable outcome measures
- Biopsy should be performed in patients not responding to an initial course of treatment and if raised lesions develop
  Target 100%

Vulval eczema

Aetiology
Eczematous and lichenified diseases, as classified by ISSVD,[22] includes:
- Atopic: the 'allergic' type often seen in people who also have hay fever or asthma.
- Allergic contact: due to skin contact to a substance to which the individual is sensitive.
- Irritant contact: due to skin contact with irritating chemicals, powders, cleaning agents, etc.

Clinical Features

Symptoms
- Vulval itch
- Soreness

Signs
- Erythema
- Lichenification and excoriation
- Fissuring

Complications
- Secondary infection

Diagnosis
- Clinical presentation (as above).
- General examination of the skin to look for other signs of dermatitis

Management
Further Investigation
- Patch testing[23,24] – standard battery and medicaments (III,B)
- Biopsy (IV,C) – only if atypical features or failure to respond to treatment

Treatment
Recommended Regimens
- Avoidance of precipitating factor (IV,C)
- Use of emollient soap substitute (aqueous cream should not be applied as a moisturiser due to the risk of irritant effects, Hydramol can be a suitable alternative)

- Topical corticosteroid – the choice of preparation will depend on severity, 1% Hydrocortisone ointment in milder cases, or betamethasone valerate 0.025% or clobetasol propionate 0.05% for limited periods if severe or lichenified. A combined preparation containing antifungal and/or antibiotic may be required if secondary infection suspected. Apply once daily.(IV,C)

Follow-up

- As clinically required
- Long-term follow up and psychological support may be needed

Auditable Outcomes

- Patients should be given a full explanation of their condition with written information Target 100%

Lichen simplex

Aetiology

Categorised into 4 main groups.

- Underlying dermatoses, i.e. atopic dermatitis, allergic contact dermatitis, superficial fungal (tinea and candidiasis) infections
- Systemic conditions causing pruritus, i.e. renal failure, obstructive biliary disease (primary biliary cirrhosis and primary sclerosing cholangitis), Hodgkin's lymphoma, hyper- or hypothyroidism, and polycythaemia rubra vera
- Environmental factors: heat, sweat, rubbing of clothing, and other irritants such as harsh skincare products.
- Psychiatric disorders: anxiety, depression, obsessive-compulsive disorder, and dissociative experiences are often associated with the condition. Emotional tensions in predisposed people (i.e., those with an underlying predisposition for atopic dermatitis, asthma, and allergic rhinitis) can induce itch and thus begin the chronic itch-scratch cycle[25,26].

Clinical Features

Symptoms

- Vulval itch
- Soreness

Signs

- Lichenification i.e. thickened, slightly scaly, pale or earthy-coloured skin with accentuated markings, maybe more marked on the side opposite the dominant hand.
- Erosions and fissuring.
- Excoriations as a result of scratching may be seen
- The pubic hair is often lost in the area of scratching

Complications

- Secondary infection

Diagnosis

- Clinical presentation (as above). Psoriasis of the vulva is usually less itchy and lesions are bright red, often glazed and well demarcated and frequently involves natal cleft
- History including mental state examination where indicated
- General examination of the skin to look for other signs of psoriasis or lichen simplex elsewhere

Management

Further Investigation

- Screening for infection (e.g. *Staphylococcus aureus, Candida albicans*)
- Dermatological referral for consideration of patch testing[23] – standard battery and medicaments (III,B)
- Ferritin[27] (III,B)
- Biopsy (IV,C)

Treatment

Recommended Regimens

- Avoidance of precipitating factor (IV,C)
- Use of emollient soap (some people may have a reaction to Aqueous cream when it is used as an emollient. For this reason it is recommended only as a soap substitute and not an emollient).
- Topical corticosteroid – potent topical steroids are required when treating lichenified areas e.g. betamethasone or clobetasol for limited periods. A combined preparation containing antifungal and/or antibiotic may be required if secondary infection suspected. Apply once or twice daily.(IV,C)
- A mildly anxiolytic antihistamine such as hydroxyzine or doxepin at night is helpful
- The symptoms of pruritus often respond fairly quickly to a topical steroid but, unless the lichenification resolves, the itch–scratch cycle will remain and the symptoms will recur. A graduated reduction in the frequency of application of the topical steroid is helpful, over about 3-4 months
- Cognitive behavioural therapy may be helpful if there are co-existing mental health issues

