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British Association of Dermatologists guidelines for the management of lichen sclerosus 2018

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NICE has accredited the process used by the British Association of Dermatologists to produce clinical guidelines. The renewed accreditation is valid until 31 May 2021 and applies to guidance produced using the process described in Updated guidance for writing a British Association of Dermatologists clinical guidance – the adoption of the GRADE methodology 2016. The original accreditation term began on 12 May 2010. More information on accreditation can be viewed at www.nice.org.uk/accreditation.

1.0 PURPOSE AND SCOPE

The overall objective of the guideline is to provide up-to-date, evidence-based recommendations for the management of lichen sclerosus (LS) in adults (18+ years), children (0-12 years) and young people (13-17 years). The document aims to:

- offer an appraisal of all relevant literature up to July 2017, focusing on any key developments
- address important, practical clinical questions relating to the primary guideline objective.
- provide guideline recommendations and if appropriate research recommendations

The guideline is presented as a detailed review with highlighted recommendations for practical use in primary care and in secondary care clinics, in addition to an updated Patient Information Leaflet (PIL; available on the BAD website, http://www.bad.org.uk/for-the-public/patient-information-leaflets).

1.1 Exclusions

The guideline does not cover complex surgical techniques used in the management of selected cases of LS or the management of squamous cell carcinoma (SCC) in LS.

2.0 METHODOLOGY

This set of guidelines has been developed using the BAD's recommended methodology[1] (see summary in Appendix K) with reference to the Appraisal of Guidelines Research and Evaluation (AGREE II) instrument [www.agreetrust.org][2] and the Grading of Recommendations Assessment, Development and Evaluation (GRADE).[3] Recommendations were developed for implementation in the UK National Health Service (NHS).

The guideline development group (GDG), which consisted of consultant dermatologists, patient representatives and a technical team (consisting of a guideline research fellow and project manager providing methodological and technical support), established several clinical questions pertinent to the scope of the guideline and a set of outcome measures of importance to patients, ranked according to the GRADE methodology (see section 2.1).

A systematic literature search of PubMed, MEDLINE, EMBASE, Cochrane and AMED databases was conducted to identify key articles on LS up to July 2017; search terms and strategies are detailed in the supplementary information (Appendix L). Additional references relevant to the topic were also isolated from citations in reviewed literature. Evidence from included studies was graded according to the GRADE system (high, moderate, low or very low quality). Recommendations are based on evidence drawn from systematic reviews of the literature pertaining to the clinical questions identified; the summary of findings with forest plots (Appendix D), GRADE evidence profiles indicating the quality of evidence (Appendix E), clinical evidence summary (Appendix B), summary of included studies (Appendix F),

narrative findings for non-comparative studies (Appendix G), summary of topical steroids (Appendix H), tables Linking the Evidence To the Recommendations (LETR) (Appendix C), PRISMA flow diagram (Appendix I) and list of excluded studies (Appendix J) are detailed as a web appendix. The strength of recommendation is expressed by the wording and symbols as shown in Table 1.

Strength	**Wording**	**Symbols**	**Definition**
Strong recommendation *for* the use of an intervention	"Offer" *(or similar, e.g. "Use", "Provide", "Take", "Investigate", etc.)*	↑↑	Benefits of the intervention outweigh the risks; most patients would choose the intervention whilst only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policy makers, it would be a useful performance indicator.
Weak recommendation *for* the use of an intervention	"Consider"	↑	Risks and benefits of the intervention are finely balanced; most patients would choose the intervention but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policy makers, it would be a poor performance indicator where variability in practice is expected.
No recommendation		Θ	Insufficient evidence to support any recommendation.
Strong recommendation *against* the use of an intervention	"Do not offer"	↓↓	Risks of the intervention outweigh the benefits; most patients would *not* choose the intervention whilst only a small proportion would; for clinicians, most of their patients would *not* receive the intervention.

Table 1: Strength of recommendation ratings

2.1 Clinical Questions and Outcomes

The GDG established a clinical question pertinent to the scope of the guideline. (See supplementary information Appendix A for full review protocol).

In patients with lichen sclerosus:

Treatment	What are the clinical outcomes and cost effectiveness of therapies? • Topical corticosteroids • Topical calcineurin inhibitors • Testosterone and other hormonal treatments • Surgery • Cryotherapy • Photodynamic therapy • Phototherapy • Laser • Systemic therapies
	Additionally, the GDG also aims to answer the following questions based on the evidence, if possible, or on consensus: 1. What is the most appropriate treatment regimen? 2. Is maintenance treatment required? 3. What follow-up protocols are needed?

