

# CELLULITIS TREATMENT FOR PEOPLE WITH LYMPHOEDEMA: UK AUDIT

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## Abstract

**Background:** A group of UK clinicians (under the auspices of the British Lymphology Society [BLS] and the Lymphoedema Support Network [LSN]) drew up consensus guidelines on the management of cellulitis in patients with lymphoedema in 2005 (available at: [www.thebls.com](http://www.thebls.com)). **Aims:** To determine whether the guidelines were being followed and to assess the effectiveness of the treatment recommended in the guidelines. **Methods:** Questionnaires to be completed by patients after an episode of cellulitis were distributed by the LSN and BLS members. **Results:** 396 responses were received during the 18-month data collection period. The average age of respondent was 60 years. 86% were female and 55% had cancer-related lymphoedema. People treated at home received 42 different drug doses/combinations of 17 antibiotics. Only 13.8% received the recommended first-line antibiotic, amoxicillin alone. The median duration of treatment was 7.5 days (interquartile range [IQR] 7–14). 26.8% of people treated at home required a second course of antibiotics. 24% of the groups required hospital treatment. **Conclusions:** Despite the publication of consensus guidelines, most patients were treated with antibiotics different from those recommended as first-line and for a shorter duration. There was, however, no evidence from this audit that this affected the outcome. **Declaration of interest:** None.

## Key words

Cellulitis  
Lymphoedema  
Antibiotics  
Guidelines  
Streptococcus

Cellulitis/erysipelas/acute inflammatory episodes (AIEs) are common, well-known complications of lymphoedema. The terms describe an acute infection of the skin and subcutaneous tissue associated with a rapid onset, spreading erythema, increased temperature to the affected area, swelling and malaise (Bisno and Stevens, 1996; Cooper and White, 2009). Dupuy et al (1999) explored the risk factors for erysipelas of the leg. Lymphoedema was the greatest risk and was present in 18% of cases examined. In addition, Maher (2008) investigated patient reported triggers for an increase in arm swelling,

The most commonly reported reason for increased swelling was infection.

In the UK there is a perceived variation in opinion as to how these infections should be treated. Many 'generalists' use anti-staphylococcal antibiotics as they feel that staphylococci are the major cause of infections. The difficulties in obtaining a positive culture and distinguishing clinically between the signs and symptoms of streptococcal and staphylococcal infections do not help (Brook and Frazier, 1995; Bisno and Stevens, 1996; Cox et al, 1998; Eron et al, 2003). However, the general view among lymphoedema specialists in the UK is that streptococci are the major cause and therefore anti-streptococcal antibiotics are preferred (Mortimer, 2000; Cox et al, 1998).

Members of the UK Lymphoedema Support Network (LSN), a national group for patients with lymphoedema, report that many general medical practitioners do not recognise the problem of cellulitis in patients suffering from lymphoedema and are also uncertain about how to treat it.

In response to these issues, the LSN together with the British Lymphology

Society (BLS) brought together a group of UK clinicians to draw up some consensus guidelines for the management of cellulitis in lymphoedema in 2005. The guidelines are based on the concept that most episodes of cellulitis in lymphoedema are caused by  $\beta$ -haemolytic streptococci. Amoxicillin was chosen by the consensus group for the management of cellulitis in lymphoedema, as it is said to have greater tissue penetration than phenoxymethylpenicillin.

The guidelines (summarised in *Table 1*) have been made available as a printed leaflet by the LSN and are also on the BLS and LSN websites. Patients are encouraged to take a copy of the leaflet to their GP.

## Method

### Study aims

Having introduced the guidelines in the UK, the aims of the audit were to determine whether the recommendations were being followed and also to try to measure the effectiveness of the treatment recommended.

