ACUTE INFLAMMATORY EPISODES IN A LYMPHOEDEMATOUS LIMB

Acute inflammatory episodes (AIEs), often called cellulitis, are common in lymphoedema:

- mild: pain, increased swelling, erythema (well-defined or blotchy)
- severe: extensive erythema with well-defined margins, increased swelling, blistering and weeping skin; often accompanied by fever, nausea and vomiting, pain and, when the leg is affected, difficulty in walking.[1]

Management strategy

Preventive measures

Patients should be educated about:

- why they are susceptible to AIEs, i.e. skin crevices harbour bacteria, stagnant fluid, reduced immunity[2]
- the consequences of AIEs, i.e. increased swelling, more fibrosis, decreasing response to treatment for reducing limb size
- the importance of daily skin care, i.e. to improve and maintain skin integrity. Risk factors include cracked or macerated interdigital skin, dermatitis, limb wounds (including leg ulcers), and weeping lymphangiectasia (leaking lymph blisters on the skin surface)
- reducing risk, for example, by reducing the swelling, protecting hands when gardening, cleaning cuts, treating fungal infections (**terbinafine** cream o.d. for two weeks) and ingrowing toenails[3]
- the importance of seeking prompt medical attention and treatment; in situations when accessing medical care may be difficult, e.g. holidays, provide a 2-week supply of amoxicillin 500mg q8h (clindamycin 300mg q6h for those allergic to penicillin) to patients who have had an AIE in the past.

Non-drug treatment

- compression garments should not be worn until the limb is comfortable
- daily skin hygiene should be continued; washing and gentle drying
- emollients should not be used in the affected area if the skin is broken.
- if severe, bed rest is essential with the affected limb elevated in a comfortable position and supported on pillows. [3,4]

Drug treatment

AIEs should be treated promptly with antibiotics to prevent increased morbidity from increased swelling and accelerated fibrosis. It is often difficult to isolate the responsible pathogen. Although cellulitis in a non-lymphoedematous limb is commonly caused by *Staphylococcus aureus*, most AIEs are probably caused by Group A *Streptococci*.[1,5-7] The advice of the British Lymphology Society/Lymphoedema Support Network (October 2006) is summarized in Table 1 (see also www.lymphoedema.org/bls).

The advice of a microbiologist should be obtained in unusual circumstances, e.g. an AIE developing shortly after an animal lick or bite, and when the inflammation fails to respond to the recommended antibiotics.

Remember: AIEs are painful: analgesics should be prescribed regularly and p.r.n.

Table 1 Antibiotics for acute inflammatory episodes[a]

Situation	*First-line antibiotics*	*If allergic to penicillin*	*Second-line antibiotics*	*Comments*
Acute AIE + septicaemia (inpatient admission)	Amoxicillin IV 2g q8h or benzylpenicillin 1.2–2.4g q6h + gentamicin IV 5mg/kg o.d.[b]	Clindamycin IV 600mg q6h [8]	Clindamycin IV 600mg q6h (if poor or no response by 48h)	Switch to amoxicillin 500mg q8h or clindamycin 300mg q6h when: • temperature down for 48h • inflammation much resolved • falling CRP
Acute AIE (home care)	Amoxicillin 500mg q8h[c]	Clindamycin 300mg q6h	If fails to resolve, convert to IV regimen as in row 1, column 2	Continue antibiotics for at least 2 weeks after the inflammation begins to resolve; complete resolution may take 1–2 months
Prophylaxis if 2+ AIEs p.a.	Phenoxymethylpenicillin 500mg o.d. (1g if weight >75kg)	Erythromycin 250mg o.d. or clarithromycin 250mg o.d	Clindamycin 150mg o.d. or clarithromycin 250mg o.d.	After 1 year, halve the dose of phenoxymethylpenicillin; if an AIE develops after discontinuation, treat the acute episode and then commence *life-long* prophylaxis
Emergency supply of antibiotics 'in case of need' (when away from home)	Amoxicillin 500mg q8h	Clindamycin 300mg q6h	If fails to resolve, or constitutional symptoms develop, convert to IV regimen as in row 1, column 2 above	

a. PO unless stated otherwise
b. generally limit gentamicin to 7 days
c. if Staphylococcus aureus infection suspected (pus formation, crusted dermatitis), add flucloxacillin 500mg q6h.

Supply
Amoxicillin (non-proprietary)
Capsules 250mg, 500mg, 14 days @ 500mg t.d.s. = £3.
Oral suspension 125mg/5ml, 250mg/5ml, 14 days @ 500mg t.d.s. = £9.
Injection (powder for reconstitution) containing **amoxicillin** (as sodium salt), 1g vial = £1.

Co-amoxiclav (non-proprietary)
Tablets containing **co-amoxiclav 500/125** (**amoxicillin** 500 mg and **clavulanic acid** 125mg (as potassium salt)), 14 days @ 1 t.d.s. = £28.
Oral suspension containing **co-amoxiclav 250/62** (**amoxicillin** 250mg and **clavulanic acid** 62.5mg (as potassium salt))/5ml, 14 days @ 10ml t.d.s. = £34.