The GDG also established two sets of outcome measures of importance to patients (treatment) which were agreed by the patient representatives, one for female patients and one for male patients, ranked according to the GRADE methodology,[4] data on which are extracted from included studies (see Appendix K):

Females		**Males**	
Quality of life (improvement of symptoms)	9	Quality of life (improvement of symptoms)	9
Restoration of sexual function*	9	Restoration of sexual function*****	9
Abolition of risk of vulval cancer*	9	Abolition of risk of penile cancer*****	9
Serious adverse events	8	Serious adverse events	8
Physician global assessment	6	Restoration of urinary function	7
Patient global assessment	5	Physician global assessment	6
Minor adverse events	4	Patient global assessment	5
		Minor adverse events	4
*Adults and young people only Outcomes ranked 7, 8 and 9 are critical for decision-making; those ranked 4, 5 and 6 are important but not critical for decision making.			

3.0 SUMMARY OF RECOMMENDATIONS

There are few randomized controlled trials (RCTs) to support the following guidelines for the management of LS. The following recommendations and ratings were agreed upon unanimously by the core members of the GDG and patient representatives. For further information on the wording used for recommendations and strength of recommendation ratings see section 2. Good practice point (GPP) recommendations are derived from informal consensus.

The GDG is aware of the lack of high-quality evidence for these recommendations, therefore, strong recommendations with an asterisk (*) are based on available evidence, as well as consensus and specialist experience. Further information about other therapies where there is less evidence are discussed in the supplementary information section.

All people (children, young people & adults: male and female)

R1 (GPP) All people with LS should be managed by a healthcare professional experienced (secondary care specialist or GP with specific training) in treating the condition

R2 (GPP) Commence treatment of LS following a firm clinical diagnosis or with histological confirmation, where necessary

R3 (GPP) Undertake a full history for all people with LS, including dyspareunia and psychosexual issues. Document urinary symptoms. Perform a detailed examination documenting architectural change at baseline (using a diagram or photograph, according to patient preference)

R4 (GPP) Advise all people with LS to avoid all irritant and fragranced products

R5 (GPP) Provide all people with LS up-to-date patient information on the condition http://www.bad.org.uk/for-the-public/patient-information-leaflets

R6 (GPP) All people treated for LS should be followed up (see algorithm) to assess response to treatment and to advise on long-term control

Adult females

R7 (↑↑) Offer* all females with anogenital LS clobetasol propionate (CP) 0.05% ointment on a regimen for 3 months (once a day for a month, alternative days for a month, twice weekly for a month), combined with a soap substitute and a barrier preparation

R8 (GPP) Discuss the amount of topical treatment to be used, the site of application and the safe use of an ultra-potent topical steroid with the patient.

R9 (↑↑) Offer* continued use of CP 0.05% for ongoing active LS disease (see algorithm)

R10 (↑) Consider an individualized treatment regimen of topical steroid to maintain disease control and prevent scarring in females with ongoing active LS disease despite good compliance. Treatment should be titrated to maintain symptoms and resolution of skin thickening and ecchymosis although pallor may not completely resolve.

R11 (GPP) Consider referral to a specialist vulval clinic in all females (including children & young people) with LS not responding to a topical steroid, or if surgical management is being considered

R12 (↑) Consider intralesional triamcinolone (1-2 mg) in females with LS with topical steroid-resistant, hyperkeratotic areas after intra-epithelial neoplasia or malignancy has been excluded by biopsy

Adult males

R13 (↑↑) Offer* all males with genital LS CP 0.05% ointment once daily for 1-3 months with an emollient as a soap substitute and as a barrier preparation

R14 (GPP) Discuss the amount of topical treatment to be used, the site of application and the safe use of an ultra-potent topical steroid with the patient

R15 (GPP) Consider a repeat course of topical treatment for 1-3 months in those who relapse

R16 (↑) Consider intralesional triamcinolone in males with LS with topical steroid-resistant, hyperkeratotic areas following biopsy to ensure no intra-epithelial neoplasia or malignancy

R17 (↑↑) Offer* all males with phimosis caused by LS who do not respond to an ultra-potent topical steroid after 1-3 months, referral to an experienced urologist for circumcision

R18 (GPP) Offer males with urinary symptoms due to LS referral for a urology opinion and further investigation and management of lower urinary tract symptoms

R19 (GPP) Offer treatment for meatal involvement by LS with CP 0.05% ointment applied once daily via cotton wool bud or meatal dilator for 1 to 3 months prior to referral to a urologist specialized in the management of LS.

R20 (GPP) Offer all males with a urethral stricture due to LS referral to a urologist specialized in the management of LS. A urologist may consider treatment for a urethral stricture with CP introduced into the urethra via a urinary catheter or meatal dilator, depending on stricture length, before proceeding to surgical treatment options.

R21 (↑↑) Offer all males with LS who have failed to respond to topical steroids and/or circumcision referral for a specialist urology opinion on other surgical treatment options, for example total or partial glans resurfacing and split-skin grafting

R22 (GPP) Advise obese males with LS and a buried penis to lose weight. Further referral to a specialist urologist and bariatric services may be required.

