

1. Introduction and Who Guideline applies to

This guidance applies to all staff at UHL, GPs and Lymphoedema nurse specialists at UHL and LOROS caring for adult patients with lymphoedema who develop cellulitis.

Clinical guidelines are 'guidelines' only. The interpretation and application of clinical guidelines will remain the responsibility of the individual practitioner. If in doubt, consult a senior colleague or expert.

2. Guideline Standards and Procedures

Cellulitis is an acute spreading inflammation of the skin and subcutaneous tissues characterised by pain, warmth, swelling and erythema. Cellulitis is sometimes called erysipelas, lymphangitis.

In lymphoedema, attacks may be variable in clinical presentation and may differ from classical cellulitis. Most episodes are believed to be caused by beta haemolytic Group A Streptococci (Mortimer 2000, Cox 2009). However, microbiologists consider Staph aureus to be the cause in some patients (e.g. Chira and Miller, 2010).

Episodes can occur very rapidly, within hours, and may be accompanied by severe systemic upset with a high temperature and rigors; others may be milder with a normal or slightly raised temperature. Increased swelling to the affected area may be present and there may be diffuse/blotchy erythema as opposed to a well-demarcated area seen in classical cellulitis. Inflammatory markers (ESR, CRP, PV) may be raised. It is difficult to predict the response to treatment. Cellulitis can be difficult to diagnose and to distinguish from other causes of inflammation particularly in the legs e.g. lipodermatosclerosis. Cellulitis most commonly affects one leg, whereas lipodermatosclerosis most commonly affects both legs.

A Cochrane review concluded that it was not possible to define the best treatment for cellulitis in general based upon existing evidence (Kilburn et al 2010). Furthermore, the treatment of cellulitis in lymphoedema may differ from conventional cellulitis.

These guidelines attempt to rationalise the approach to management and to make recommendations for use of antibiotics for cellulitis in adult patients with lymphoedema. Prompt and effective treatment is essential to avoid further damage to the lymphatics of the affected part, since this may predispose to further attacks and deterioration in lymphoedema.

- It is important to check the nature of any 'penicillin allergy' to confirm it's veracity e.g. anaphylaxis /widespread rash.
- Patients who have experienced an anaphylactic reaction should not be given cephalosporins.

For all patients regardless of level of systemic upset

- All patients need to rest and elevate the affected part.
- Remove all compression garments during an acute attack as they may push infection proximally. However, they should be replaced as soon as the affected area is comfortable enough to tolerate them. The compression garment may need to be reviewed to check fit as the area may become more swollen after an episode of cellulitis.
- Consider analgesia as appropriate, for pain
- Look for predisposing factors such as skin injury, possible distal infection e.g. sore throat, tooth abscess, tinea pedis, indwelling device and treat as appropriate.
- When inflammation has subsided, the patient can return to normal exercise.
- Return to work depends upon the patient's occupation and there being no deterioration when normal levels of exercise are established
- Consider admission if the patient becomes systemically unwell
- Antibiotics should be continued until all signs of acute inflammation have resolved; this may take 1-2 months and the course of antibiotics should be for **no less** than 14 days from the time a definite clinical response is observed.
- Skin changes e.g. discolouration or staining, may persist for months or longer and do not necessarily require on-going antibiotics
- Oedema can be a side effect of medication (e.g. calcium channel blockers). Review all drugs the patient is taking.