Follow-up

- Mild disease – as clinically required
- Severe disease (i.e. when using potent topical steroids) – 1 month then as required

Auditable Outcome Measures

- Patients should be given a full explanation of their condition with written information Target 100%

Vulval psoriasis

Aetiology

Psoriasis is a chronic inflammatory epidermal skin disease affecting approximately 2% of the general population. Genital psoriasis may present as part of plaque or flexural psoriasis or, rarely, as the only area affected.

Clinical Features

Symptoms

- Vulval itch
- Soreness
- Burning sensation

Signs

- Well demarcated brightly erythematous plaques
- Often symmetrical
- Frequently affects natal cleft
- Usually lacks scaling due to maceration
- Fissuring

Complications

- May be worsened due to Koebner effect by irritation from urine, tight-fitting clothes or sexual intercourse.

Diagnosis

- Clinical presentation [as above.]
- General examination of the skin and nails to look for other signs of psoriasis

Management

Further Investigation

- Skin punch biopsy if the diagnosis is in doubt

Treatment[28]

Recommended Regimens

- Avoidance of irritating factors
- Use of emollient soap substitute
- Topical corticosteroid - weak to moderate steroids are preferred but if insufficient to induce a response then intensive short term potent steroid such as clobetasol propionate 0.05% may be used. A combined preparation containing antifungal and/or antibiotic may be required if secondary infection suspected (e.g. Trimovate®).(IV, C)
- Coal-tar preparations – may be used alone or combined or alternated with topical steroids. However, these preparations can cause irritation and folliculitis. (IV, C)
- Vitamin D analogues such as Talcalcitol – alone or in combination with corticosteroid, however their usefulness may be limited by causing irritation. (IV, C)

Onward referral

- Referral to a multidisciplinary vulval clinic is recommended for unresponsive or recalcitrant cases, or those in whom systemic therapy is considered.
- Systemic treatments: if required for severe and extensive psoriasis may help genital lesions but not recommended for isolated genital psoriasis.

Follow-up

- Mild disease – as clinically required
- Severe disease – (i.e. when using potent topical steroids) 1 month then as required

Auditable Outcome Measures

- Patients should be given a full explanation of their condition with written information Target 100%

Other Vulval Dermatoses

Many other skin conditions can affect the vulva. Where the diagnosis is not obvious patients should be referred to a combined vulval clinic or to a dermatologist.

Vulval intraepithelial neoplasia (VIN)[2]

Aetiology

This is a vulval skin condition which may become cancerous if left untreated. It is confirmed by histological diagnosis. In Genitourinary Medicine clinics the commonest aetiological agent is Human papillomavirus (HPV) this is known as usual type and is mainly associated with HPV 16[29]. A second type, generally not HPV related occurs in conjunction with lichen sclerosus or lichen planus (known as differentiated type)[30]. The risk of progression to squamous cell carcinoma is much greater with the differentiated type of VIN and needs specialised management. VIN is commoner in immunocompromised women.[31] Smoking is also a risk factor.

Clinical Features

Symptoms

- Lumps
- Burning and itch / irritation
- Asymptomatic
- Pain

Signs

- Clinical appearance is very variable
- Raised white, erythematous or pigmented lesions occur and these may be warty, moist or eroded (pigmented lesions were previously known as Bowenoid papulosis)
- Multifocal lesions are common

Complications

- Development of squamous cell carcinoma (SCC) has been reported in between 9%[32] and 18.5% of women[33]
- Recurrence is common and progression to cancer can occur following previous treatment [33]
- Psychosexual consequences have also been described (especially following surgical treatment)[34]

Diagnosis

- Biopsy – histology shows loss of organisation of squamous epithelium with a variable degree of cytological atypia which is graded as undifferentiated or differentiated[30] and by depth. Multiple biopsies may be required as there is a risk of missing invasive disease[35]

Management

Further investigation

- Ensure that cervical cytology remains up to date - there is an association with cervical intraepithelial neoplasia (CIN)[36] (this is probably only applicable to those due to HPV) (IV,C)
- All patients with VIN should be referred for up-to date colposcopy to exclude CIN and VIN. If there are any peri-anal lesions, referral for anoscopy is recommended (IV, C).

