

2007 UK National Guideline on the Management of Vulval Conditions

Clinical Effectiveness Group British Association Sexual Health and HIV

Scope and Purpose

The main objective is to aid recognition of the signs and symptoms and complications of vulval conditions which may present in Genitourinary Medicine clinic attendees. This guideline offers recommendations on the diagnostic tests and treatment regimes needed for the effective management of the following vulval conditions:

- Vulval lichen sclerosus
- Vulval lichen planus
- Vulval dermatitis
- Vulval Intraepithelial Neoplasia (including Paget's disease)
- Vulval vestibulitis
- Vulvodynia

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

Stakeholder involvement

This guideline was reviewed by the Clinical Effectiveness Group of BASHH and their comments incorporated.

Introduction and Methodology

Vulval conditions often present to Genitourinary Medicine clinics. They represent a disparate group of conditions with a variety of causes, affecting a particular anatomical site. These guidelines concentrate on a selected group of conditions, which may be managed by Genitourinary Physicians, either alone or in conjunction with other specialists. 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. The guideline has been updated by reviewing the previous guideline and medical literature since its publication.

Management

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 moisturiser¹ (IV,C)
- Avoid tight fitting garments which may irritate the area¹(IV,C)
- Avoid use of spermicidally lubricated condoms
- Patients should be given a detailed explanation of their condition with particular emphasis on the 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)
- The patient's GP should be informed.

Sexual partners

- Contact tracing is not required unless screening detects a sexually transmitted infection.

Vulval Lichen Sclerosus²

Aetiology

This is an inflammatory condition of unknown aetiology. It is thought to be an autoimmune condition and recent evidence has shown autoantibodies to extracellular matrix protein 1³. There is an increased frequency of other autoimmune disorders in females with lichen sclerosus.⁴

Clinical Features

Symptoms

- Itch / irritation
- Soreness
- Dyspareunia
- Urinary symptoms
- Other symptoms, e.g. constipation, can occur as a result of disruption of the normal architecture
- Can be asymptomatic

Signs

- Patchy pale, atrophic appearance
- Erosions, blistering and purpura in some cases
- Fissuring
- Hyperkeratosis can occur
- Changes may be localised or in a 'figure of eight' distribution including the perianal area

Complications

- Loss of architecture may be manifest as loss of the labia or midline fusion
- Development of squamous cell carcinoma⁵ (actual risk uncertain but small)

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.⁶

Management

Further investigation

- Biopsy: is a necessity if the diagnosis is uncertain or coexistent vulval intraepithelial neoplasia (VIN) / squamous cell carcinoma (SCC) is suspected

- Investigation for autoimmune disease, especially thyroid dysfunction (i.e T4 and TSH) as it is often asymptomatic and has been found be associated⁴
- Skin swab: to exclude secondary infection especially of excoriated lesions
- Patch testing: if secondary medicament allergy suspected

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

- Very potent topical steroids⁷ e.g. Clobetasol propionate 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 2-3 months. There is no evidence on the optimal regimen. (III,B)
- Maintenance treatment may be required and can either be with weaker steroid preparations or less frequent use of very potent steroids.
- 30gm of very potent steroid should last at least 3 months
- Ointment bases are less allergenic but the choice of base will depend on patient tolerability

Alternative regimens

- A very potent topical steroid with antibacterial and antifungal e.g. Dermovate NN (if available) or an additional preparation that combats secondary infection (such as Nystaform), may be appropriate if secondary infection is a concern.
- Surgery¹¹ – For the treatment of coexistent VIN / SCC or fusion. Disease tends to recur around the scar.(III, B).

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).⁸ This study, which included males and females and genital and extragenital 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.⁹

(IIb) Local irritancy was the most common side effect with both tacrolimus and pimecrolimus but usually improved after the initial period of use.

- Oral retinoids, e.g. acitretin¹⁰ – these may be effective in severe recalcitrant disease (Ib) but should only be given by a specialist such as a dermatologist, experienced in the use of these agents.
- UVA1 phototherapy has been reported as successful in a small number of cases.¹² (III,B)

Pregnancy and Breast-feeding

- Topical steroids are safe to use while pregnant or breast-feeding although some practitioners would advise against potent topical steroids.
- 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.