Children & young people – female

R23 (GPP) Refer female children and young people with LS to specialized vulval services (vulval clinic, paediatric dermatologist or urologist experienced in managing LS)

R24 (GPP) Consider referral to specialist vulval clinic in females (also adults) with LS not responding to topical steroid, or if surgical management is being considered

R25 (↑↑) Offer* all females with anogenital LS CP 0.05% ointment on a regimen for 3 months (once a day for a month, alternative days for a month, twice weekly for a month) with an emollient as a soap substitute and as a barrier preparation

R26 (GPP) Discuss the amount of topical treatment to be used, the site of application and the safe use of an ultra-potent topical steroid with the patient.

R27 (↑) Consider an individualized treatment regimen of topical steroid to maintain disease control and prevent scarring in females with ongoing active LS disease despite good compliance

Children & young people – male

R28 (↑↑) Offer* a trial of an ultra-potent topical steroid applied once daily for 1 to 3 months combined with emollients and barrier preparations to all male children & young people with phimosis caused by LS.

R29 (↑↑) Offer all male children with phimosis caused by LS who do not respond to topical steroids after 1 to 3 months, referral to a paediatric urologist for a circumcision. Disease of the glans unmasked by circumcision should be treated with a potent topical steroid once daily for 1 to 3 months.

R30 (GPP) Send* all circumcision specimens in males with LS for histological examination

Extragenital disease

R31 (↑) Consider potent topical steroids, acitretin, methotrexate and phototherapy for people with extragenital LS

Insufficient evidence to support any recommendation

(Θ) Currently, there is insufficient evidence to recommend the following interventions for people with LS:

- Topical calcineurin inhibitors
- Systemic retinoids

List of key future research recommendations (FRRs)

FRR1 What is the role of topical calcineurin inhibitors in treating people with LS?

FRR2 What is the role of topical steroids in preventing malignancy in genital LS in females?

FRR3 What is the course of LS after puberty in females?

FRR4 What is the optimal surgical management of females with fusion over the clitoris?

FRR5 Would acitretin in combination with a topical steroid be more effective than monotherapy in treating people with resistant LS?

FRR6 What is the safety and efficacy of adalimumab in males with urethral stenosis caused by LS?

FRR7 To set up a national registry for extensive extragenital LS to identify the treatments involved and outcomes achieved.

FRR8 What is the role of urine in the pathogenesis of genital LS and paediatric genital LS?

FRR9 Is there a role for systemic therapy in genital LS?

FRR10 What proportion of patients with LS remit completely?

4.0 ALGORITHM

The recommendations and discussions in the LETR (see Appendix C in the supplementary information) and consensus specialist experience were used to produce management pathways for adult patients. Similar algorithms have been published elsewhere (https://bssvd.org/education-and-training/guidelines-and-clinical-standards/documents/Lichen-Sclerosus-management.pdf).

See separate PDF files for the 2 algorithms.

5.0 INTRODUCTION

5.1 Definition

LS is an inflammatory scarring dermatosis, characterized by a lymphocytic response, that has a predilection for the genital skin in both sexes.[5-7]

The old terms ‘balanitis xerotica obliterans’ and ‘kraurosis vulvae’ are synonymous terms for LS and should not be used. The suffix ‘et atrophicus’ has been dropped, as it is recognized that some cases of LS are associated with a hypertrophic, rather than atrophic, epithelium. The term ‘leukoplakia’ (meaning white plaque) is not a diagnostic entity and is descriptive only, as many conditions may present with white plaques. There are instances when it can be difficult to differentiate between LS and lichen planus (LP) on the basis of the clinical and histological features,[8] and these cases appear to constitute an overlap syndrome. Clinically, these cases can be associated with hyperkeratosis and a poor response to ultra-potent topical corticosteroids.

5.2 Aetiology

The aetiology of LS is contested. There is evidence to suggest that autoimmune mechanisms are involved in its pathogenesis.[9-12] An increased incidence of tissue-specific antibodies[13] and associations with other autoimmune diseases, especially thyroid disease, has been documented in women with LS,[14-16] but this is not the case in men.[17,18] The transcriptosome of male genital LS shows no evidence of patterns of gene expression associated with autoimmune diseases or infectious diseases.[19] The presence of circulating extracellular matrix protein antibodies has been demonstrated in both sexes.[20,21] In males LS is associated with an increased body mass index (BMI)[22,23] and has been associated with coronary artery disease, diabetes mellitus and tobacco use.[23]. Crucially in males LS is associated with urinary occlusion because of microincontinence created by the dysfunctional performance of the naviculomeatal fossa and meatal lips as a low-pressure valve.[24] LS rarely occurs in boys circumcised at birth and this may support the concept that a moist environment under the foreskin predisposes to LS.[17] The association of LS with urostomy and ileostomy suggests that moisture and irritation may play a role in the aetiology of LS.[25] Urine contact may be relevant to the association of LS with hypospadias[26] and hypospadias repair in cases without prior LS can be complicated by LS. Trauma is known to predispose to LS and it may appear in surgical wounds and following radiotherapy and sunburn.[27-29]

