

Consensus Document on the Management of Cellulitis in Lymphoedema

Cellulitis is an acute spreading inflammation of the skin and subcutaneous tissues characterised by pain, warmth, swelling and erythema. In lymphoedema, attacks are variable in presentation and, because of differences from classical cellulitis, are often called acute inflammatory episodes. Cellulitis will be the term used here (related terms: erysipelas, lymphangitis). Most episodes are believed to be caused by *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).

Some episodes are accompanied by severe systemic upset, with high fever and rigors; others are milder, with minimal or no fever. Increased swelling of the affected area may occur. Inflammatory markers (CRP, ESR) may be raised. It is difficult to predict response to treatment.

A recent 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.

With this background, this consensus document makes recommendations about the use of antibiotics for cellulitis in patients with lymphoedema, and advises when admission to hospital is indicated. Prompt treatment is essential to avoid further damage to the lymphatics of the affected part which in turn may predispose to repeated attacks.

1. ACUTE ATTACK OF CELLULITIS

1.1 A decision whether hospital admission is indicated should be based on the level of systemic upset i.e. if:

- signs of septicaemia (hypotension, tachycardia, severe pyrexia, confusion, tachypnoea or vomiting) are an absolute indication for admission;
- continuing or deteriorating systemic signs, with or without deteriorating local signs, after 48hrs of antibiotic treatment;
- unresolving or deteriorating local signs, with or without systemic signs, despite trials of first and second line antibiotics.

1.2. Management at home

1.2.1. It is essential that the patient is closely monitored, ideally by the GP. To establish a baseline to monitor progress, record:

- extent and severity of rash – if possible, mark and date the edge of the erythema (may be difficult in lymphoedema as the rash is often blotchy);
- level of systemic upset;

CRP/ESR/white cell count may be helpful in diagnosis and monitoring of treatment.

Microbiology of any cuts or breaks in the skin should be considered before antibiotics are started.

- 1.2.2.** Oral amoxicillin 500mg 8-hourly is the treatment of choice. If there is any evidence of *Staph aureus* infection e.g. folliculitis, pus formation or crusted dermatitis, then flucloxacillin 500mg 6-hourly should be prescribed in addition or as an alternative.

Microbiologists suggest that the use of single agent Flucloxacillin for all cellulitis covers both *Strep.* and *Staph.* infections. This is, therefore, an acceptable alternative. (See www.thebls.co.uk or www.lymphoedema.org for more detailed discussion of the relative merits of Amoxicillin and Flucloxacillin).

- 1.2.3.** Patients who are allergic to penicillin should be prescribed erythromycin 500mg 6-hourly or clarithromycin 500mg 12-hourly (see also 3.1-3.3).

- 1.2.4.** If there is no or a poor response (unresolving inflammation or development of systemic symptoms) to oral amoxicillin after 48 hours, then clindamycin 300mg 6-hourly should be substituted as second line oral treatment.

- 1.2.5.** Antibiotics should be continued until all signs of acute inflammation have resolved; this may mean taking antibiotics for 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 / staining may persist for months or longer following severe cellulitis and do not necessarily require ongoing antibiotics.

- 1.2.6.** Bed rest and elevation of the affected part is essential. Avoid compression garments during the acute attack. However, they should be replaced as soon as the affected area is comfortable enough to tolerate them.

- 1.2.7.** Appropriate analgesia, e.g. paracetamol, as necessary. It is probably advisable to avoid NSAIDS e.g. ibuprofen during the acute attack. On occasions these medications may be associated with rare complications such as necrotizing fasciitis.

- 1.2.8.** When the inflammation is sufficiently reduced, wearing of compression garments and normal levels of exercise may resume. A return to work depends on the patient's occupation, and there being no deterioration when normal levels of exercise are established.

- 1.2.9** Unusual circumstances, e.g. animal bite or lick preceding an attack, or a failure of infection to respond to above recommendations, should prompt discussions with a local microbiologist.

1.3. Management in hospital

- 1.3.1.** Choice of antibiotics in hospital is usually made according to local guidelines. Hospital guidelines commonly recommend single agent i.v. Flucloxacillin 2g 6hly, as this is felt to cover both *Staph.* and *Strep.* infections (Leman and Mukherjee, 2005)

- 1.3.2.** If there is no or a poor response to this regimen after 48 hours, clindamycin 600mg 6-hourly iv should be substituted.

- 1.3.3.** Penicillin allergic patients should receive clindamycin as in 1.3.2.
- 1.3.4.** For the treatment of ano-genital cellulitis the recommended first line treatment is amoxicillin 2g 8-hourly iv plus gentamicin 5mg/kg iv daily; dose to be adjusted according to renal function and assay. NB: Local hospital guidelines may differ from this.
- 1.3.5** Monitoring of CRP / ESR / WCC / temperature is recommended and microbiology of any cuts or breaks in the skin before antibiotics started. Blood cultures may be appropriate.
- 1.3.6** Extent and severity of rash – if possible, mark and date the edge of the erythema (may be difficult in lymphoedema as the rash is often blotchy).
- 1.3.7.** A switch to oral treatment with amoxicillin 500mg 8-hourly, or clindamycin 300mg 6-hourly should not be made before:
- Temperature down for 48 hours;
 - Inflammation much resolved;
 - CRP falling.
- then continue as in 1.2.5 to 1.2.9.