Follow-up

- After 2-3 months to assess response to treatment
- Active disease should be assessed as clinically required
- 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 recalcitrant to treatment and if raised lesions develop Target 100%

Vulval Lichen Planus

Aetiology

Lichen planus is a skin condition that can occur on any area of keratinised skin and the genital and oral mucosa. More rarely it affects the conjunctiva and oesophagus. It is an inflammatory condition of unknown aetiology. In some cases there is overlap between lichen sclerosis and lichen planus.

Clinical Features

Symptoms

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

Signs

There are overlapping subtypes:

- 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. As erosions heal synaechiae and scarring can develop.¹³ This type is also seen in the oral mucosa although synaechia are uncommon. The term vulvo-vaginal gingival syndrome is used in severe cases. The presenting symptom is usually of pain.
- Guttate, annular and plaque: the most common types on keratinised skin. Lesions are polygonal papules, which sometimes merge to give plaques or annular lesions. The papules are purple, ranging from mauve to dark purple/brown. They are shinier than the surrounding skin. A white network known as Wickham's striae can be seen on the surface of the lesions. Lesions are most commonly seen on the wrists. This pattern is uncommonly seen on vulval mucosa where it usually presents with pruritus.
- Hypertrophic: raised keratotic lesions are most commonly seen on the legs.
- Flexural: groins and sub-mammary folds can be affected by both erosive and non-erosive lichen planus.¹⁴
- Lacy network: this change is seen in genital and oral mucosa. It is often asymptomatic but studies have shown that in patients with oral lichen planus asymptomatic vulval lichen planus occurs in over a third of patients.¹⁵
- Vulval splitting: this problem can be the cause of severe dyspareunia. In one study biopsy of clinically normal vulval skin in patients with recurrent splitting showed lichen planus in three of 9 cases. Other findings were infection with *Candida* and chronic dermatitis.¹⁶

The perianal area is less often involved than in lichen sclerosus but the vagina can be involved particularly in erosive lichen planus.

Complications

- Scarring, including vaginal synaechiae
- Development of squamous cell carcinoma: In one study the incidence was as high as 3%.¹⁷

Diagnosis

- Characteristic clinical appearance. Involvement of the vagina is very much more common in lichen planus than lichen sclerosus. Skin changes elsewhere can be helpful but overlaps between lichen planus, lichen sclerosus and even subacute and discoid lupus are 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.

- Investigation for autoimmune disease especially of the thyroid (i.e T4 and TSH if there is any suspicion of abnormality)³
- 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.¹⁸

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

- Very potent topical steroids e.g. Clobetasol propionate.(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.¹⁷ 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.

Alternative regimens

- A very potent topical steroid with antibacterial and antifungal e.g. Dermovate NN may be appropriate if secondary infection is a concern

Research findings and unlicensed treatments

- Topical calcineurin inhibitors. (IIb) Tacrolimus 0.1% has been shown to give short-term relief.¹⁹ In practice many patients find stinging on application too severe to persist with treatment. Topical pimecrolimus is better tolerated. A study of 10 patients showed total response in 6 of the nine who could tolerate treatment and partial response in 3.²⁰ As discussed in the section of lichen sclerosus the long-term risks are unknown and of this is emphasised by the report of malignant change in oral lichen planus following the use of topical tacrolimus.²¹
- There are many single case reports and small series of the use of a wide variety of treatments including retinoids, immunosuppressives and antibacterials. Most of these reports are of treatment of cutaneous or oral lichen planus.

Pregnancy and Breast-feeding

- Topical steroids are safe to use while pregnant or breast-feeding although some practitioners would advise against potent topical steroids.