### The questionnaire

The questionnaire was divided into four sections (*Box 1*). The first was designed

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**Table 1**

**Summary of consensus guidelines for the treatment of cellulitis in people with lymphoedema**

**Home management**

- ▶▶ Oral amoxicillin 500mg 8-hourly for at least 14 days
- ▶▶ If patient is penicillin allergic: oral clindamycin 300mg 6-hourly for at least 14 days

**Hospital management**

- ▶▶ Local hospital guidelines for iv antibiotics: amoxicillin 2g 8-hourly or benzylpenicillin 1.2–2.4g 6-hourly + gentamicin 5mg/kg daily. (Most hospitals use benzylpenicillin + flucloxacillin)
- ▶▶ If penicillin-allergic: clindamycin 600mg 6-hourly
- ▶▶ Change to oral antibiotics when signs of improvement, these include:
  - ~ Temperature down for 48 hours
  - ~ Inflammation much resolved
  - ~ C-reactive protein (CRP) falling

**Antibiotics 'in case'**

Patients who have had a previous attack should carry a two-week supply of antibiotics (amoxicillin 500mg 8-hourly or clindamycin 300mg 6-hourly if penicillin-allergic) with them when away from home for any length of time, e.g. on holiday

**Recurrent cellulitis**

Antibiotic prophylaxis should be offered to patients who have two or more attacks of cellulitis per year:

- ▶▶ Penicillin V 500mg daily (1g if weight >75kg)
- ▶▶ If penicillin allergic: erythromycin 250mg daily, or if this is not tolerated clarithromycin 250mg daily can be used as an alternative

to identify demographic details about the patient and signs and symptoms of this infection. This included age, gender, site(s) of swelling and cause of lymphoedema. This section also asked the patient to recall any previous episodes of cellulitis and whether they were receiving prophylactic antibiotics.

The following two sections related to the treatments received. Patients were asked to complete different sections depending upon whether they were treated at home and/or in hospital. They were asked to record the name(s) and duration of the antibiotics taken and to identify who prescribed the course.

The final section was designed to evaluate the effectiveness of the treatment(s). This was measured by the requirement for a second course of antibiotics, the length of time to recovery and rash resolution. It is acknowledged

that patient rated outcomes are subjective and therefore produce weaker findings than objective outcome markers.

**Distribution**

Questionnaires were distributed to patients across the UK through the LSN (a questionnaire was sent to every member) and by lymphoedema specialists. The questionnaires were made available on the LSN/BLS websites and additional copies were sent out to patients from the coordinating centre in Derby. Completed questionnaires were returned using a freepost address to encourage returns, and articles were published in the LSN newsletter, *Lymphline*, to publicise the project. Patients were asked to complete a questionnaire after an episode of cellulitis between March 2007 and September 2008. If a patient experienced multiple episodes of cellulitis during the data collection period, they were asked to complete one questionnaire for each episode.

**Table 2**

**Type or cause of lymphoedema**

Type/cause	Percent (%)
Cancer related	55
Primary	26
Cellulitis	3
Surgery (non cancer)	2
Trauma	1.5
Post-thrombotic	1
Not specified/ unknown/other	11.5

**Analysis**

Descriptive analysis and comparisons were undertaken. Comparison between the treatments suggested by the guidelines and other treatments were made. The Chi squared and the Mann Whitney U test were undertaken to identify whether any differences observed between the groups demonstrated statistical significance.

**Results**

**Demographics**

Over the 18-month data collection period, 396 responses were received. The average age of respondent was 60 years and 86% were female. 51% of the group reported having lymphoedema of the legs, 36% arm oedema and the remainder had head and neck, breast, trunk, genital oedema or a combination of the above. *Table 2* details the type or cause of lymphoedema.

**Symptoms**

The recognised symptoms of cellulitis: redness, heat, increased swelling and feelings of being generally unwell were acknowledged by over 80% of the sample. Symptoms of experiencing a rash and a raised temperature were less frequently recorded but recognised by over 50% of the group. Other symptoms recalled included itchiness, pain, blistering and subsequent wounds, nausea and vomiting. This is illustrated in *Table 3*.

**Previous cellulitis**

76% of the group had experienced a previous episode(s) of cellulitis, the median number of episodes in the previous year was 1 (interquartile range [IQR], 1–2) and

**Box 1: Audit of the treatment of skin infections in people with lymphoedema**

The Consensus Document on the Management of Cellulitis was reproduced as an LSN fact sheet in March 2006. We would like to see if these guidelines have been helpful. We would therefore be most grateful if, in the event of your experiencing a skin infection (or cellulitis), you would kindly complete and return this questionnaire. Please complete one questionnaire for each episode of cellulitis once the episode has resolved. If you experience more than one infection, we would be grateful if you would complete a questionnaire for each episode. All of the information shared by you in this questionnaire will be anonymous.