Genetic associations and associations with HLA class II antigens are seen in males and females.[19,30-32] A family history is reported in 12% of patients with LS.[33] Vulval LS is associated with epigenetic alterations in expression of isocitrate dehydrogenase enzymes and hydroxymethylation.[34] Controversy remains regarding the role of *Borrelia* infection as an aetiological agent; although several studies have shown that this association does not occur in the USA, some doubt still remains in Europe.[35] There is no evidence for a link between LS and *Borrelia burgdorferi* in the UK.[36] The role for TNFα in the pathogenesis of LS has been reported and early reports suggest promising outcomes for treatment of male LS with adalimumab.[37,38]

5.3 Incidence and patterns

The true incidence of LS is unknown, and probably underestimated as it is either asymptomatic or under-recognized.[39] The estimated prevalence in adult females is up to 3%[40] and 0.07% in males.[41] Genital LS in females has two peak ages of presentation - in the pre-pubertal and post-menopausal years.[42] There is also a bimodal onset in males, with age peaks in young boys and in adult men.[17,43]

5.4 Clinical features

a. Adult female anogenital

Itch is the main symptom, but pain may be a consequence of erosions or fissures. Rarely LS may be asymptomatic and is an incidental finding on examination. In those with itch, this is often worse at night and may be sufficiently severe to disturb sleep. Dyspareunia occurs in the presence of erosions, fissures or introital narrowing. Urinary symptoms and urinary incontinence are reported by women with LS[44,45] but have been shown to be less common than in the general population in another.[45,46]

The typical lesions are porcelain-white papules and plaques, often associated with areas of ecchymosis. Follicular delling may be prominent, and occasionally hyperkeratosis is a prominent feature. The characteristic sites are the interlabial sulci, labia minora, clitoral hood, clitoris and perineal body. LS is a scarring dermatosis and may cause resorption of the labia minora, sealing of the clitoral hood and covering of the clitoris. The vagina and cervix are not involved (in contrast to LP), unless there is a significant vaginal prolapse when the mucosa may become keratinized and develop the disease.[47,48] Perianal lesions occur in women in 30% of cases. There may be extension to the buttocks and genitocrural folds.

b. LS in pregnancy

LS can koebnerize and may first arise in obstetric scars. There are few reports of the effects of pregnancy on LS but clinical experience suggests that it does improve with less treatment required. However, topical steroids can be safely continued during pregnancy and in the post delivery period, if needed. If the LS is well controlled, without significant scarring, vaginal delivery is not contra-indicated and a controlled delivery by an experienced midwife with early episiotomy to prevent tearing. The preferred mode of delivery should be discussed with the patient and their obstetrician.

c. Child female anogenital

The lesions are similar to those in adult women, but ecchymosis may be very striking and potentially mistaken as evidence of sexual abuse. However, the two are not mutually exclusive as some cases of LS may possibly be caused or aggravated by sexual abuse through koebnerization.[49] Features that should arouse suspicion of this include LS arising in older pre-pubertal girls, poor response to treatment, the presence of associated sexually transmitted infection or other symptoms or signs of abuse.

Perianal involvement is a frequent finding in young girls, who may present with constipation because of painful fissuring in this area. Dysuria can also result from fissuring.

Although childhood LS often improves at puberty, there may be cases that persist into adulthood[50] and the patient should be made aware of this. Long term follow-up may needed for those patients with ongoing disease activity. Malignancy has not been reported in girls but scarring can occur.

d. Adult male genital

The common sites of involvement of LS in adult men are the glans penis, coronal sulcus, frenulum and prepuce. Perianal disease is rarely, if ever, seen in males. The presenting complaint is often difficulty with sexual intercourse (male dyspareunia).[17] Tightening of the foreskin (constrictive posthitis) may lead to paraphimosis, phimosis and painful erections. One report documents that 30% of phimosis occurring in adults was due to LS,[51] although another study of 75 subjects with severe phimosis identified LS in only 11%.[52] Other presenting complaints are due to the appearance of lesions or changes in urinary stream, but itch is not a prominent symptom. Urological symptoms are reported in 10% of patients.[17] In a urological practice, urethral disease was reported to occur in 20% of patients and meatal disease in 4%.[53] The perimeatal area may be involved and post-inflammatory scarring may lead to stenosis and obstruction. Initial meatal disease may lead to problematic voiding with subsequent progression to urethral disease[6] and the extent of involvement ranges from purely meatal to panurethral.[54] It has been suggested that early treatment of meatal disease may prevent progression to urethral involvement and urethral strictures.[55] These complications may require a multidisciplinary approach with input from both a dermatologist and urologist.