- 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.
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Follow-up

- At 2-3 months to assess response to treatment
- Active disease should be assessed as clinically required
- 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 recalcitrant to treatment and if raised lesions develop Target 100%

Vulval dermatitis²

Aetiology

- Irritant, allergic, atopic or seborrhoeic
- Secondary – e.g. to iron deficiency in Lichen simplex²², or after candidal infection

Clinical Features

Symptoms

- Vulval itch
- Soreness

Signs

- Erythema
- Lichenification
- Fissuring

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
- General examination of the skin to look for other signs of psoriasis

Management

Further Investigation

- Screening for infection (e.g. *Staphylococcus aureus*, *Candida albicans*)
- Dermatological referral for consideration of patch testing²³ – standard battery and medicaments (III,B)
- IgE and RAST tests or prick tests especially for latex allergy in eczema provoked by condoms III
- Ferritin²² (III,B)
- Biopsy (IV,C)

Treatment

Recommended Regimens

- Avoidance of precipitating factor (IV,C)
- Use of emollient soap substitute
- Topical corticosteroid – the choice of preparation will depend on severity, 1% Hydrocortisone in milder cases, or betamethasone or clobetasol for limited periods if severe or lichenified, or to break the itch-scratch cycle. A combined preparation containing antifungal and/or antibiotic may be required if secondary infection suspected. Apply once or twice daily.(IV,C)

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 vulva clinic or to a dermatologist.

Vulval Intraepithelial Neoplasia (VIN)²

Aetiology

This is a histological diagnosis and is a combination of conditions of different aetiologies. In Genitourinary Medicine clinics the commonest aetiological agent is Human papillomavirus (HPV) (most frequently type 16). VIN is commoner in immunocompromised women²⁴. It is also associated with dermatological conditions such as lichen sclerosus²⁵.

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
- Persistent or atypical lesions, or those with associated induration should be biopsied.

Complications

- Development of squamous cell carcinoma (SCC)

Diagnosis

- Biopsy – Histology shows loss of organisation of squamous epithelium with a variable degree of cytological atypia which is graded VIN I, II and III.

Management

Further investigation

- Annual cervical cytology +/- colposcopy – there is an association with cervical intraepithelial neoplasia (CIN)²⁶ (this is probably only applicable to those due to HPV) (IV,C)
- Management may be by GU Physicians alone or in consultation with other disciplines, depending on local expertise.

Treatment

Most studies and research relate to VIN III. Multifocal lesions can be treated in the same manner as single lesions, but may have a higher recurrence rate²⁷.

Recommended Regimen

- Local excision^{27,28} – this is the treatment of choice for small well circumscribed lesions as it has the lowest rate of recurrence on follow up.(III,B)

Alternative Regimens

1. Local destruction – by laser²⁷ (III,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. 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. (IIb, B)
3. Photodynamic therapy – using systemic or topical agents has proven useful in some small trials²⁷.(III,B)

4. Supervision²⁸ – some lesions will spontaneously regress. This may be the best policy for VIN I and II. However there is a risk of progression and patients should be made aware of this (IV,C).
5. Vulvectomy – this has been effective but recurrence may occur and function and cosmesis will be impaired (IV,C)²⁷
6. 5 fluorouracil cream³⁰ – 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).

Pregnancy and Breast-feeding

- Imiquimod cream is not licensed in pregnancy
- 5 Fluorouracil should be avoided in pregnancy

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)³¹

Auditable Outcome Measures

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

Vulval Paget's Disease^{2,32}

Aetiology

This is a rare form of intraepithelial neoplasia. The aetiology is unknown.

Clinical Features

Symptoms

- Localised itch

Signs

- Red, crusting, lesion. May look eczematous

Complications

- Development of adenocarcinoma

Diagnosis

- Biopsy- Single cells or clusters infiltrate the squamous mucosa. Nuclei have large nucleolus and are hyperchromatic and the cytoplasm contains mucin.

Management

Further Investigation

- There is an association with adenocarcinoma elsewhere (<15%) so investigation for other tumours would be advised (IV,C)
- Referral to a local specialist recommended

Treatment

Recommended regimen

- Wide local excision (III,B)

Follow up

- Regular follow up is required as there is a significant risk of recurrence. This should be undertaken by the local specialist.