Benzylpenicillin sodium
Crystapen® (Britannia)
Injection (powder for reconstitution) 600mg/vial, 1.2g/vial, 7 days @ 1.2g q6h = £1; *contains Na^+ 3.36mmol/1.2g vial*.

Phenoxymethylpenicillin potassium (non-proprietary)
Tablets 250mg, 14 days @ 500mg q.d.s. = £6.
Oral solution 125mg/5ml, 250mg/5ml, 14 days @ 500mg q.d.s. = £9.

Gentamicin sulphate (non-proprietary)
Injection 40mg/ml, 1ml amp, 2ml amp, 2ml vial all = £1.50.

Flucloxacillin sodium (non-proprietary)
Capsules 500mg, 14 days @ 500mg q.d.s. = £15.
Oral solution 125mg/5ml, 250mg/5ml, 14 days @ 500mg q.d.s. = £39.
Injection (powder for reconstitution) 250mg vial, 500mg vial, 1g vial, 14 days @ 500mg q.d.s. = £112.

Clindamycin (non-proprietary)
Capsules **clindamycin** (as hydrochloride) 150mg, 14 days @ 150mg o.d. or 300mg q.d.s. = £8 and £64 respectively.

Dalacin C® (Pharmacia)
Capsules **clindamycin** (as hydrochloride) 75mg, 150mg, 14 days @ 150mg o.d. or 300mg q.d.s. = £8 and £64 respectively.
Injection **clindamycin** (as phosphate) 150mg/ml, 2ml amp, 4ml amp, 14 days @ 600mg q.d.s. = £691.

Erythromycin (non-proprietary)
Capsules enclosing e/c granules **erythromycin** 250mg, 14 days @ 250mg o.d. = £3.
Oral suspension **erythromycin** (as ethyl succinate) 125mg/5ml, 250mg/5ml, 500mg/5ml, 14 days @ 250mg o.d. = £3.

Erythrocin® (Abbott)
Tablets **erythromycin** (as stearate) 250mg, 14 days @ 250mg o.d. = £2.

Clarithromycin (non-proprietary)
Tablets 250mg, 500mg, 14 days @ 250mg o.d. = £10.

Ciprofloxacin hydrochloride (non-proprietary)
Tablets 100mg, 250mg, 500mg, 750mg, 14 days @ 500mg b.d. = £4.

Terbinafine
Lamisil® (Novartis)
Cream 1%, 15g tube = £5, 30g tube = £9.

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1 Mortimer P (2000) Acute inflammatory episodes. In: RG Twycross *et al.* (eds) *Lymphoedema*. Radcliffe Medical Press, Oxford, pp.130–139.
2 Mallon E *et al.* (1997) Evidence for altered cell-mediated immunity in postmastectomy lymphoedema. *British Journal of Dermatology.* **137**: 928–933.
3 Twycross RG *et al.* (2000) *Lymphoedema.* Radcliffe Medical Press, Oxford.
4 Twycross RG *et al.* (in press) *Symptom Management in Advanced Cancer* (4e). palliativedrugs.com Ltd, Nottingham.
5 Sabouraud R (1892) Sur la parasitologie de l'elephantiasis nostras. *Annales de Dermatologie et de Syphiligraphie.* **3**: 592.
6 Stevens FA (1954) The behavior of local foci causing recurrent streptococcal infections of the skin, subcutaneous tissues, and lymphatics. *Surgery, Gynecology and Obstetrics.* **99**: 268–272.
7 Chambers J and McGovern K (2004) Dental work as a cause of acute inflammation of a lymphoedematous limb. *Palliative Medicine.* **18**: 667–668.
8 Bisno AL and Stevens DL (1996) Streptococcal infections of skin and soft tissues. *New England Journal of Medicine.* **334**: 240–245.

PCF GUIDELINES: ACUTE INFLAMMATORY EPISODES (AIES) IN LYMPHOEDEMA

AIEs, often called cellulitis, are common in lymphoedema. They are often associated with septicaemia (e.g. fever, flu-like symptoms, hypotension, tachycardia, delirium, nausea and vomiting). It may be difficult to identify the infective agent, but *Streptococcus* is the mostly likely pathogen.

Evaluation

1 Clinical features
- mild: pain, increased swelling, erythema (well-defined or blotchy)
- severe: extensive erythema with well-defined margins, increased swelling, blistering and weeping skin; often accompanied by fever, nausea and vomiting, pain and, when the leg is affected, difficulty in walking.

2 Diagnosis is based on pattern recognition and clinical judgement. The following information should be solicited.
- present history: date of onset, precipitating factor (e.g. insect bite or trauma), treatment received to date
- past history: details of previous AIEs, precipitating factors, antibiotics taken
- examination: include sites of lymphatic drainage to and from inflamed area.