Table 1**Oral Antibiotic Treatment for Mild to Moderate Infection**

Indication	1 st line Treatment	2 nd Line Treatment	Duration of Treatment	Comments
No/Minimal Systemic Upset				Monitor patient closely Record: <ul style="list-style-type: none"> • Extent and severity of rash • Patient's temperature • Level of systemic upset : CRP/ESR/white count may be helpful in diagnosis and monitoring of treatment. • Microbiology of any skin disturbance e.g. open wounds/cuts/ breaks in skin before antibiotics are started
Mild to moderate cellulitis	Oral flucloxacillin 1g qds	If penicillin Allergic – oral doxycycline PO 200mg od	14 days (minimum duration)	<ul style="list-style-type: none"> • If no / poor response (unresolving inflammation) in 72hours, increase oral flucloxacillin to 2g qds • Review all cases after one week • If clinical improvement - complete course
Patient with minimal systemic upset who shows no response or worsens on flucloxacillin after 72 hours.	Oral doxycycline 200mg od		14 days	If symptoms persist, but signs of improvement continue for a total of three weeks. Occasionally longer courses of up to six weeks may be required
Patient with minimal systemic upset who shows no response to doxycycline after one week	Discuss with microbiologist			Consider dermatology referral if the diagnosis of cellulitis is in doubt or there are other rashes that may require diagnosis and treatment.

Consider admission at any point if patient becomes systemically unwell.

Indications for Hospital Admission

A decision whether hospital admission is indicated should be based on the level of systemic upset:

- Signs of septicaemia (hypotension, tachycardia, severe pyrexia, confusion, tachypnoea or vomiting) are an absolute indication for admission and the UHL Red Flag Sepsis pathway should be considered for patient management.
- Continuing or deteriorating systemic signs, with or without deteriorating local signs, after 48 hours of antibiotic treatment
- Unresolving or deteriorating local signs, with or without systemic signs, despite trials of first and second line oral antibiotics

Table 2

IV Antibiotic Treatment for Severe Infection

Indication	1 st line Treatment	2 nd Line Treatment	Duration of Treatment	Comments
Systemic Upset	Flucloxacillin IV 2g qds	If penicillin allergic vancomycin IV (Dose dependent upon the patient's weight and calculated creatinine clearance : See UHL antibiotic website for vancomycin regimen)	Continue IV treatment for 48 hours	Consider the following Blood cultures Swabs from: •Edge of ulcers •Any weeping or blistered skin •Macerated or fissured areas between toes FBC, U&E's, CRP, ESR, PV Monitor temperature Review daily
Infection resolving after 48hours and patient able to tolerate oral medication	Switch IV to oral flucloxacillin 1g qds	If penicillin allergic switch to oral doxycycline 200mg od	Continue for a total of 14 days	A switch to oral treatment should not be made before : • Temperature down for 48hours • Inflammation resolving • CRP and WBC falling.
No response after 48 hours	Discuss with microbiologist and refer to dermatologist			

Anogenital Cellulitis - patient systemically unwell	Amoxicillin IV 2g tds plus gentamicin IV 7mg/kg once daily; dose adjusted according to renal function and assay	If penicillin allergic, discuss with microbiologist	Continue IV treatment for 48hours	Consider blood tests and swabs as above Monitor temperature Review daily
Infection resolving after 48hours	Switch IV to oral amoxicillin 500mg tds	If allergic to penicillin, discuss with microbiologist	Continue for a total of 14 days	If patient weighs 100kg or more or BMI >30, double the dose of oral amoxicillin to 1g tds

Table 3

Treatment for Animal Lick or Bite Wound

Indication	1 st line	2 nd Line Treatment	Duration of Treatment	Comments
No/Minimal Systemic Upset	Oral co-amoxiclav 625mg tds	If penicillin allergic: oral metronidazole 400mg tds and doxycycline 200mg od	14 days	Send a wound swab for culture
With systemic upset	Co-amoxiclav IV 1.2g tds	If penicillin allergic ciprofloxacin PO 500mg bd plus metronidazole IV 500mg bd	Discuss with microbiologist	Admit to Infectious Disease Unit Discuss with microbiologist in all cases of animal licks or bites

Table 4

Treatment for MRSA Infection

Indication	1 st line Treatment	2 nd Line Treatment	Duration of Treatment	Comments
MRSA Infection	Discuss with microbiologist			

Table 5**Treatment for Fungal Infections - Fungal infections can cause cellulitis**