Auditable Outcome Measures

- Referral to local specialist Target 100%

Vulval Pain Syndromes

Provoked Vestibulodynia (Vulval Vestibulitis)^{33,34,35}

Aetiology

The aetiology is unknown and the condition is diagnosed on clinical grounds. It is also known as focal vulvitis or vestibulitis.

Clinical Features

Symptoms

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

Signs

- Focal tenderness at the vestibule and may be associated with erythema over Skene's and Bartholin's ducts³³
- There are no signs of an acute inflammatory process

Complications

- Vaginismus

Management

Further Investigation

- Screening to exclude infection may be helpful as many women present with symptoms attributed to chronic candidiasis.
- Biopsy – this may show non-specific inflammation, but can be used to exclude other dermatoses.

Treatment

There are numerous treatments described, however there is a lack of well-designed clinical trials. General advice on vulval care should be given.

Recommended Regimens

- Observation – the natural history is that remission can occur in up to 50% of patients with vulval vestibulitis
- Soothing agents e.g. emollients such as aqueous cream².
- Topical local anaesthetic³⁴ –Lidocaine (as 5% ointment, or 2% gel) may be used to control symptoms during sexual intercourse or as an adjunct to other treatment (IV,C)
- Behavioural therapy³⁶ – this may be used alone or as an adjunct to other therapy (IIa,B)
- Biofeedback³⁷ – has been used with good effect (III,B)
- Integrated model of care – involving medical evaluation and treatment, psychotherapy, physiotherapy and dietary advice has been shown to improve symptoms³⁸ (IV,C)

- Pain Modifiers – e.g. Amitriptyline in small doses (gradually titrated from 10mg up to 100 mg according to response and side effects³⁹. This may alleviate symptoms in a proportion of women but has not been effectively studied. IV,C Gabapentin⁴⁰ or pregabalin are also being used. (IV C)

Alternative Regimens

- Topical steroids alone and in combination with other agents (e.g. Trimovate)^{34,41} (IV,C)
- Surgery - Perineoplasty has been used with some success. Sub - total perineoplasties (with or without interferon) have also lead to improvement in some patients. Vestibuloplasty was not shown to be effective when compared to perineoplasty. Surgery may be suitable for intractable cases, but failure rates are higher if pain was present from first intercourse or was constant^{42,43}.(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%

Dysaesthetic vulvodynia^{35,36,44}

Aetiology

The aetiology is unknown and the condition is diagnosed on clinical grounds.

Clinical Features

Symptoms

- Pain that is longstanding and unexplained. Often in older women. Often associated urinary symptoms such as frequency.

Signs

- The vulva appears normal
- Pain on light touch over the labia. Can also occur on the trunk.

Management

Further investigation

- No specific investigation required.

Treatment

Recommended regimens

- Soothing agents e.g. emollients such as aqueous cream².
- Topical local anaesthetic³⁹– Lidocaine (as 5% ointment, or 2% gel) may be used to control symptoms during sexual intercourse or as an adjunct to other treatment (IV,C)

- Pain modifiers – Amitriptyline in small doses (up to 50mg daily)(IV,C)⁴⁴, Gabapentin⁴⁰ or pregabalin is also being used. (IV,C)

Follow up

- As clinically required

Auditable outcomes

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

Qualifying statement

The recommendations in this guideline may not be appropriate for use in all clinical situations. Decisions to follow these recommendations must be based on the professional judgement of the clinician and consideration of individual patient circumstances and available resources.

All possible care has been undertaken to ensure the publication of the correct dosage of medication and route of administration. However, it remains the responsibility of the prescribing physician to ensure the accuracy and appropriateness of the medication they prescribe.

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Conflict of Interest

None

Evidence Base

A Medline search was performed from 2001 up to 2006, using Keywords – Vulval disease, Lichen sclerosus, Lichen planus, Vulval intraepithelial neoplasia, Vulval vestibulitis, focal vulvitis, vulvodynia, vulval pain syndromes, vulval dermatoses, vulval eczema, and vulval itch. A search of the Cochrane database was also performed. Related articles were also checked.

Editorial Independence

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

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