3 Establish a baseline
- extent and severity of rash: if well demarcated outline with pen and date
- level of systemic upset: temperature, pulse, BP, CRP, white cell count
- swab cuts or breaks in skin for microbiology before starting antibiotics.

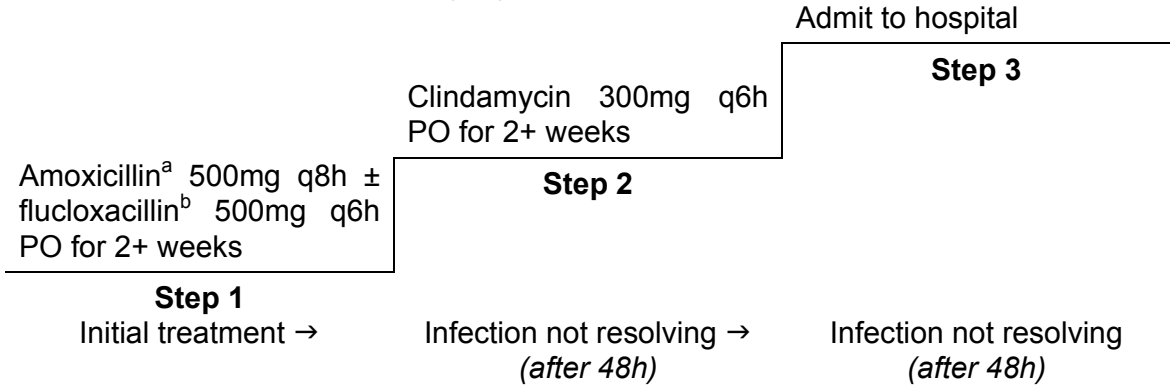
4 Arrange admission to hospital for patients with septicaemia or who deteriorate or fail to improve despite antibiotics.

Antibiotics

5 AIEs should be treated promptly with antibiotics to prevent increased morbidity (increased swelling, accelerated fibrosis). Continue antibiotics for at least 2 weeks after the inflammation begins to resolve; complete resolution may take 1–2 months.

6 The advice of a microbiologist should be obtained in unusual circumstances, e.g. an AIE developing shortly after an animal bite, and when the inflammation fails to respond to the recommended antibiotics.

7 *Standard treatment at home (PO):*



a. if a history of penicillin allergy, start on Step 2
b. add if features suggest *Staph. aureus* infection, e.g. folliculitis, pus, crusted dermatitis.

8 *Standard treatment in hospital (IV):* choice of antibiotics may vary with local policy. The following are the recommendations of the British Lymphology Society and Lymphoedema Support Network. Switch to PO amoxicillin or clindamycin when no fever for 48h, inflammation settling and CRP falling (see 7 above).

Step 1	Step 2	Step 3
IV Amoxicillin[a,b] 2g q8h+ IV gentamicin[c] 5mg/kg daily	IV Clindamycin 600mg q6h	Consult microbiologist
Initial treatment →	Infection not resolving → *(after 48h)*	Infection not resolving *(after 48h)*

a. IV benzylpenicillin 1.2–2.4g q6h is an alternative to IV amoxicillin
b. if a history of penicillin allergy, start on Step 2
c. dose adjusted according to renal function.

9 If ≥2 AIEs/year, review skin condition and skin care regimen, and consider further steps to reduce limb swelling. Start antibiotic prophylaxis with:
- phenoxymethylpenicillin 500mg (1g in those >75kg) o.d. for two years; halve the dose after one year if no recurrence
- if allergic to penicillin, erythromycin 250mg o.d. or clarithromycin 250mg o.d.
- if an AIE develops despite antibiotics, switch to clindamycin 150mg o.d. or clarithromycin 250mg o.d.
- if an AIE develops after discontinuation of antibiotics after 2 years, treat the acute episode, and then commence life-long prophylaxis.

General

10 Remember:
- bed rest and elevation of the affected limb on pillows is essential
- AIEs are painful; analgesics should be prescribed regularly and p.r.n.
- compression garments should not be worn until limb is comfortable
- daily skin hygiene should be continued; washing and gentle drying
- emollients should not be used in the affected area if the skin is broken.

11 Patients should be educated about:
- why they are susceptible to AIEs, i.e. skin crevices harbour bacteria, stagnant fluid, reduced immunity
- the consequence of AIEs, i.e. increased swelling, more fibrosis, decreased response to treatment
- the importance of daily skin care, i.e. to improve and maintain skin integrity
- reducing risk, for example, by reducing the swelling, protecting hands when gardening, cleaning cuts, treating fungal infections (**terbinafine** cream o.d. for two weeks) and ingrowing toenails
- obtaining prompt medical attention if an AIE occurs and, if a history of AIEs, taking a 2-week supply of amoxicillin 500mg q8h (clindamycin 300mg q6h if allergic to penicillin) for emergency use when away from home.