Indication	1st line	2nd Line Treatment	Duration of Treatment	Comments
Fungal infection	Terbinafine cream od-bd		14 days	Swab area for Candida sp Scrape area for tinea pedis Maintenance treatment, provided skin is unbroken, with alcohol wipes daily.
If no response or substantial or extensive rash on feet				Refer to dermatologist
Fungal nail Infections				Refer to dermatologist Not usually cause of cellulitis

Table 6**Secondary Antibiotic Prophylaxis for Patients with Recurrent Episodes**

Indication	1 st line Treatment	2 nd Line Treatment	Duration of Treatment	Comments
Prophylaxis after 2 or more episodes in a year	Oral penicillin V 250mg bd	If penicillin allergic oral erythromycin 250mg OD If intolerant to erythromycin oral clarithromycin 250mg OD	2 years or more	Review annually If patient weighs 100kg or more or BMI 33 or over, use oral penicillin V 500mg bd or oral erythromycin 500mg OD in penicillin allergy Caution: <ul style="list-style-type: none"> Erythromycin and clarithromycin can both increase plasma concentration of statins and may cause increased risk of myopathy. Be aware of concurrent use and review the need for the statin. If statin definitely required : for patients who are penicillin allergic, but not anaphylaxis the recommended prophylactic antibiotics are cephalexin 125mg nocte/doxycycline 50mg od.
Recurrence whilst on prophylaxis				Suspend prophylaxis Treat acute episode and resume once infection resolved
Multiple recurrences (second and more)	Oral doxycycline 100mg od			Discuss with microbiologist Suspend prophylaxis to treat recurrence and resume once infection resolved
Antibiotic supply in case of holiday and travel	Oral flucloxacillin 1g qds	If penicillin allergic: Oral doxycycline 200mg od	14 days	Patients who have had previous attacks of cellulitis should ask the lymphoedema clinic or their GP to supply two weeks antibiotics to take on holiday. Commence antibiotics as soon as familiar symptoms of cellulitis start. A medical opinion should be sought as soon as possible
Patient undergoing intensive decongestive lymphatic drainage (DLT) with a history of cellulitis in the past during DLT	Oral penicillin V 250mg bd	If penicillin allergic oral erythromycin 250mg bd If intolerant to erythromycin, oral clarithromycin 250mg bd	For the duration of the intensive treatment	Patients who have not had previous episodes of cellulitis do not require antibiotics during intensive treatments If patient weighs more than 100kg or more or BMI >30, use oral penicillin V 500mg bd or oral erythromycin 500mg bd in penicillin allergy Patients already receiving prophylactic antibiotics should receive a therapeutic course of antibiotic for the duration of the intensive treatment (see Table 1)

Anogenital cellulitis	Oral trimethoprim 100mg nocte	If trimethoprim allergic, discuss with microbiologist	2 years or more	
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Guidelines for Cessation of Antibiotic Prophylaxis

- Prophylaxis should be continued long term - two years or more
- Risk factors for recurrent cellulitis including cracked, macerated inter-digital skin, dermatitis, open wounds including leg ulcers and weeping lymphangiectasia (leaking lymph blisters on the skin surface) should be treated.
- Skin care including the use of emollients should be part of routine maintenance.
- Consider discontinuation after 2 years of successful prophylaxis, particularly if the risk factors described above have been successfully addressed. However, if there are ongoing significant risk factors, continuing prophylaxis should be considered.
- Prophylaxis may need to be life-long if relapse occurs when antibiotics are discontinued after two years of successful prophylaxis
- Discontinue antibiotic prophylaxis while antibiotics are being taken to treat acute cellulitis.

Table 7

Prophylaxis against Fungal Infections

Indication	1 st Line Treatment	2 nd Line Treatment	Duration of Treatment	Comments
Fungal Infections	Clotrimazole 1% (Canesten) cream od			Use in morning before putting on footwear
Soggy Skin	Stellisept skin cleanser			Use with water to wash feet
Recurrence	Refer to dermatologist			

Caution, the antibiotic doses recommended in this guidance are intended for adult patients with normal renal and liver function, are not applicable to pregnant or breast feeding patients unless otherwise stated. Refer to Microbiologist/Pharmacist for further advice in these patients

Drug Interactions :

The prescriber should check individual drug interactions.