e. Child male genital

The most frequent presentation is phimosis. The reported incidence of LS in boys with phimosis ranges from 12% to 100%.[56-59] Involvement of the glans has been reported to occur in 56% of boys and meatal involvement in 37%.[60] Perianal involvement, as in adult men, is extremely rare. There is a report of a rare complication of renal failure following meatal obstruction.[61] Phimosis caused by LS may be complicated by preputial stones.[62]

f. Extragenital male, female and children

The classical sites for extragenital lesions are the upper trunk, axillae, buttocks and lateral thighs, and these are involved most frequently in adult women. Rarer sites include the mouth, face, scalp, hands, feet and nails.[63,64] The typical lesions are porcelain-white plaques, which may have follicular dells and areas of ecchymosis, similar to the genital lesions. There may be difficulty in distinguishing the lesions from those of morphoea. The clinical types of extragenital LS include an extensive bullous form,[65,66] annular, Blaschkoid

and keratotic variants.[67] Koebnerization is very common at extragenital sites, arising at pressure points, old surgical and radiotherapy scars and at sites of trauma including urostomies.[25,68]

5.5 Assessment and investigations

a. Biopsy

LS is a clinical diagnosis and a confirmatory biopsy, is not always necessary when the typical clinical features are present. This is particularly true in children and men. However, histological examination is recommended if there are atypical features or diagnostic uncertainty and is essential if there is any suspicion of neoplastic change. As LS is less common in young adult females presenting in the reproductive years, a biopsy should be considered to confirm the diagnosis before starting treatment.

The site of the biopsy is important and should be taken from the most active sclerotic area. Good clinico-pathological correlation with active discussion between clinician and pathologist is vital, particularly in relation to the diagnosis of differentiated intra-epithelial neoplasia.

A biopsy must always be considered in patients if:

1. There is a suspicion of neoplastic change, i.e. a persistent area of hyperkeratosis, erosion or erythema, or new warty or papular lesions. Several mapping biopsies may be required if there is extensive abnormality. If there are any lesions highly suspicious of a squamous cell carcinoma, the patient should be referred urgently to a gynae-oncologist, or specialist urologist in males, for excision of the whole lesion for adequate staging.
2. The disease fails to respond to adequate treatment
3. Circumcision is performed: the foreskin should always be sent for histology to exclude penile intra-epithelial neoplasia (PeIN) and confirm the diagnosis but non-specific features do not exclude LS. Although an obligate factor in the pathogenesis of LS, the foreskin is not always the seat or a site of disease.
4. In extragenital LS, which has features mimicking morphoea
5. There are pigmented areas, to exclude an abnormal melanocytic proliferation
6. Alternative or additional therapy to a potent topical steroid is to be used
7. Urological surgery is being considered for urethral disease for confirmation of LS[69]

b. Immunology

An auto-antibody screen to look for associated auto-immune disease is only useful if there are clinical features to suggest an auto-immune disorder.

c. Microbiology

Swabs are not required routinely but may be indicated in erosive or topical steroid resistant disease to exclude herpes simplex or candida as additional complicating problems.

5.6 Complications

5.6.1. Malignancy

Squamous cell carcinoma (SCC) has been described in genital LS of the usual and verrucous histological subtypes.[70-72] SCC is not associated with extragenital LS. Melanoma, basal cell carcinoma and Merkel cell carcinoma have all been reported in patients with vulval LS and melanoma in male genital LS[73] but no studies prove that there is an increased frequency of these tumours. There appear to be two pathogenetic mechanisms for genital SCC: firstly, SCC in younger patients is associated with the oncogenic types of human papilloma virus (HPV, specifically high risk HPV 16 and HPV 18); and secondly, in older patients, the association is with a chronic scarring dermatosis such as LS (or LP) with little evidence of a link with HPV.[74-76] Differentiated vulval intra-epithelial neoplasia (VIN) or PeIN associated with a dermatosis, is a precursor of SCC but can be challenging to diagnose histologically.[77] Local recurrence of a vulval SCC is greater in those with LS.[78]

a. SCC in females with genital LS

This risk of developing malignancy is approximately 3.5% to 5%.[6,42,79] However, histopathological examination of vulval SCCs indicates that about 60% occur on a background of LS.[80-82] LS may act as both an initiator and promoter of carcinogenesis by mechanisms that seem to be independent of HPV. However, HPV may be found in VIN associated with LS.[83]

SCC of the vulva should be managed by gynaecological oncologists as surgery has to be individualized according to the tumour size and location, particularly in early invasive disease.

b. SCC in men with genital LS

An association between LS and penile SCC has also been reported.[53,70,84,85] The maximum rate is 12.5% and the minimum is 0%.[17,86] The overall rate is probably 4-5% as in women.[42] Histological evidence of LS can be found in about 23% to 40% of penile carcinomas.[85,87,88] In a ten-year multi-centre cohort of 130 males with genital LS, histological changes of SCC were found in eight, verrucous carcinoma in two and PeIN in one.[89]

Rarely, chronic LS related urethral stricture disease is associated with an SCC of the urethra.