- 1a)** Please indicate the site of swelling: Arm  Left  Right   
 (Please tick all that apply) Leg  Left  Right   
 Other .....
- 1b)** I am ..... years of age.
- 1c)** I am Male  Female
- 1d)** What is the type or cause of your lymphoedema? .....
- 1e)** Have you had previous episodes of skin infection in the area affected by lymphoedema? Yes  No   
 If 'Yes', how many episodes have you experienced in the last year? .....
- 1f)** Were you taking 'low' dose antibiotics to try to prevent cellulitis (prophylactic antibiotics) before this infection? Yes  No   
 If 'Yes', please give the name of the antibiotic, the dose and how often you took it (e.g. once per day, twice per day) .....

Please give details of this episode of cellulitis. Please tick the appropriate box(es)

- 1g)** Which area was affected by cellulitis? .....
- 1h)** Affected area was: Red  Hot  More swollen  Rash present
- 1i)** Did you experience a general feeling of being unwell? Yes  No
- 1j)** Did you experience a raised temperature? Yes  No   
 Please describe any other symptoms: .....
- 1k)** How long was it after you first noticed these symptoms before you started the first course of antibiotics?
- 1l)** Are you allergic to any antibiotics? Yes  No   
 If 'Yes', which antibiotics are you allergic to? .....

If you remained at home for your antibiotic treatment please complete the questions in section two and four. If you were admitted to hospital for your treatment please complete sections three and four. If your treatment started at home and then required hospital admission, please complete all sections.

**Section Two: (treatment started at home)**

- 2a)** What were the first antibiotics taken (name of antibiotic, dose and how many times per day you took them)? .....
- 2b)** Who prescribed these antibiotics? GP  Hospital doctor  Other  .....
- Was this an 'in case supply' (antibiotics already prescribed for you in case of an infection)? Yes  No
- 2c)** How long did you take them for? .....

**Section Three: For hospital admissions**

- 3a)** How long were you in hospital for? .....
- 3b)** If you are aware, please give details of the antibiotics given:  
 (If possible, please give details of the drug name(s), dose, how frequently they were given, whether they were given to you by mouth or intravenously and the length of treatment) .....

**Section Four: For all respondents**

- 4a)** Were further courses of antibiotics taken for this particular episode of infection? Yes  No   
 (If possible, please give details of name, dose, how many times per day you took them, the reason for the second course and length of time taken) .....
- 4b)** Were any other treatments or medication prescribed for this episode of cellulitis e.g. pain killers, diuretics ('water tablets')? Yes  No   
 (If possible, please give details of name, dose and reason for taking) .....
- 4c)** How long was it before you felt better? .....
- 4d)** How long was it before the redness/rash resolved? .....

Thank you for your time and help in completing this questionnaire.

We aim to collect responses to this questionnaire for one year and will publish the results in a future issue of Lymphline.

**Table 3**

**Symptoms experienced**

Symptoms of cellulitis	Percent (%)
Redness	91
Heat	90
More swollen	81
Rash	53
Feeling generally unwell	82
Fever, raised temperature	69

ranged from 0 to 10. Of this group, 16% had not experienced an episode in the last year but 45.8% had experienced two or more episodes.

12.6% were receiving prophylactic antibiotics before the reported cellulitic episode, the most commonly recalled being phenoxymethylpenicillin (Table 4).

**Treatment in hospital**

94 people (24%) required hospital treatment, with a mean stay of eight days ( $\pm 10.25$  SD). 66% of this group were hospitalised from the initial onset of the acute episode and 33% with unresolved cellulitis following a course of oral antibiotics at home.

All but two hospitalised patients received intravenous (IV) antibiotics. However, half could not recall the name or dose of the drug given.

There was a variety in the drugs that were administered, with 21 combinations of 15 different drugs given. The most common combination was of IV flucloxacillin and benzylpenicillin (18.4%).

**Treatment at home**

84% of patients treated at home were prescribed antibiotics by their general practitioner (GP). The others were prescribed by a hospital doctor, an out-of-hours doctor, at a walk-in clinic or by a nurse (district nurse and lymphoedema nurse).