Common interactions include:

- Statins and macrolides e.g. erythromycin and clarithromycin.
- *Many antibiotics alter the anti-coagulant effect of coumarins e.g. warfarin. It is advised that interactions are checked before prescribing antibiotics for patients on coumarins*

For information on contraindications, cautions, drug interactions and adverse effects refer to the British National Formulary (www.bnf.org) or the Medicines Compendium (www.medicines.org.uk)

3. Education and Training

None

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Prescribing of antibiotics in line with the guidance	Audit of patients with cellulitis seen in the Lymphoedema clinic at LOROS	Dr C Cooke (Consultant in Palliative Medicine)	Before next review	

5. Supporting References

- Chira S and Miller LG (2010) Staphylococcus aureus is the most common identified cause of cellulitis: a systemic review. *Epidemiology and Infection*, 138, 313-317
- Cox NH (2009) Chapter 41, Streptococcal cellulitis / erysipelas of the lower leg in Williams H, Bigby M, Diepan T, Herxheimer A, Naldi L and Rzany B (Eds) *Evidence-Based Dermatology*, Second Edition, Oxford, Blackwell Publishing
- Mortimer P (2000) Acute Inflammatory Episodes. In Twycross R, Jenns K and Todd J, (Eds) *Lymphoedema*, Oxford, Radcliffe Medical Press, p130-139
- Olszewski WL. Episodic dermatolymphangioadenitis (DLA) in patients with lymphedema of the lower extremities before and after administration of benzathine penicillin: a preliminary study. *Lymphology*. 1996 Sep;29(3):126-31.
- Vignes S, Dupuy A. Recurrence of lymphoedema-associated cellulitis(erysipelas) under prophylactic antibiotherapy: a retrospective cohort study.*J Eur Acad Dermatol Venereol*. 2006 Aug;20(7):818-22.
- Kilburn SA, Featherstone P, Higgins B, Bridle R (2010) Interventions for cellulitis and erysipelas, *Cochrane Database of Systemic Reviews* No 6
- Health Protection Agency (2008) Antimicrobial resistance and prescribing in England, Wales and Northern Ireland, London, Health protection Agency
- Ko DSC, Lerner R, Klose G et al (1998) Effective treatment of lymphedema of the extremities, *Archives of surgery* 133, 452-458
- Leman P and Mukherjee D (2005) Flucloxacillin alone or combined with benzylpenicillin to treat lower limb cellulitis : a randomized controlled trial. *Emergency medicine journal*, 22, 342-346
- Picard M et al (2019) Cross-reactivity to Cephalosporins and carbapenems in penicillin-allergic patients : two systematic reviews and meta-analyses *J Allergy Clin Immunol Pract* - in press

6. Key Words

Lymphedema, cellulitis

CONTACT AND REVIEW DETAILS	
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Details of Changes made during review: Minor changes for clarity and to keep in line with recommendations of the British Lymphology Society.	

Appendix:

BMI approximate calculations (to be used if unable to obtain height and weight)

- At 5 foot 2 inches (1.58m) an individual would have a BMI of >33 if they weighed more than 12 stone 13lbs (82kg).
- At 5 foot 4 inches (1.62m) an individual would have a BMI of >33 if they weighed more than 13 stone 8lbs (86kg).
- At 5 foot 7 inches (1.7m) an individual would have a BMI of >33 if they weighed more than 15 stone (95kg).
- At 5 foot 10 inches (1.78m) an individual would have a BMI of >33 if they weighed more than 16 stone 10lbs (106kg).
- At 6 foot 1 inches (1.86m) an individual would have a BMI of >33 if they weighed more than 17 stone 13lbs (114kg).

N.B.

‘This information is based on a Censensus Document produced by medical experts and facilitated by the Lymphoedema Support Network. The document, originally produced in October 2005, is jointly owned by the British Lymphology Society and the Lymphoedema Support Network’.