Venous leg ulcers: Infection diagnosis and microbiological investigation

Quick reference guide for primary care: For consultation and local adaptation
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About Public Health England

Public Health England
Wellington House
133-155 Waterloo Road
London SE1 8UG
Tel: 020 7654 8000
www.gov.uk/phe
Twitter: @PHE_uk
Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Professor Cliodna McNulty
For queries relating to this document, please contact cliodna.mcnulty@phe.gov.uk or sarah.alton@phe.gov.uk.

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Foreword – Aims and adaptations

Audience
- primary care prescribers in general practice and out of hours settings; including doctors, nurses and pharmacists
- those giving first point of contact for management of infected venous leg ulcers in adults

Aims
- to provide a simple, effective, economical and empirical approach to the management of venous leg ulcers, when infection is suspected
- to minimise the emergence of antibiotic resistance in the community

Implications
- the guidance should lead to more appropriate antibiotic use
- use of this guidance may influence laboratory workload, which may have financial implications for laboratories and primary care commissioners

Production
- the guidance has been produced in consultation with the Association of Medical Microbiologists, general practitioners, nurses, specialists, and patient representatives
- the guidance is in agreement with other publications, including CKS, SIGN and NICE
- the guidance is fully referenced and graded
- the guidance is not all-encompassing; it is meant to be ‘quick reference’
- if more detail is required we suggest referral to the websites and references cited
- the guidance will be updated every three years, or more frequently if there are significant developments in the field

Poster presentation of guidance
- the summary table is designed to be printed out as a poster for use in practice
- the rationale and evidence is designed to be used as an educational tool for you, and your colleagues and trainees, to share with patients as needed

Local adaptation
- we would discourage major changes to the guidance, but the format allows minor changes to suit local service delivery and sampling protocols
- to create ownership agreement on the guidance locally, dissemination should be agreed and planned at the local level between primary care clinicians, laboratories and secondary care providers

We welcome opinions on the advice given. Please email any evidence or references that support your requests for change so that we may consider them at our annual review. Comments should be submitted to Professor Cliodna McNulty, Head of PHE Primary Care Unit, Microbiology Laboratory, Gloucestershire Royal Hospital, Great Western Road, Gloucester GL1 3NN.
Email: cliodna.mcnulty@phe.gov.uk
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Quick reference guide

BACKGROUND

CKS □ A venous leg ulcer is defined as “the loss of skin below the knee on the leg or foot, which takes more than 6 weeks to heal”. 1D
☐ An assessment should be carried out by a healthcare professional trained in leg ulcer management. This should include clinical history; Doppler studies to exclude arterial insufficiency; 2B+, 3C assessment of pain, odour and discharge; oedema; venous eczema and infection; assessment of risk factors and comorbidities. 3C, 4C, 5C

NICE □ If a leg ulcer is associated with signs of venous hypertension (eg varicose veins), NICE recommends referral to a vascular service. 6D

SIGN □ Ulcerated legs should be washed normally in tap water and carefully dried with a smooth, soft material. 2D, 7C Management includes cleaning, debriding and dressing the ulcer; 1A+ applying compression therapy if the ulcer is not infected; 8A+, 9A+, 10A+ arranging a follow-up to assess the ulcer. 1A+, 4C

MICROBIOLOGY AND VENOUS LEG ULCERS

☐ Routine bacteriological samples should not be taken. 11B+, 12C, 13C Treat the patient not the culture results. 1D, 2B+, 5C
☐ All venous leg ulcers contain bacteria. Most bacteria are colonisers; only in some instances does clinical infection occur. 5C, 14B+, 15A-
☐ In patients with chronic venous leg ulcers, only use systemic antibiotics if there is evidence of clinical infection. 4C, 11B+, 16A+
☐ Do not use antibiotics routinely in venous leg ulcers. Overuse of antibiotics will select for resistant organisms. 5C, 11B+, 16A+

WHEN SHOULD I TAKE A MICROBIOLOGICAL SAMPLE FROM A VENOUS LEG ULCER?