41.8% of respondents took antibiotics that had been prescribed before the episode as an 'in case' supply.

**Table 4**

**Details of antibiotic prophylaxis**

Prophylactic antibiotics (n=44)		Percent (%)
Phenoxymethylpenicillin	250mg/day	6.8
	500mg/day	43.2
	1000mg/day	11.4
Flucloxacillin	500mg/day	4.5
Clarithromycin	250mg/day	6.8
Cefalexin	250mg/day	2.3
Clindamycin	150mg/day	6.8
Erythromycin	250mg/day	11.4
Others/missing		6.8

42 combinations of 17 different antibiotics were prescribed. The most commonly recalled were flucloxacillin alone (23.5%). Amoxicillin alone was prescribed in 13.8% of cases and the recommended amoxicillin 500mg TDS for 14 days was given to 4% of all respondents. The details of the antibiotics taken at home are presented in Table 5.

The median duration of antibiotic course was 7.5 days (IQR 7–14). However, there were some patients who received antibiotics for a longer period of time, 180 days being the longest duration that was reported.

**Second course of antibiotics**

Respondents were asked to provide details about the second antibiotic course taken. 30 patients who were treated in hospital were discharged with a course of oral antibiotics.

81 patients (26.8%) treated at home received a second course of antibiotics. This included 26 patients (8.6%) who received an extended course of the first antibiotic taken, either at the same or a reduced dose. It can be inferred that for this group of patients, the infective episode was responding to the first antibiotic course but had not completely resolved at this time.

34 patients (11.3%) received a different antibiotic for the second course. The requirement of a different type of antibiotic is interpreted as a marker of effectiveness of the original treatment, in

**Table 5**

**Oral antibiotic course taken at home**

Drug	Percent (%)
Flucloxacillin	23.5
Amoxicillin	13.8
Erythromycin	12.2
Phenoxymethylpenicillin and flucloxacillin	5.2
Clarithromycin	3.5
Co-fluampicil	3.1
Clindamycin	2.4
Others	18.6

that the infection had not responded to the first antibiotic prescribed. Responses detailing the second antibiotic were missing for 21 patients.

**Recovery time**

Respondents were asked to state how long it was until any rash/redness had resolved and until they felt better.

The median time for the discoloration resolving was seven days (IQR 5–14). The range varied greatly from 1–180 days.

The median time until respondent rated recovery was seven days (IQR

Table 6

### Comparison of antibiotic course taken and the percentage requiring a second course of antibiotics

Antibiotic course	Amoxicillin	Others
% requiring second course of antibiotics	10% (4/40)	12/1% (29/240)
Antibiotic course	Amoxicillin	Flucloxacillin
% requiring second course of antibiotics	10% (4/40)	9.6% (5/52)

Table 7

### Comparison of the length of first antibiotic course and percentage requiring a second course of antibiotics, chi squared test

Duration of first course (days)	7	14	p value
% requiring second course of antibiotics	10.6 (11/104)	7.2 (6/83)	0.429

4–17). Similarly, there was variation in the responses ranging from a single day to 180 days.

#### Did following the consensus document improve the outcome?

Statistical analysis was undertaken to identify whether there were significant differences between the recovery time and number of antibiotic courses required for those who received treatment, as recommended in the consensus document and those who received other antibiotics. Comparisons were made between respondents who required a second course of a different antibiotic and the original antibiotic prescribed. Respondents who required an extended course of the original antibiotic were included in the group whose cellulitis resolved following one course of antibiotics, as it was felt that this pattern of prescribing probably reflected at least a partial response to the first course.

#### Were further courses of antibiotics required?

Table 6 presents the percentage of respondents who required a second course of antibiotics, comparing amoxicillin to all other first antibiotics taken at home and then amoxicillin to flucloxacillin. There was no obvious difference in the percentage of patients requiring a second course of antibiotics when amoxicillin or other antibiotics were taken as the

first course. Comparable proportions of patients required a second course of antibiotics when those who were prescribed amoxicillin were compared to respondents who received flucloxacillin. The numbers in the groups being compared were too small to enable the chi squared test to be undertaken.