The role of HPV in penile LS-associated SCC has also been debated. Some studies using PCR have documented a negligible frequency of HPV in LS,[90,91] but other studies have suggested a frequency of up to 33%.[92,93] An additional feature that has been linked with penile LS-associated SCC is the occurrence of a prominent lichenoid infiltrate on long standing, chronic LS, suggesting disease reactivation.[94]

5.6.2 Scarring

a. Introital narrowing

Anterior and/or posterior fusion of the labia can lead to a narrowing of the introitus. If significant and causing dyspareunia or difficulty with micturition, surgery may need to be considered, using part of the posterior vaginal wall in the reconstruction to prevent further

adhesions and stenosis due to koebnerization.[95,96] Topical steroids, together with the use of vaginal dilators must be used post-operatively to prevent re-adhesion.[97] The topical steroid can be started 48 hours post-operatively once daily until area fully epithelialized and then reduced in frequency on an individual basis to maintain control of symptoms and signs.

b. Pseudocyst of the clitoris

Occasionally, clitoral hood adhesions seal over the clitoris and keratinous debris builds up underneath forming a painful pseudocyst. These patients should be reviewed with a gynaecologist with a special interest in vulval disease. Division of adhesions may be needed if symptomatic or recurrently infected.[98,99]

c. Phimosis

Phimosis is due to preputial scarring. Phimosis can make a topical steroid difficult to apply to the diseased inner aspect of the foreskin and methods of applying the topical steroid should be reviewed; one option is to introduce the topical steroid using a cotton wool bud. If the phimosis has failed to respond to a potent topical steroid the patient should be referred for circumcision. If the disease is still active at the time of surgery it is important to continue topical steroids to prevent koebnerization and further scarring, particularly around the coronal sulcus.

d. Adhesions and frenulum disease

Adhesions may be transcoronal or subcoronal. Often there is a mixed presentation. They may be reduced manually by the patient during treatment with ultrapotent topical steroid or they may require surgical reduction usually during circumcision.

Frenulum scarring may be the cause of significant sexual morbidity and has a variable response to topical steroids. Frenuloplasty may be necessary usually in the context of complete circumcision.

e. Meatal stenosis in males

If this results in an impaired urinary stream, referral for urological assessment is advisable. Before referral a meatal stenosis can be treated with a topical steroid introduced via cotton wool bud or meatal dilator for 1 to 3 months.

f. Urethral stricture

Although LS may start at the meatus, the condition may spread proximally to involve the penile and bulbar urethra.[53] Urethral involvement is reported to occur in 20% of males with LS.[53] All male patients with LS should be questioned about urinary symptoms and, if present, referral to a specialist urologist for further investigation is needed. Prior to invasive surgery for a urethral stricture, a urologist may consider treatment with a topical steroid applied to the urethra via a urinary catheter or meatal dilator, depending on the length of the stricture.[69]

5.6.3 Sensory abnormalities

a. Vulvodynia

Vulvodynia may occur after any inflammatory condition of the vulva or vestibule. Typically, the patient remains symptomatic despite objective clinical improvement or resolution of the skin lesions. Neuropathic pain does not respond to topical corticosteroids, and treatment must be directed to this entity.

b. Penile dysaesthesia

Men may develop a similar problem, with an abnormal burning sensation on the glans or around the urethral meatus. The management is as for females.

5.6.4 Psychosexual problems

LS has a significant impact on quality of life,[100-102] particularly on sexual functioning.[103] Psychosexual issues are common and may persist after successful treatment.[104] Patients who have any chronic genital disorder will often lose their interest in sexual activity, leading to problems with sexual dysfunction.[105,106] It is important to give the patient the opportunity to express their concerns about their sexual function, and to offer a referral to someone with the necessary expertise to address these problems. Menopause may also have an effect on sexual function which may be helped by hormone replacement.

6.0 TREATMENT FAILURE

If treatment with topical corticosteroids appears to fail to bring LS under control then it is important to consider the following:

- Is non-compliance an issue? Sometimes patients may be alarmed at the contents of the package information insert warning against the use of topical corticosteroids in the anogenital area. Patients with poor eyesight and/or limited mobility or flexibility may not be able to apply the medication appropriately. It is also important to ensure that the treatment is being applied in an adequate amount and to the correct site.

- Has the correct diagnosis been made? If a biopsy was not done previously, it should be considered to exclude differential diagnoses including lichen planus, mucous membrane pemphigoid or genital intra-epithelial neoplasia. Another differential diagnosis is vitiligo but this does not cause any architectural change and is asymptomatic; however, vitiligo may coexist with LS.