☐ If there are any of the following criteria that indicate the presence of infection: 2B+, 11B+, 13C
  • increased odour or increased exudate from the ulcer
  • enlarging ulcer with abnormal bleeding or bridging granulation tissue
  • increased disproportionate pain
  • cellulitis (particularly if spreading), lymphangitis or lymphadenopathy
  • pyrexia, systemic inflammatory response syndrome or sepsis
☐ Samples should always be collected before antibiotics are started. 12C, 17B-
☐ Only patients with a non-healing or atypical venous leg ulcer should be referred for consideration of biopsy. 2D, 4C, 14B+

HOW SHOULD I TAKE A MICROBIOLOGICAL SWAB FROM A VENOUS LEG ULCER?

1. Use a swab with charcoal transport medium. 12C, 18B+
2. Cleanse the wound with tap water or saline to remove surface contaminants, slough and necrotic tissue. 2D, 5C, 7A+
3. Swab viable tissue that displays signs of infection, whilst rotating the swab. Alternatively, use the Levine technique in which the swab is pressed into the ulcer bed, as this displaces deeper placed organisms. 1D, 15A-
4. Send the swab to the microbiology laboratory as soon as possible to aid survival of fastidious organisms. 12C
☐ For all specimens include all clinical details (patient details, site, nature of wound and current or recent treatment), to enable accurate processing and reporting of the specimen. 13C
**INTERPRETING THE LABORATORY REPORT**

- The result will only provide information about the organisms present and their antibiotic susceptibilities. The results will not tell you if infection is present in a venous leg ulcer, as this is a clinical diagnosis.  
- All venous leg ulcers are colonised by bacteria, which may progress to a level of so-called "critical colonisation". Above this, healing is delayed and significant infection occurs. No simple test can differentiate colonisation from infection. Early colonisation of venous leg ulcers is not considered adverse to healing.  
- Group A \( \beta \)-haemolytic streptococci can be associated with significant infection and delayed healing. When diagnosed, these infections justify early, aggressive, systemic antimicrobial therapy.  
- Other streptococci, *Staphylococcus aureus* and anaerobes may be associated with clinical infection. Most other bacterial colonisation of wounds is not considered to adversely affect healing.  
- Treatment to be based on signs of infection, as inclusion of antibiotic susceptibilities on the report does not mean that an organism is significant or that it requires antibiotics.  

**WHEN SHOULD I USE ANTISEPTICS OR ANTIBIOTICS IN VENOUS LEG ULCERS?**

- Topical antiseptics may be of benefit to individual patients, but are not routinely recommended in the treatment of venous leg ulcers. Some evidence supports the use of cadexomer iodine for critically colonised ulcers or early infection, but further research is required before recommendations can be made about other agents.  
- Systemic antibiotics are indicated in the presence of locally spreading cellulitis or other signs of clinical infection.  
- Give patient “safety net instructions” and review swab results at three days to determine the need for antibiotics.  
- First line treatment if there is locally spreading cellulitis or other signs of clinical infection:  
  - empirical therapy with oral flucloxacillin, 500mg-1g (dependent on BMI), four times a day, to cover staphylococci and Groups A, C and G streptococci. If penicillin-hypersensitive, clarithromycin, 500mg, twice daily; if penicillin-hypersensitive and on statins, doxycycline, 200mg stat and then 100mg daily. If cellulitis is persistent, clindamycin is an alternative, 300-450mg, four times daily; stop clindamycin if diarrhoea develops. All antibiotics to be prescribed for 7 days; if there is slow response, continue for a further 7 days.  
- Discuss with local microbiologist for any antibiotic advice needed, or treatment choice for MRSA.  
- Consider need for referral to secondary care if infection is non-responsive or patient is systemically unwell.  

**KEY:** = good practice point
GRADING OF GUIDANCE RECOMMENDATIONS

The strength of each recommendation is qualified by a letter in parenthesis. This is an altered version of the grading recommendation system used by SIGN.