Table 7 compares the percentage of respondents who required a second course of antibiotics to the length of the first course of antibiotics. Responses were only counted if they were specified as seven days ( $n=104$ ) or 14 days ( $n=83$ ). The results were similar; 10.6% compared to 7.2%. The chi squared test demonstrated that this difference was not significant ( $p=0.429$ ).

#### Respondent rated recovery time

Table 8 compares the first antibiotic course received to respondent rated recovery time. The median time for recovery is the same for the groups being compared. The differences between the two groups lie in the interquartile ranges.

The Mann Whitney U test tests whether the populations tested are the same and Table 8 demonstrates that the differences are not significant ( $p=0.96$  and  $0.985$ ).

Comparing recovery time to duration of antibiotic course (Table 9) using the Mann

Whitney U test demonstrated a statistically significant difference between the groups. The median time until feeling better was the same for both groups but the interquartile ranges differed. Both the 25th and 75th percentile were greater for the group that received a 14-day course, indicating that this group took longer to recover. The Mann Whitney U test demonstrated a trend to significance ( $p=0.063$ ).

The times taken for any rash/redness to resolve were different. The raw data demonstrated that the median and interquartile ranges were greater indicating that the rash/redness took longer to resolve for the group who received a 14-day course of antibiotics ( $p=0.006$ ).

These results suggest that patients received a 14-day course of antibiotics if they had not fully improved after a seven-day course.

## Discussion

The responses received demonstrate that the consensus guidelines are not being followed in most cases. Reasons for this could include; availability of the guidelines to GPs, belief in the guidelines, and differences between the consensus guidelines and individual hospital policies.

There are few other existing guidelines on the management of cellulitis. These are not specific to the treatment of lymphoedema-associated infections and do not advocate the same antibiotic regimens (Eron et al, 2003; Clinical Resource Efficiency Support Team [CREST], 2005). Flucloxacillin alone appears to be the oral antibiotic of choice, despite an acknowledgement that the majority of cellulitis infections are streptococcal in origin. The CREST guidelines rationalised their choice as they recognised flucloxacillin to have an effect on streptococcal bacteria as well as staphylococcal. French guidelines on the management of erysipelas/necrotising fasciitis recommend pristinamycin where available, or amoxicillin as an alternative (Société Française de Dermatologie, 2001).

A recent review of streptococcal cellulitis/erysipelas of the lower leg considers in detail, among other aspects, the diagnostic difficulties, the limited



**Table 8**

**Comparison of the first antibiotic course taken and time to feeling better/rash resolution. Mann Whitney U Test**

Antibiotic course	Amoxicillin (33)	Others (215)	p value
Time to feeling better? Median (IQR)	7 (4.5–12)	7 (4–17)	0.96
Antibiotic course	Amoxicillin (33)	Others (215)	p value
Time to rash resolving? Median (IQR)	7 (4–24)	7 (5–14)	0.985

**Table 9**

**Comparison of the length of first antibiotic course and time to recovery/rash resolution, Mann Whitney U Test**

Duration of first course	7 (94)	14 (77)	p value
Time to feeling better? Median (IQR)	7 (4–14)	7 (5–17)	0.063
Time to rash resolving? Median (IQR)	7 (4–12)	10 (5–7)	0.006

evidence for the choice of the best antibiotic treatment regimen and the case for prophylaxis (Cox, 2008). There have been no randomised control trials comparing benzylpenicillin with flucloxacillin, but one study found no difference in the efficacy of IV flucloxacillin alone compared with IV flucloxacillin and benzylpenicillin in combination (Leman and Mukherjee, 2005). The authors suggest that adding benzylpenicillin provides no advantage. Flucloxacillin and benzylpenicillin both have antistreptococcal activity with low minimum inhibitory concentrations (MICs) and the main argument against using benzylpenicillin alone is the possibility of non-streptococcal infection (Cox, 2008). Patients with cellulitis and lymphoedema have not been specifically studied.

Individual hospitals tend to have their own guidance on the management of cellulitis, differentiating clinical presentation into separate classes which influence the antibiotic drug, route and dose prescribed. This may explain the responses from this audit for the group who received their first treatment in hospital. The most frequently reported IV antibiotics were a combination of flucloxacillin and benzylpenicillin, and not the suggested amoxicillin or benzylpenicillin combined with gentamicin. Similarly, Cox et

al (1998) reported flucloxacillin alone or in combination as the most commonly used antibiotic for patients treated in hospital for cellulitis of the leg.