- Is there an additional superimposed problem such as the development of a contact allergy to the medication (refer for patch testing), urinary incontinence (refer for urological advice), herpes simplex infection or candidiasis (treat infection appropriately)? Some patients can have LS and psoriasis together which may be more difficult to control.[107,108]

- Those patients with hyperkeratotic LS often require further treatment and should be referred to a specialist clinic. Systemic retinoids maybe considered in this group.

- Has the patient developed vulvodynia/penodynia? If the LS has been successfully treated, but the patient remains symptomatic, often with burning or soreness being a predominant symptom rather than itch, always consider vulvodynia/penodynia.

- Has the patient presented with a tight phimosis? Phimosis can make a topical steroid difficult to apply to the diseased inner aspect of the foreskin and methods of applying

the topical steroid should be reviewed; one option is to introduce the topical steroid using a cotton wool bud. If the phimosis is sufficiently tight that the application of a topical steroid is impossible, the patient should be referred to a urologist for a circumcision.

- Has topical treatment failed in an obese male? These patients may find topical treatment difficult to apply as, the penis becomes buried. Treatment should be directed at correcting obesity and this may involve bariatric surgery if conservative methods of weight loss fail.[109] Subsequently the patient may require penile reconstruction [110] combined with removal of the suprapubic and lateral fat pads.[111]

7.0 FOLLOW-UP

Follow-up is needed for patients with LS to assess response to treatment, confirm good control of the disease and to check for complications. It is also an opportunity to provide patient education and to ensure that patients know how to manage their disease well. The frequency and length of follow-up must be tailored to the patient.

7.1 Adult females

Those patients with uncomplicated disease that responds well to topical treatment need limited follow-up. Two follow-up visits after the initial consultation are suggested: one at 3 months to assess response to treatment and to check that the patient is using the topical corticosteroid appropriately, and a second assessment 6 months later to ensure that the patient is confident in treating their problem and to take the opportunity to discuss any residual problems before discharging to the care of their primary physician. Emollients should be continued and if the patient needs to apply a topical steroid regularly, it is suggested that they see their primary care physician once a year. However, as over half of women discharged from UK vulval clinics are not subsequently followed up in primary care appropriately,[112] it is important that instructions for self-monitoring are fully understood.

The risk of malignancy in uncomplicated genital LS that has been diagnosed and treated appropriately is small and in females there is growing evidence that LS under good control has a reduced risk of scarring and risk of malignancy.[113] Written instructions should be given to the patient at the time of their discharge from the clinic explaining that any change of symptoms, lack of response to topical treatment, new areas of erosion, ulceration or the development of any lumps must be reported to their family practitioner straight away, who will then make an urgent referral back to an appropriate specialist.

Long-term follow-up in a secondary-care specialist clinic is appropriate for females with ano-genital LS associated with ongoing troublesome symptoms, atypical disease, previous cancer or any type of VIN, or pathological uncertainty about intra-epithelial neoplasia.[114] Biopsies of persistent erosions, ulcers, hyperkeratotic and fixed erythematous areas are advised to exclude intraepithelial neoplasia or invasive SCC.

Females who require surgery for severe fusion leading to functional difficulties need close follow-up post-operatively with intensive topical steroid treatment to prevent recurrence of fusion.

7.1.1 Children and young people – female

Girls with LS should be seen at 3 months after the initial consultation and then 6 months later. Emollients can be continued and maintenance treatment with a topical steroid may be required.[115] Follow-up should continue until at least puberty in all cases but any child with atypical or poorly responsive disease should be under long term follow-up in a specialised clinic.

7.2 Adult males

Follow-up should occur at 3 months after diagnosis and the initial course of topical steroid. Symptoms should be recorded, particularly those relating to sexual and urinary function. If the disease has responded well to topical steroids a further review 6 months later is recommended. At this stage, if disease remission has continued, the patient can be discharged. It is essential that written information is provided outlining symptoms and signs which may suggest disease relapse and those which may be related to malignant change. As in females, patients should see their general practitioner who will refer back to secondary care for further assessment.

Those men who require circumcision at 3 months because of persistent disease unresponsive to topical steroids, should be reviewed after surgery. Circumcision following a tight phimosis may reveal active disease on the glans and in the coronal sulcus which will require further treatment with a topical steroid. The results of biopsies taken during surgery must be reviewed, as they may confirm the clinical diagnosis of LS; biopsies from suspicious areas suggestive of PeIN or SCC must be reviewed and appropriate treatment instigated. For many patients, circumcision may cure their disease and they can be discharged after the post-operative follow-up visit.

Patients with active ongoing disease will require long-term follow-up. At each review, symptoms, particularly urinary and sexual, should be assessed and any changes suggestive of PeIN or SCC (persistent area of well-defined erythema, erosion, ulceration, papule or nodule) should be biopsied. Patients with urinary symptoms should be referred to a urologist for flow-rate and post-void residual volume measurement to identify urethral involvement by LS; ultimately, referral to a specialist urologist for management of a urethral stricture or meatal stenosis may be needed. Where medical treatment has failed, patients should be offered referral to discuss other surgical treatment options such as division of coronal adhesions, frenuloplasty and glans resurfacing with split-skin grafting. Following surgery, patients should continue under review as LS may recur after surgical treatment and follow-up treatment with topical steroids may be required. Men who are discharged because their disease is in remission should be aware that LS can recur after many years[116] and that they and should seek referral to specialist services if there are signs of disease recurrence.