<table>
<thead>
<tr>
<th>STUDY DESIGN</th>
<th>RECOMMENDATION GRADE</th>
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<tbody>
<tr>
<td>Good recent systematic review and meta-analysis of studies</td>
<td>A+</td>
</tr>
<tr>
<td>One or more rigorous studies; randomised controlled trials</td>
<td>A-</td>
</tr>
<tr>
<td>One or more prospective studies</td>
<td>B+</td>
</tr>
<tr>
<td>One or more retrospective studies</td>
<td>B-</td>
</tr>
<tr>
<td>Non-analytic studies, eg case reports or case series</td>
<td>C</td>
</tr>
<tr>
<td>Formal combination of expert opinion</td>
<td>D</td>
</tr>
</tbody>
</table>

This guidance was originally produced in 2006 by the South West GP Microbiology Laboratory Use Group, in collaboration with the Association of Medical Microbiologists, general practitioners, nurses and specialists in the field. This guidance was reviewed and updated in 2016, with input from Professor Cliodna McNulty; Dr Philippa Moore; Professor David Leaper and Jacqui Fletcher (Cardiff University); the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI); the British Society for Antimicrobial Chemotherapy (BSAC); the British Infection Association (BIA); the Royal College of General Practitioners (RCGP); the Royal College of Nursing (RCN); general practitioners; specialists in the field; and patient representatives. Full consensus of the recommendations made was given by all guidance developers and reviewers prior to the dissemination of this guidance. All comments received have been reviewed and incorporated into the guidance, where appropriate. For detailed information regarding the comments provided and action taken, please email sarah.alton@phe.gov.uk. Public Health England works closely with the authors of the Clinical Knowledge Summaries.

If you would like to receive a copy of this guidance with the most recent changes highlighted, please email sarah.alton@phe.gov.uk.

For detailed information regarding the search strategies implemented and full literature search results, please email sarah.alton@phe.gov.uk.
References and rationale

   RATIONALE: A detailed guideline defining a venous leg ulcer as “the loss of skin below the knee on the leg or foot, which takes more than six weeks to heal”. This guideline states that management of a venous leg ulcer should include: cleaning and dressing the ulcer; applying compression therapy; taking a wound swab and prescribing an antibiotic; arranging a follow-up to assess the ulcer. This guideline offers advice on the most effective way to take a wound swab and suggests that samples should only be collected in the presence of clinical infection. It also defines the symptomatic criteria that may indicate infection, and suggests that antibiotics should only be started if these criteria are met. Finally, this guideline states that referral to secondary care should be considered if the infection is non-responsive or the patient is systemically unwell.

   RATIONALE: A detailed guideline providing evidence-based recommendations on the management of venous leg ulcers. The guideline provides advice on the assessment of the leg, the importance of Doppler studies, and the use of dressings and compression in treating venous leg ulcers. SIGN recommend that ulcerated legs should be washed normally in tap water and carefully dried. This guideline clearly states that routine bacteriological samples should not be taken in the absence of clinical infection (cellulitis; pyrexia; increased pain; rapid extension of area of ulceration; malodour; increased exudate). It is also advised that only patients with a non-healing or atypical venous leg ulcer should be referred for consideration of biopsy, and that colonisation of wounds does not necessarily mean that a wound is infected. Finally, this guideline states that antibiotics should not be started unless there is clear sign of clinical infection.

   RATIONALE: A review article discussing the assessment, diagnosis and treatment of venous leg ulcers. The authors outline the range of elements an assessment should encompass, including: full clinical history, examination to identify risk factors, varicose vein assessment, and Doppler studies.

   RATIONALE: A review article outlining the correct protocol for the successful treatment of venous leg ulcers. This article suggests that a thorough assessment should be conducted.
on initial meeting, including a physical examination and assessment of pain. It also states that debridement, compression therapy, topical dressings, and antibiotics are the recommended treatment for venous leg ulcers; but that antibiotics should only be started in the presence of clinical infection. This article suggests that patients with a non-healing venous leg ulcer that has been present for more than three months should undergo biopsy to rule out malignancy. It also outlines the likely pathogens to be found in an infected venous leg ulcer.