In the present audit, the prescribing of oral flucloxacillin alone for patients receiving treatment at home was more frequently reported than amoxicillin alone. A high proportion of these were prescribed by the patient's GP. In their paper, Cox et al (1998) concluded that it is important to consider staphylococci and other organisms in the management of cellulitis, particularly in cases with preceding wounds. However, they also recommend that treatment must include an anti-streptococcal agent. The prescribing reported in this audit would comply with these recommendations.

The Health Protection Agency's 2008 annual report on antimicrobial resistance and prescribing reported resistance to clindamycin (5.1%), erythromycin (5.6%) and tetracycline (14%) when treating group A streptococci. No resistance to penicillin has been observed in the UK or elsewhere and the report recommends penicillin as the therapeutic drug of choice in the treatment of group A streptococci infections. This, therefore, supports the approach taken in the BLS/LSN guidelines.

It is not known how many GPs have access to the consensus document. The questionnaire was completed by patients and did not seek to identify whether the healthcare professional treating the patient had access to the consensus document and based the rationale for the treatment on this. The consensus document appears to be the only guidance that suggests amoxicillin as the first line antibiotic. It is not known on what GPs based their prescribing decision upon. It could have been local guidelines or national ones such as the NHS Clinical Knowledge Summaries ([www.cks.nhs.uk/home](http://www.cks.nhs.uk/home)). The latter recommends flucloxacillin as first line treatment following the CREST guidance.

The audit asked patients to complete a questionnaire after an episode of cellulitis had resolved. This retrospective data collection method relied on the patient's ability to recall the event. The questionnaire did not ask for corroboration from the treating professional to confirm the episode or details of the patient's recovery time. Not all respondents identified having the recognised signs and symptoms of cellulitis, thereby raising questions about the accuracy of the diagnosis. 9% didn't report redness of the affected area and 18% did not feel generally unwell at the time of the infective episode. However, all of the respondents were treated with antibiotics, either by a doctor or using an 'in case' supply, which is suggestive of confirmation by a healthcare professional or previous experience of cellulitis.

It is acknowledged that recovery time varies between patients and that some are left with chronic skin changes after the cellulitis has resolved. Length of time taken for the rash to resolve varied from a few days to many months. It is not known whether patients who reported a long recovery were experiencing resultant chronic skin changes.

A further limitation of this method of data collection from a self-selected group is that it is unknown whether this was a representative sample of all patients with lymphoedema. Questionnaires were distributed through the LSN to its members. It could be inferred that this is a proactive group of patients with a strong interest in their condition which may, therefore, bias

the results. It is not known from where each respondent received the questionnaire.

There is a lack of evidence for the duration of antibiotic course required to resolve an infective episode and the length of antibiotics required once the episode appears to be resolving. The CREST guidelines suggest that IV antibiotics can be switched to oral antibiotics within 3.5 days. In uncomplicated cases, the length of antibiotic treatment recommended is one to two weeks. However, patients with lymphoedema have been recognised as a group susceptible to complicated infections which may require longer treatment (Eron, 2003; CREST, 2005).

Cox (1998) recorded the length of antibiotics taken to resolve cellulitis after discharge from hospital. This study reviewed patients treated for cellulitis of the leg in a district hospital. The duration ranged from 0 days to six months, the mean and median differed at 14 days and seven days respectively. 12% were advised to take antibiotics for a further four weeks following discharge. Two patients from the 92 sampled were known to have lymphoedema prior to the cellulitis and six patients had chronic oedema after the episode. The proportion of patients requiring a prolonged course of antibiotics was greater in Cox's 2006 study (49%). However, the percentage of patients recognised to have persistent oedema before the infective episode was also larger, 46% (79 out of 171 patients).

Masmoudi et al (2005) undertook a 10-year retrospective study identifying 26 cases of upper limb erysipelas post breast cancer treatment. All of the patients reviewed required IV antibiotics, 16 were known to have lymphoedema before the episode and an additional two patients following the erysipelas. The duration of antibiotics used ranged from 11 to 27 days, the average being 16 days.