7.2.1 Children and young people – male

A proportion of boys presenting with phimosis due to LS will respond to topical steroids.[117] Children with phimosis unresponsive to topical steroids are referred to a urologist for

circumcision. Following surgery, the boys should be reviewed to assess residual disease which may be present in the glans and /or the meatus[118] and to review the histopathology of the circumcision specimen. Topical steroid therapy should be initiated to remaining active areas of LS. As in men, any child with ongoing active disease should remain under review. Obese children and those who have had surgical interventions, including a hypospadias repair, are at a greater risk of persistent disease.[60,119]

7.3 Extragenital LS

Patients with extragenital disease do not need prolonged follow-up unless they are on systemic agents where follow-up should adhere to relevant guidance on drug monitoring. If they have had phototherapy, a follow-up visit would be needed to assess response to treatment.

8.0 RECOMMENDED AUDIT POINTS

In the last 20 consecutive patients is there clear documentation of:

1. Is there documentation of the history, including urinary symptoms and sexual and psychosexual symptoms?
2. Has a biopsy been performed in patients with clinically active LS that has not responded to treatment in females?
3. Has a topical steroid of adequate potency and duration been used prior to circumcision in males with symptomatic LS?
4. Are all circumcision specimens sent for histology to confirm the diagnosis of LS and to exclude PeIN which will aid in the future management of the patient?
5. Have patients discharged from the clinic been given advice on when to seek advice if further symptoms occur?

The audit recommendation of 20 cases per department is to reduce variation in the results due to a single patient, and allow benchmarking between different units. However, departments unable to achieve this recommendation may choose to audit all cases seen in the preceding 12 months.

9.0 STAKEHOLDER INVOLVEMENT AND PEER REVIEW

The draft document and supporting information was made available to the BAD membership, British Dermatological Nursing Group (BDNG), Primary Care Dermatological Society (PCDS), British Society for Paediatric Dermatology (BSPD), British Society for the Study of Vulval Disease (BSSVD), British Association of Sexual Health and HIV (BASHH), Royal College of Obstetrics & Gynaecology (RCOG), Royal College of General Practitioners (RCGP), Royal College of Paediatrics & Child Health (RCPCH), British Association of Urological Surgeons, British Association of Paediatric Urologists (BAPU), British Association of Urological Nurses (BAUN), British Association of Urological Pathologists (BAUP) and urology and gynaecology colleagues for comments, which were actively considered by the

GDG. Following further review, the finalized version was sent for peer-review by the Clinical Standards Unit of the BAD, made up of the Therapy & Guidelines Sub-committee (T&G), prior to submission for publication.

10.0 LIMITATIONS OF THE GUIDELINE

This document has been prepared on behalf of the BAD and is based on the best data available when the document was prepared. It is recognized that under certain conditions it may be necessary to deviate from the guidelines and that the results of future studies may require some of the recommendations herein to be changed. Failure to adhere to these guidelines should not necessarily be considered negligent, nor should adherence to these recommendations constitute a defence against a claim of negligence.

11.0 PLANS FOR GUIDELINE REVISION

The proposed revision date for this set of recommendations is scheduled for 2023; where necessary, important interim changes will be updated on the BAD website.

SUPPORTING INFORMATION

Additional supporting information including the study selection PRISMA flow diagram, summary of findings with forest plots, GRADE evidence profiles indicating the quality of evidence, clinical evidence summary, summary of included studies, narrative findings for non-comparative studies, summary of topical steroids, LETR, list of excluded studies and search strategy may be found in the online version of this article.

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Footnote:

This is an updated guideline prepared for the British Association of Dermatologists (BAD) Clinical Standards Unit, which includes the Therapy & Guidelines Sub-committee. Members of the Clinical Standards Unit that have been involved are: PM McHenry [Chairman T&G], TA Leslie, S Wakelin, RYP Hunasehally, M Cork, GA Johnston, N Chiang, FS Worsnop, D Buckley, G Petrof, A Salin, N Callachand [British National Formulary], C Saunders [British Dermatological Nursing Group], AA Salad [BAD Scientific Administrator], LS Exton [BAD Guideline Research Fellow], MF Mohd Mustapa [BAD Clinical Standards Manager].

CONFLICTS OF INTEREST

FL: Secretary of the European College for Study of Vulval Disease (2008-16) (specific); CB: Principal Investigator and research grant holder for investigation into male genital lichen sclerosus, HPV and penis cancer – Sir John Fisher & Skin Treatment and Research (START) Trusts, EADV.

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