Treatment [37,38]

Most studies and research relate to full thickness VIN. Multifocal lesions can be treated in the same manner as single lesions, but may have a higher recurrence rate[28].

. Recommended Regimen

- Local excision[39] – this is the treatment of choice for small well circumscribed lesions as it has the lowest rate of recurrence on follow up.(III,B)
- Imiquimod cream 5% - partial and complete clinical and histological regression has been shown in small studies but treatment limited by side effects. Only short term follow up data is available. This is an unlicensed indication. (Ib,A)[40,41]
- Vulvectomy – this has been effective but recurrence may occur and function and cosmesis will be impaired (IV,C)[34,39]

Alternative Regimens

1. Local destruction – a variety of techniques have been evaluated [30, 32], including carbon dioxide laser and ultrasonic surgical aspiration [42], photodynamic therapy[39], cryotherapy [32], laser[39].(IIa, B) There are anecdotal reports of treatment with diathermy. Involvement of skin appendages can occur and recurrence may ensue if the appropriate depth of treatment is not achieved. The recurrence rates at follow-up tend to be higher than for excision, but cosmesis is usually good.
2. 5 fluorouracil cream [43] – may lead to resolution of some lesions but results are variable and side effects are common. No consensus on usefulness or regimen. This is an unlicensed indication. (IV,C).
3. Supervision[35] – some lesions will spontaneously regress. This may be the best policy for partial thickness VIN. However there

is a risk of progression and patients should be made aware of this (IV, C).

Pregnancy and Breast-feeding

- Imiquimod and 5 fluorouracil creams are not licensed in pregnancy

Onward referral

- Cases of VIN should be assessed in a multidisciplinary vulval clinic, or have input from gynaecology regarding assessment for surgical excision[1].

Follow-up

- Close follow-up is mandatory. Although resolution may occur VIN III particularly has a significant rate of progression (6.5% in one study)[33]

Auditable Outcome Measures

- Follow up of cases until 5 years after resolution Target 80%

Vulval pain

International Society for the Study of Vulvovaginal Diseases [ISSVD] defines vulvodynia as 'vulvar discomfort, most often described as burning pain, occurring in the absence of relevant visible findings or a specific, clinically identifiable, neurologic disorder'. [44]

Vulvodynia is categorised, by the ISSVD, as generalised or localised; provoked, unprovoked or a mixture of the two.

Localised provoked vulvodynia [vestibulodynia]

Aetiology

Likely to be multifactorial; a history of vulvovaginal candidiasis, usually recurrent, is the most commonly reported feature. Experimental animal study supports this association.[45]

Clinical Features

Symptoms

- Vulval pain – frequently felt at the introitus at penetration during sexual intercourse or on insertion of tampons. There is usually a long history.

Signs

- Focal tenderness elicited by gentle application of a cotton wool tip bud at the introitus or around the clitoris
- There are no signs of an acute inflammatory process

Complications

- Sexual dysfunction
- Psychological morbidity

Diagnosis

- Clinical diagnosis made on history and examination

Management

Further investigation

- After exclusion of other treatable causes no further investigation is required

Treatment

The British Society for the Study of Vulval Disease [BSSVD] recommends a multidisciplinary approach to patient care and that combining treatments can be helpful in dealing with different aspects of vulval pain. [46,47]

Recommended regimens

- Avoidance of irritating factors
- Use of emollient soap substitute
- Topical local anaesthetics e.g. 5% lidocaine ointment or 2% lidocaine gel should be used with caution as irritation may be caused. The application should be made 15-20 minutes prior to penetrative sex and washing off the lidocaine just before sex or the use of condom by the partner can reduce the risk of transfer resulting in penile numbness. Oral contact should be avoided (IVC)