Woo et al (2000) monitored the symptoms experienced and recovery time from cellulitis in a group of patients with cancer-related lymphoedema and compared this to a matched control group. The mean duration of fever, tachycardia and cellulitis was significantly longer in patients with lymphoedema than those without.

In this audit the time to recovery was similar for respondents regardless of the antibiotic prescribed. The median recovery time and rash resolution was seven days for the group that received amoxicillin and those who received other antibiotics. The median recovery time was the same for patients who received a seven-day course of antibiotics or a 14-day course. Patient rated time for any rash/redness to resolve was significantly different when the two groups were compared, the median resolution time was greater for the group who received a 14-day course of antibiotics. It is not known why the groups differed. However, it could be inferred that the group who received a 14-day course were being treated for a severe episode of cellulitis or were given an extended course of antibiotics as the rash had not resolved by seven days.

One of the arguments used in favour of prescribing a longer course of antibiotics is that, although patients with lymphoedema may respond to a shorter course, they may be more likely to develop an early recurrence of cellulitis than those taking 14 days of antibiotics. The time to the next episode of cellulitis was, however, not recorded in this audit.

Approximately 25% of respondents treated at home required an extended or second course of antibiotics to resolve the episode. From the literature available, it does not appear that the number of antibiotic courses required to treat an episode of cellulitis has been studied.

This audit has confirmed that cellulitis is a recurrent problem for people with lymphoedema, 75% of the sample had experienced a previous episode of cellulitis. The consensus document recommends that prophylactic antibiotics are started following two or more episodes of cellulitis in one year: 45.8% of respondents had experienced at least two episodes in the previous year; however, fewer than expected respondents (12.6%) were taking antibiotic prophylaxis.

There are a few studies that were designed to investigate the efficacy of prophylactic treatments. A Cochrane review (Badger et al 2004) identified and reviewed four eligible randomised control trials (RCTs) designed to investigate the

treatments prescribed prophylactically to reduce and prevent AIEs in patients with lymphoedema. The review failed to identify enough good quality evidence to draw conclusions about the efficacy of the treatments reviewed.

The type and route of prophylactic antibiotics studied vary. Sjoblom et al (1993) studied the effect of prophylactic penicillin in patients with recurrent cellulitis and venous insufficiency or lymphatic congestion. The rate of recurrence appeared to decrease for the group who received antibiotics, however, this was not statistically significant. Low dose erythromycin as prophylaxis was compared to a placebo in a group of patients with recurrent episodes of cellulitis or erysipelas, the presence of lymphoedema was not recorded (Kremer et al, 1991). No patient who received the study drug experienced an infective episode while taking the medication, compared to eight patients (50%) in the placebo group. Three patients who had received erythromycin had their treatment changed to penicillin due to gastro-intestinal side-effects.

Prophylaxis using intra muscular penicillin has also been studied. Vignes and Dupuy (2006) monitored time to recurrence in patients with upper limb lymphoedema and recurrent cellulitis who received long-term prophylaxis. 23 of the 48 women sampled experienced an episode of cellulitis during the four-year median follow-up period. The median duration of time free from cellulitis was 2.7 years, and two-thirds of the sample did not have recurrence within the first two years of treatment. The total number of prior infective episodes was provided but information was not given specifying the frequency before prophylaxis.

Olzewski (1996) observed that long-term antibiotic prophylaxis using IV penicillin was required. This study aimed to offer treatment for one year to patients with recurrent dermatolymphangioadenitis (DLA). This was extended for all 45 patients due to the tendency of recurrence after prophylaxis cessation. 9% of patients experienced a recurrent episode while receiving treatment in a group of patients who reported episodes of DLA that ranged from one to six episodes per year.

A study currently in progress has been designed to provide evidence to determine the role of prophylactic penicillin. This RCT to investigate whether prophylactic antibiotics can prevent further episodes of cellulitis (erysipelas) of the leg compares the number of recurrent episodes of cellulitis of the leg(s) in patients receiving prophylactic penicillin V or a placebo (PATCH). The study recruits patients following a first episode of cellulitis and recurrence offering six and 12 months of treatment respectively. Patients are followed up for up to 18 months after completing the randomised study drug. The randomisation process is stratified for the presence of oedema to prevent bias between the two groups. The results are awaited with interest.