**RATIONALE:** A review article providing a methodological mechanism for wound assessment, accompanied by photographic examples. This article states that a full clinical history should be taken, including; patient details, history of ulceration, and ulcer characteristics. It also suggests that all open wounds are colonised by bacteria, but routine bacteriological sampling should only be conducted if infection is suspected. This article states that removal of necrotic tissue is key, and reports that antibiotics should only be prescribed in the presence of infection.


**RATIONALE:** A guideline from NICE on varicose veins, recommending referral to a vascular service if a leg ulcer is associated with signs of venous hypertension.


**RATIONALE:** A Cochrane review of 11 trials, which determined the effects of water compared with other solutions for wound cleansing. The authors conclude that tap water can be used to cleanse wounds and there is some evidence that its use can reduce infection. It is also stated that high quality drinking water may be just as good as saline when used to cleanse wounds.


**RATIONALE:** A Cochrane review of 59 randomised controlled trials, which determined to evaluate the clinical effectiveness of compression bandaging and stocking systems in the treatment of venous leg ulceration. The authors conclude that venous leg ulcers heal more rapidly with compression than without, and that multi-component systems are more effective than single-component compression.


**RATIONALE:** A report of a randomised trial, which found that patients with venous leg ulcers treated with four-layer compression are significantly more likely to heal than those treated with an adhesive single-layer bandage.


**RATIONALE:** A systematic review and meta-analysis reviewing the evidence of the effectiveness of dressings applied to venous leg ulcers. This review explicitly states that multi-layer component compression bandaging is the most effective in the treatment of venous leg ulcers. It also suggests that there is some evidence that cadexomer iodine can aid healing so may be considered as a topical antiseptic.


**RATIONALE:** A review article stating that routine microbiological sampling of venous leg ulcers without clinical signs of infection is often pointless. It also outlines the potential bacteria found in clinically infected venous leg ulcers and suggests that antibiotics are only recommended in the presence of locally spreading cellulitis or other signs of infection.


**RATIONALE:** A PHE document outlining the standards required for bacteriological investigation and processing of skin, superficial and non-surgical wound swabs. This document suggests that routine swab cultures are of questionable clinical value if there is no sign of infection. It also states that specimens should be collected before antimicrobial therapy is started, and provides details on how to optimise results from a wound swab. The guideline describes how to take a microbiological sample and the importance of using appropriate transport medium and transporting the specimen to the microbiology laboratory as soon as possible.


**RATIONALE:** A highly detailed paper stating that only clinical infection should prompt a practitioner to sample a wound for microbiological analysis, as routine biopsy specimens are impractical in the management of venous leg ulcers. This paper outlines the importance of correct procedure in collecting and transporting microbiological specimens.
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and including all clinical and patient details on a sample. It is also stated that the majority of open wounds are polymicrobial, but only some of these bacteria cause clinical infection. If infection is present, treatment with topical and systemic antibiotics is crucial, and there is some evidence for the potential benefits of cadexomer iodine as a topical antiseptic.

RATIONAL: A prospective study, which states that no consistent association has been made between colonisation and infection of open leg wounds. This paper also determines that wound biopsies do not contribute significantly to the patient management of venous leg ulcers.

RATIONAL: A study examining the diagnostic validity of three different swab techniques in identifying chronic wound infection. This paper states that all secondary wounds are colonised by many types of bacteria, but this does not mean that they are infected. Of the 83 wounds analysed in this paper, 30 (36%) were infected. The authors conclude that swab specimens obtained using Levine’s technique had the highest accuracy.

RATIONAL: An updated Cochrane review of 45 randomised controlled trials, established to determine the effects of systemic, topical antibiotics and antiseptics on the healing of venous leg ulcers. The authors state that the evidence does not currently support the routine use of systemic antibiotics in venous leg ulcers, especially with the increasing problem of bacterial resistance in the community. There is, however, some evidence in support of cadexomer iodine as a topical preparation. This review suggests that all wounds are colonised by bacteria and, at a certain level, some bacteria can cause significant infection and delay healing. The authors conclude that antibacterial preparations should only be used in cases of clinical infection, as bacterial colonisation alone is not considered adverse to healing.