- Physical therapies
  - Pelvic floor muscle biofeedback[48] (III,B)
  - Vaginal transcutaneous electrical nerve stimulation [TENS] (Ib,A) [49]
  - Vaginal trainers (III,B) [50]

- Cognitive behaviour therapy (III,C) [51]

Alternative Regimens

- Pain modifiers – the benefit of drugs such as tricyclic antidepressants, gabapentin and pregabalin is not clear. Amitriptyline gradually titrated from 10mg up to 100 mg according to response and side effects may be beneficial in some women (IVC)
- Surgery – Modified vestibulectomy may be considered in cases where other measures have been unsuccessful. Patients who have responded to topical lidocaine prior to sex have a better outcome. (IIIB) [52,53]

Follow-up

- As clinically required
- Long-term follow-up and psychological support may be needed

Auditable Outcomes

- Patients should be given a full explanation of their condition with written information Target 100%

Unprovoked Vulvodynia

Aetiology
The aetiology is unknown and the condition is best managed as a chronic pain syndrome.

Clinical Features

Symptoms
- Pain that is longstanding and unexplained.
- May be associated with urinary symptoms such as interstitial cystitis[54]

Signs
- The vulva appears normal

.

Complications
- Sexual dysfunction
- Psychological morbidity

Diagnosis
- Clinical diagnosis made on history and examination having excluded other causes.

Management

Further investigation
- After exclusion of other treatable causes no further investigation is required

Treatment
The British Society for the Study of Vulval Disease [BSSVD] recommends a multidisciplinary approach to patient care and that combining treatments can be helpful in dealing with different aspects of vulval pain.[46]

Treatment resistant unprovoked vulvodynia may require referral to a pain clinic.

Recommended regimens
- Use of emollient soap substitute
- Pain modifiers – tricyclic antidepressants are well established in chronic pain management. Few studies have specifically examined the effect in vulvodynia however amitriptyline is frequently first line treatment; dosage should be increased by small increments starting at 10mg up to 100mg daily according to the patient's response[55] (III,B)
  Note: a recent randomised study has not confirmed the beneficial effect of amitriptyline. (Ib, A)[56]
- If unresponsive or unable to tolerate the side effects, gabapentin[57](III,B) or pregabalin[58] may be used (IIb,B)

Alternative regimens

- Topical local anaesthetic e.g. 5% lidocaine ointment or 2% lidocaine gel. A trial of local anaesthetic may be considered although irritation is a common side effect. (IV,C)
- Cognitive behavioural therapy and psychotherapy[59] (IIb,B)
- Acupuncture[60] (IIb, C)

Follow up

- As clinically required

Auditable outcomes

- Patients should be given a full explanation of their condition with written information Target 100%

Editorial independence

This guideline was commissioned, edited and endorsed by the BASHH CEG without external funding being sought or obtained.

Declarations of interest

All members of the guideline writing committee completed the BASHH conflict of interest declaration detailed below at the time the guidelines final draft was submitted to the CEG.

Cost implications

These guidelines have been revised to include a much wider group of conditions than included in previous guidance. Many of these conditions already do present to GUM setting initially. Where appropriate, onward referral to Dermatology is recommended and is therefore unlikely to impact greatly on the cost of managing these chronic conditions

Appendix 1

Levels of evidence and grading of recommendations

Level of evidence
Ia Meta-analysis of randomised controlled trials
Ib At least one randomised controlled trial
IIa At least one well designed controlled study without randomisation
IIb At least one other type of well-designed quasi-experimental study
III Well designed non-experimental descriptive studies
IV Expert committee reports or opinions of respected authorities

Grading of recommendation
A Evidence at level Ia or Ib
B Evidence at level IIa, IIb or III
C Evidence at level IV

Acknowledgments
Dr John Evans-Jones provided feedback during the consultation period