1.4. Antibiotics “in case”

- 1.4.1.** The risk of further attacks of cellulitis in lymphoedema is high. It is recommended that patients who have had an attack of cellulitis should carry a two week supply of antibiotics with them particularly when away from home for any length of time, e.g. on holiday. Amoxicillin 500mg tds is recommended or, for those allergic to penicillin, erythromycin 500mg qds or clarithromycin 500mg bd. Antibiotics should be started **immediately** if familiar symptoms of cellulitis develop but a medical opinion should be sought as soon as possible.
- 1.4.2.** There is evidence that decongestive lymphatic therapy (DLT) reduces the frequency of attacks (Ko et al 1998). Control of the swelling is therefore important. Patients undergoing intensive DLT and known to have suffered cellulitis in the past during DLT may benefit from antibiotic cover in case cellulitis is provoked.
- Patients who have not experienced previous episodes of cellulitis do not require antibiotics during intensive treatments.
 - It is recommended that patients with a history of previous episode(s) of cellulitis during DLT are prescribed a prophylactic dose of antibiotic for the duration of the intensive treatment.
 - For patients already receiving prophylactic antibiotics it is recommended that a therapeutic course of antibiotics are prescribed for the duration of the intensive treatment.
- 1.4.3.** Patients undergoing surgical procedures on the lymphoedematous region should receive a therapeutic course of antibiotics commenced before surgery (oral or iv

as appropriate) as described previously (see points 1.2.2 or 1.2.3) or as indicated by the procedure.

2. RECURRENT CELLULITIS

- 2.1.** Antibiotic prophylaxis should be considered in patients who have two or more attacks of cellulitis per year. Penicillin V 250mg bd (500mg bd if BMI \geq 33, refer to end for guide) should be the first choice. The dose may be reduced to 250mg daily after one year of successful prophylaxis. Prophylaxis may need to be life-long if relapse occurs when antibiotics are discontinued after a two year period of successful prophylaxis. For those allergic to penicillin, erythromycin 250mg bd is recommended; if this is not tolerated then clarithromycin 250mg daily is an alternative (see also 3.1-3.3). It is recommended that patients requiring antibiotic prophylaxis for ano-genital cellulitis should receive trimethoprim 100mg daily taken at night.
- 2.2.** Apart from the swelling, other 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. Treatment of inter-digital fungus should be with application of terbinafine cream daily for two weeks. This may be followed by maintenance treatment, providing the skin is unbroken, with alcohol wipes daily.
- 2.3.** It may not be possible to fully prevent further episodes of cellulitis even with prophylactic antibiotics. However, there may be a reduction in the frequency of cellulitis and / or the severity of episodes. If the response to first line prophylactic antibiotics is inadequate then alternative strategies including trials of other prophylactic antibiotics e.g. clindamycin 150mg daily or cefalexin 125mg daily or doxycycline 50mg daily may need to be considered. In these circumstances, review by local specialist lymphoedema services and advice from microbiologists is recommended. There is a need to balance the use of certain antibiotics (eg clindamycin, cefalexin) as prophylaxis against the risk of predisposing to C.difficile infections.
- 2.4.** The Health Protection Agency's 2008 annual report on antimicrobial resistance and prescribing reported that no resistance to penicillin has been observed in the UK or elsewhere when prescribed for the treatment of group A Streptococci.

3. DRUG INTERACTIONS.

- 3.1.** It is recommended that the prescriber checks individual drug interactions particularly when prescribing macrolides e.g. erythromycin, and clarithromycin. The most common interactions are outlined below (3.3-3.4).
- 3.2.** Patients who have experienced an anaphylactic reaction to penicillin should not be given antibiotics from the cephalosporin family e.g. cefuroxime, cefotaxime, ceftazidime and cefalexin.
- 3.3.** For patients receiving a statin e.g. simvastatin or atorvastatin who are penicillin allergic (not anaphylaxis) the recommended first line antibiotics are cefalexin 500mg taken 8-hourly or doxycycline 200mg taken for the first day and then 100mg daily. Patients requiring prophylactic antibiotics should be offered cefalexin 125mg taken at night or doxycycline 50mg daily.

- 3.4. It is known that many of the different groups of antibiotics alter the anti coagulant effect of coumarins e.g. warfarin. It is advised that the interactions are checked before prescribing antibiotics for patients receiving coumarins.

4. RECOMMENDATIONS FOR THE TREATMENT OF CELLULITIS IN CHILDREN WITH LYMPHOEDEMA.

- 4.1. As in adults, cellulitis in children may present with local symptoms of pain, discomfort, redness or swelling with or without general ill health and malaise. It is important to treat early and recognise that those children who present with systemic symptoms of infection or have deteriorating local signs should be seen in hospital and treated aggressively with intravenous antibiotics.
- 4.2. The management of cellulitis in children with lymphoedema should follow the previous sections (1-3) with reference to appropriate documents (e.g. BNF) to determine the required antibiotic dose(s).
- 4.3. It has been suggested that children requiring hospital admission should receive amoxicillin plus flucloxacillin. If there is any suspicion of toxic shock syndrome clindamycin should be prescribed in addition to amoxicillin and flucloxacillin.

References:

- Chira S. and Miller L.G (2010) Staphylococcus aureus is the most common identified cause of cellulitis: a systemic review, *Epidemiology and Infection*, 138, 313-317.
- Cox N.H, (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.
- Health Protection Agency (2008) Antimicrobial resistance and prescribing in England, Wales and Northern Ireland, London, Health Protection Agency.
- Kilburn SA, Featherstone P, Higgins B, Brindle R (2010) Interventions for cellulitis and erysipelas, *Cochrane Database of Systematic Reviews*, 6.
- Ko D.S.C, Lerner R, Klose G et al (1998) Effective treatment of lymphoedema 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 randomised controlled trial, *Emergency Medicine Journal*, 22, 342-346.
- Mortimer P (2000) Acute inflammatory episodes. In Twycross R, Jenks K and Todd J, (Eds), *Lymphoedema*, Oxford, Radcliffe Medical Press, p130-139.

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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).