RATIONAL: A review paper written by an expert panel, in which the authors state that the first dose of antibiotic therapy should be administered as soon as culture specimens
are obtained. The authors list the likely colonising and infecting pathogens for specific types of skin and soft tissue infections. The importance of considering patient characteristics when determining the correct antibiotic dosing is also underlined. This paper suggests flucloxacillin and clindamycin as the recommended antimicrobial therapy for class 2 and 3 skin and soft tissue infections.


RATIONALE: A study evaluating various transport swabs for their ability to preserve bacteria for 24 and 48 hours. The authors conclude that swabs using Amies plus charcoal medium have better recovery rates than those using Amies medium alone.


RATIONALE: An expert consensus outlining the most common infective organisms as streptococci and *Staphylococcus aureus*. The consensus is that people with Class I disease (no signs of systemic toxicity and no uncontrolled comorbidities) can usually be managed on an outpatient basis with oral antibiotics. Flucloxacillin 500mg QDS (or clarithromycin 500mg BD for those with penicillin allergy) are suitable oral antibiotics because they cover both staphylococci and streptococci. Clindamycin 300mg QDS is also recommended as a further alternative for people who do not respond to treatment, or have more severe disease. This document states that most cases of uncomplicated cellulitis can be successfully treated within 1-2 weeks of therapy. Consider outpatient antimicrobial therapy (OPAT) with intravenous treatment in those with Class II disease (systemically unwell or co-morbidity). Patients can usually be switched to oral treatment after 3-5 days when signs and symptoms are improving (decreased temperature, change in white cell count, and decreasing erythema and induration). Those with Class III disease (significant systemic upset, acute confusion, tachycardia, tachypnoea, hypotension or unstable comorbidities) or Class IV disease (patients with sepsis syndrome or severe life threatening infections) should be admitted urgently.


RATIONALE: An expert consensus document on the management of cellulitis in lymphoedema. The authors state that flucloxacillin 500mg should be prescribed in the presence of clinical infection (eg pus formation, folliculitis or crusted dermatitis). They also state that if the patient is allergic to penicillin, clarithromycin 500mg or clindamycin 300mg should be prescribed. Doxycycline 200mg is recommended as an alternative if the patient is penicillin-hypersensitive and taking statins (eg simvastatin or atorvastatin). Finally, the authors state that advice should be sought from a local microbiologist if the infection fails to respond to these recommendations.
Acknowledgements

QUICK REFERENCE GUIDE AUTHORS

Prof Cliodna McNulty, Head of Primary Care Unit and Honorary Visiting Professor, Public Health England and Cardiff University

Dr Philippa Moore, Consultant Microbiologist, Gloucestershire Royal Hospital

Prof David Leaper, Visiting Professor, Cardiff University

Jacqui Fletcher, Senior Professional Tutor in the Department of Dermatology and Wound Healing, Cardiff University

Dr Gerry Morrow, Clinical Editor, Clinical Knowledge Summaries

Sarah Alton, Guidance Research Assistant, Public Health England

QUICK REFERENCE GUIDE REVIEWERS

Dr Teferi Abraham, Medical Doctor, Luton and Dunstable University Hospital NHS Foundation Trust

Dr Gavin Barlow, Consultant in Infection, Hull & East Yorkshire Hospitals NHS Trust

Dr Adriana Basarab, Consultant Medical Microbiologist, University Hospital Southampton NHS Foundation Trust

Dr Justin Bendig, Consultant Microbiologist and Joint Head of Department, Epsom and St Helier University Hospitals

Dr Giuseppe Bignardi, Consultant Microbiologist, City Hospitals Sunderland NHS Foundation Trust

Valerie Bailey, Professional Practice Co-ordinator and Wales Union Learning Fund (WULF) Project Manager, Royal College of Nursing