References

1. Cruickshank ME, Hay I. Green-top Guideline 58 The Management of Vulval Skin Disorders. 2011 http://www.rcog.org.uk/files/rcog-corp/GTG58Vulval22022011.pdf
2. Neill SM, Lewis FM. Non-infective cutaneous conditions of the vulva. In Neill SM, Lewis FM eds. Ridley's 'The Vulva'. London: Wiley-Blackwell 2009
3. Neill SM, Lewis FM, Tatnall FM, Cox NH. British Association of Dermatologists' guidelines for the management of lichen sclerosus 2010. British Journal of Dermatology 2010; **163:** 672-82.
4. Oyama N, Chan I, Neill SM et al. Autoantibodies to extracellular matrix protein 1 in lichen sclerosus. Lancet 2003; 362:118-23.
5. Meyrick-Thomas RH, Ridley CM, McGibbon DH, Black MM. Lichen sclerosus and autoimmunity – a study of 350 women. Br J Dermatol 1988; 118:41-46.
6. Wallace HJ. Lichen sclosus et atrophicus. Trans St John's Hosp Dermatol Soc 1971: 57: 9-30.
7. Regauer S, Reich O. Early vulvar lichen sclerosus: a histological challenge Histopathology 2005; 47:340-7.
8. Chi CC, Kirtschig G, Baldo M, Brackenbury F, Lewis F. Wojnarowska F. Topical interventions for genital lichen sclerosus (Review). Cochrane Library 2011, Issue 12. E-pub

9. Hengge UR, Krause W, Hofmann H et al Multi-centre, phase II trial on the safety and efficacy of topical tacrolimus ointment for the treatment of lichen sclerosus. Br J Dermatol 2006; 155:1021-8.
10. Nissi R, Risteli J, Niemimaa M. Pimecrolimus cream 1% in the treatment of lichen sclerosus. Gynecol Obstet Invest 2006; 63:151-154.
11. Edey K, Bisson D, Kennedy C. Topical tacrolimus in the management of lichen sclerosus. Br J Obstet Gynaecol 2006: 113;1482
12. Fischer G, Bradford J. Topical immunosuppressants, genital lichen sclerosus and the risk of squamous cell carcinoma. J Reprod Med 2007; 52: 329-31.
13. Bousema MT, Romppanen U, Geiger JM et al. Acitretin in the treatment of severe lichen sclerosus et atrophicus of the vulva: a double-blind, placebo controlled study. J Am Acad Dermatol 1994; 30:225-231.
14. Beattie PE, Dawe RS, Ferguson J, Ibbotson SH. UVA1 phototherapy for genital lichen sclerosus Clin Exp Dermatol 2006;31:343-7.
15. Abramov Y, Elchalal U, Abramov D, Goldfarb A, Schenker JG. Surgical treatment of vulvar lichen sclerosus: a review. Obstet Gynecol Surv. 1996; 51:193-9.
16. Cooper, S.M., Dean, D., Allen, J. et al. Erosive lichen planus of the vulva: weak circulating basement membrane zone antibodies are present. Clin Exp Dermatol 2005; 30:551–556.
17. Lewis, F.M., Shah, M. & Harrington, C.I. Vulval involvement in lichen planus: a study of 37 women. Br J Dermatol 1996; 135: 89–91.
18. Genadry R, Provost TT. Severe vulvar scarring in patients with erosive lichen planus. J Reprod Med 2006; 51:67-72.
19. Cooper SM, Wojnarwowska F. Influence of treatment of erosive lichen planus of the vulva on its prognosis. Arch Dermatol. 2006; 142:362-4.
20. Mucosal vulval lichen planus: outcome, clinical and laboratory findings. Kirtschig G, Wakelin SH, Wojnarowska F. J Eur Acad Dermatol Venerol 2005; 19:301-7.
21. Rebora, A., Parodi, A. & Marialdo, G. Basiliximab is effective for erosive lichen planus. Archives of Dermatology 2002; 138: 1100–1111.
22. Lynch PJ, Moyal-Barracco M, Scurry J, Stockdale C. ISSVD Terminology and Classification of Vulvar Dermatological Disorders: An Approach to clinical diagnosis. Presented at the XXI World Congress of the ISSVD, Paris, France Sept 3-8 2011
23. Nardelli A, Degreef H, Goossens A. Contact allergic reactions of the vulva: a 14 year review. Dermatitis 2004;15:131-6
24. Haverhoek E, Reid C, Gordon L et al Prospective study of patch testing in patients with vulval pruritis. Australas J Dermatol. 2008;49(2):80-5
25. Lotti T, Buggiani G, Prignano F. Prurigo nodularis and lichen simplex chronicus. Dermatol Ther 2008; 21:42-46.
26. Lynch PJ. Lichen simplex chronicus (atopic/neurodermatitis) of the anogenital region. Dermatol Ther 2004; 17: 8-19
27. Crone AM, Stewart EJ, Wojnarowska F, Powell SM. Aetiological factors in vulvar dermatitis. J Eur Acad Dermatol Venereol 2000;14:181-6.
28. Meeuwis KA, et al. Genital psoriasis: A systematic literature review on this hidden skin disease. Acta Derm Venereol. 2011 Jan; 91(1):5-11.
29. Hording U, Daugaard S, Iversen AK et al. Human Papillomavirus 16 in vulvar carcinoma, vulvar intraepithelial neoplasia, and associated cervical neoplasia. Gynecol Oncol 1991; 42:22-26.

30. Sideri M, Jones RW, Wilkinson EJ, Preti M, Heller DS, Scurry J, et al. Squamous vulvar intraepithelial neoplasia: 2004 modified terminology, ISSVD Vulvar Oncology Subcommittee. J Reprod Med *2005*; 50(11):807-10.
31. Petry KU, Kochel H, Bode U et al. Human papillomavirus is associated with the frequent detection of warty and basaloid high-grade neoplasia of the vulva and cervical neoplasia among immunocompromised women. Gynecol Oncol 1996; 60:30-34.
32. van Seters M, van Beurden M, de Craen AJ. Is the assumed natural history of vulvar intraepithelial neoplasia III based on enough evidence? A systematic review of 3322 published patients. Gynecologic Oncology 2005 May; 97(2):645-51.
33. Jones RW, Rowan DM, Stewart AW. Vulvar intraepithelial neoplasia: aspects of the natural history and outcome in 405 women. Obstetrics and Gynecology 2005 Dec; 106(6):1319-26.
34. Andreasson B, Moth I, Jensen SB, Bock JE. Sexual function and somatopsychic reactions in vulvectomy-operated women and their partners. Acta Obstetricia ET Gynecologica Scandinavica 1986; 65(1):7-10.
35. Polterauer S,Catharina Dressler A,Grimm C, Seebacher V, Tempfer C,Reinthaller A, et al. Accuracy of preoperative vulva biopsy and the outcome of surgery in vulvar intraepithelial neoplasia 2 and 3. Int J Gynecol Pathol 2009; 28:559–62.
36. de Bie RP, van de Nieuwenhof HP, Bekkers RL, Melchers WJ, Siebers AG, Bulten J, Massuger LF, de Hullu JA. Patients with usual vulvar intraepithelial neoplasia-related vulvar cancer have an increased risk of cervical abnormalities. Br J Cancer. 2009 Jul 7; 101(1):27-31. Epub 2009 Jun 9.
37. Pepas L, Kaushik S, Bryant A, Nordin A, Dickinson HO. Medical interventions for high grade vulval intraepithelial neoplasia. Cochrane Database of Systematic Reviews 2011, Issue 4. Art. No.: CD007924. DOI: 10.1002/14651858.CD007924.pub2.
38. Kaushik S, Pepas L, Nordin A, Bryant A, Dickinson HO. Surgical interventions for high grade vulval intraepithelial neoplasia. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD007928. DOI: 10.1002/14651858.CD007928.pub2.
39. Hillemanns P, Wang X, Staehle S, Michels W, Dannecker C. Evaluation of different treatment modalities for vulvar intraepithelial neoplasia (VIN): CO(2) laser vaporization, photodynamic therapy, excision and vulvectomy. Gynecol Oncol 2006; 100(2):271-5.
40. van Seters M, van Beurden M, Kate FJ, Beckmann I, Ewing PC, Eijkemans MJ, et al. Treatment of vulvar intraepithelial neoplasia with topical imiquimod. N Engle J Med 2008; 358(14):1465-73.
41. Mathiesen O, Buus SK, Cramers M. Topical imiquimod can reverse vulvar intraepithelial neoplasia: A randomised, double-blinded study. Gynecol Oncol 2007;107(2):219-22.
42. von Gruenigen V E, Gibbons H E Gibbins K Jenison E L Hopkins M P. Surgical treatments for vulvar and vaginal dysplasia: a randomized controlled trial. Obstet Gynecol 2007; 109(4):942-7.
43. Sillman FH and Sedlis A. 5-FU/Chemosurgery in the Treatment of Vulvar Intraepithelial Neoplasia. Journal of Gynecologic Surgery. 1988, 4(3): 171-185 Journal of Gynecologic Surgery. 1988, 4(3): 171-185.