Deri Burgess, Clinical Pharmacist, First Databank

Dr Alleyna Claxton, Consultant Microbiologist, Homerton University Hospital Foundation Trust

Anna Crossley, Professional Lead for Acute Emergency and Critical Care, Royal College of Nursing

Dr Richard Cunningham, Consultant Microbiologist, Plymouth Hospitals NHS Trust

Dr Jayshree Dave, Public Health England (PHE) Consultant Medical Microbiologist, Barts and The London NHS Trust

Dr Jiten Dave, Company Director, Jrd Healthcare Limited

Dr Roopal Dave, General Practitioner, Ealing Park Health Centre

Lynn Davis, Tissue Viability Nurse Specialist, Gloucestershire Hospitals NHS Foundation Trust
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Dr Susan Dawson, Consultant Microbiologist, Great Western Hospitals NHS Foundation Trust
Rose Gallagher, Nurse Advisor Infection Prevention and Control, Royal College of Nursing
Dr Roshina Grenadira, General Practitioner (no longer in practice)
Dr Shabnam Iyer, Consultant Microbiologist, The Royal Berkshire NHS Foundation Trust
Dr David Jenkins, Consultant Medical Microbiologist and Lead Infection Prevention Doctor, University Hospitals of Leicester NHS Trust
Brenda King, Nurse Consultant, Sheffield Teaching Hospitals NHS Foundation Trust
Andrew Kingsley, Lead Nurse Healthcare Acquired Infections, Northern, Eastern and Western Devon Clinical Commissioning Group
Dr Tom Lewis, Consultant Medical Microbiologist and Lead for Antimicrobial Stewardship, Northern Devon Healthcare NHS
Prof Alasdair MacGowan, Consultant Medical Microbiologist, North Bristol NHS Trust
Dr George Moncrieff, General Practitioner, Bicester Health Centre
Dr Dilip Nathwani, Consultant Physician, NHS Tayside
Prof Andrea Nelson, Professor in Wound Healing, University of Leeds
Dr Paul O'Hallaran, General Practitioner, Hampshire Hospitals NHS Foundation Trust
Rachael Parslow, Development and Communications Co-ordinator, PRODIGY Knowledge
Dr Keith Poskitt, Consultant General and Vascular Surgeon, Gloucestershire Hospitals NHS Foundation Trust
Benjamin Rehman, Director London Medicines Information Service and Chair UK Medicines Information (UKMi), North West London Hospitals
Dr Terry Riordan, Consultant Medical Microbiologist, Royal Devon and Exeter Healthcare NHS Trust
Ruth Ropper, Lead Nurse – Tissue Viability, NHS Lothian
Dr Andrew Seaton, Consultant Physician, NHS Greater Glasgow & Clyde
Dr John Sloss, Consultant Microbiologist, County Durham and Darlington Acute Hospitals NHS Trust
Dr Jane Stockley, Consultant Medical Microbiologist, Worcestershire Acute Hospitals NHS Trust
Dr David Waghorn, Consultant Microbiologist, Buckinghamshire Healthcare NHS Trust
Dr Vivienne Weston, Consultant Microbiologist and Community Infection Control Doctor, Nottingham University Hospitals NHS Trust
Prof Peter Wilson, Consultant Microbiologist, University College London Hospitals
Dr Harry Yoxall, Medical Secretary, Somerset Local Medical Committee
Primary Care Clinicians from Cheltenham Road Surgery, Gloucester
Primary Care Clinicians from Rosebank Surgery, Gloucester

Members of the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI)

Members of the British Infection Association (BIA)

Members of the British Society for Antimicrobial Chemotherapy (BSAC)

Members of the Public Health England (PHE) Standards Unit

Members of the Royal College of General Practitioners (RCGP)

Members of the Royal College of Nursing (RCN)

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Abbreviations

**BD** = Twice daily  
**BMI** = Body mass index  
**G** = Gram(s)  
**Mg** = Milligram(s)  
**MRSA** = Methicillin-resistant *Staphylococcus aureus*  
**OPAT** = Outpatient antimicrobial therapy  
**QDS** = Four times daily