44. Moyal-Barracco M, Lynch PJ. 2003 ISSVD terminology and classification of vulvodynia: a historical perspective. J Reprod Med 2004;49(io):772-7
45. Farmer MA, Talor AM, Bailey AL et al Repeated vulvovaginal fungal infections cause persistent pain in a mouse model of vulvodynia. Sci Transi Med 2011;3(101):101ra92
46. Mandal D, Nunns D et al Guidelines for the management of Vulvodynia.Br J Dermatol 2010;162:1180–1185
47. Spoelstra SK. Dijkstra JR. van Driel MF. Weijmar Schultz WC. Long-term results of an individualized, multifaceted, and multidisciplinary therapeutic approach to provoked vestibulodynia. J Sex Med 2011 8(2):489-96.
48. Gentilcore-Saulnier E. McLean L. Goldfinger C. et al Pelvic floor muscle assessment outcomes in women with and without provoked vestibulodynia and the impact of a physical therapy program. J Sex Med 2010;7(2 Pt 2):1003-22
49. Murina F, Bianco V, Radici G, et al Transcutaneous electrical nerve stimulation to treat vestibulodynia: a randomised controlled trial. BJOG 2008 115(9):1165-70
50. Murina F, Bernorio R, Palmiotto R, The Use of Amielle Vaginal Trainers as Adjuvant in the Treatment of Vestibulodynia: An Observational Multicentric Study. Medscape J Med. 2008; 10(1): 23
51. Desrochers G. Bergeron S. Khalife S. et al Provoked vestibulodynia: psychological predictors of topical and cognitive-behavioral treatment outcome. Behav Res & Ther 2010 48(2):106-15
52. Tommola P, Unkila-Kallio L, Paavonen J. Long-term follow up of posterior vestibulectomy for treating vulvar vestibulitis. Acta Obstet Gynecol Scand 2011;90(11):1225-31
53. Eva LJ, Narain S. Orakwue CO. Luesley DM. Long-term follow up of posterior vestibulectomy for treating vulvar vestibulitis. J Reprod Med.2008; 53(6):435-40
54. Peters K, Girdler B, Carrico D, et al Painful bladder syndrome/interstitial cystitis and vulvodynia: a clinical correlation Int Urogynecol J 19;5:665-669
55. Reed BD, Caron AM, Gorenflo DW, Haefner HK.J Treatment of vulvodynia with tricyclic antidepressants: efficacy and associated factors Low Genit Tract Dis. 2006; 10(4):245-51.
56. Brown CS. Wan J. Bachmann G. Rosen R. Self-management, amitriptyline, and amitriptyline plus triamcinolone in the management of vulvodynia. J Women's Health. 2009;18(2):163-9
57. Harris G, Horowitz B, Borgida A. Evaluation of gabapentin in the treatment of generalized vulvodynia, unprovoked. Evaluation of gabapentin in the treatment of generalized vulvodynia, unprovoked. J Reprod Med. 2007; 52(2):103-6.
58. Jerome L. Pregabalin-induced remission in a 62-year-old woman with a 20-year history of vulvodynia. Pain Res Manag. 2007; 12(3):212-4.
59. Masheb RM, Kerns RD, Lozano C, et al A randomized clinical trial for women with vulvodynia: Cognitive-behavioral therapy vs. supportive psychotherapy. Pain 2009; 141(1-2):31-40.
60. Powell J, Wojnarowska F Acupuncture for vulvodynia. J R Soc Med. 1999;92(11):579-81