### Conclusions

Few patients were treated according to the recommendations in the consensus guidelines. There is, however, no evidence from the audit that the outcome of treatment was affected by this. It seems that either practitioners are unaware of the existence of the guidance or that there is a belief that staphylococci are a significant factor in cellulitis, which should therefore be treated with anti-staphylococcal antibiotics such as flucloxacillin which is also effective against streptococci.

In the audit results there was no obvious difference in the response to flucloxacillin or amoxicillin. This would be consistent with the concept that cellulitis in lymphoedema is usually caused by streptococci, since amoxicillin is ineffective against most staphylococcal infections.

Further microbiological evidence on the pathogenesis of cellulitis in lymphoedema would facilitate decision-making in the choice of the most appropriate antibiotic therapy.

It is planned that the consensus guidelines and their distribution will be reviewed this year particularly in the light of the growing problem of *Clostridium difficile* infections associated with broad spectrum antibiotic usage especially in hospitals. JL

*This paper was written on behalf of the British Lymphology Society (BLS) and Lymphoedema Support Network (LSN) Consensus Group on the treatment of cellulitis in lymphoedema.*

### References

- Badger C, Preston N, Seers K and Mortimer P. Antibiotics/ anti inflammatories for reducing acute inflammatory episodes in lymphoedema of the limbs, Cochrane Database of Systematic Reviews 2004, Issue 2, Art No. CD003143.
- Bisno AL, Stevens DL (1996) Streptococcal infection of skin and soft tissues. *N Engl J Med* 334: 240–6
- Brook I, Frazier EH (1995) Clinical features and aerobic and anaerobic microbiological characteristics of cellulitis. *Arch Surg* 130: 786–92
- Clinical Resource Efficiency Support Team (CREST) (2005) *Guidelines on the Management of Cellulitis in Adults*. CREST, Belfast
- Clinical Knowledge Summaries, Cellulitis Acute. Accessed 06/07/2009 at [www.cks.nhs.uk/cellulitis\\_acute](http://www.cks.nhs.uk/cellulitis_acute)
- Cooper R, White R (2009) Cutaneous infections in lymphoedema. *J Lymphoedema* 4(1): 44–8
- Cox NH (2006) Oedema as a risk factor for multiple episodes of cellulitis/erysipelas of the lower leg: a series with community follow up. *Br J Dermatol* 155: 947–50
- Cox N (2008) Streptococcal cellulitis / erysipelas of the lower leg. In: Williams H, ed. *Evidence-Based Dermatology*. 2nd edn. Oxford, Blackwell Publishing, Oxford: chap 41
- Cox NH, Colver GB, Paterson WD (1998) Management and morbidity of cellulitis of the leg. *J R Soc Med* 91: 634–7
- Dupuy A, Benchikhi H, Roujeau JC, et al (1999) Risk factors for erysipelas of the leg (cellulitis): case-control study. *Br Med J* 318: 1591–4
- Eron LJ, Lipsky BA, Low DE, Nathwani D, Tice AD, Volturo GA (2003) Managing skin and soft tissue infections: expert panel recommendations on key decision points. *J Antimicrob Chemother* 52: S1, i3–17
- Health Protection Agency (2008) *Antimicrobial Resistance and Prescribing in England, Wales and Northern Ireland*. Health Protection Agency, London
- Kremer M, Zuckerman R, Avraham Z, Raz R (1991) Long-term antimicrobial therapy in the prevention of recurrent soft-tissue infections. *J Infect* 22: 37–40
- Leman P, Mukherjee D (2005) Flucloxacillin alone or combined with benzylpenicillin to treat lower limb cellulitis: a randomised control trial. *Emerg Med J* 22: 342–6
- Maher J (2008) Factors precipitating an episode of lymphatic swelling. *J Lymphoedema* 3(2): 32–6
- Masmoudi A, Maaloul I, Turki H, et al (2005) Erysipelas after breast cancer treatment. *Dermatol Online J* 11(3): 12
- Mortimer P (2000) Acute inflammatory episodes. In Twycross R, Jenns K, Todd J, eds. *Lymphoedema*. Radcliffe Medical Press, Oxford: 130–9
- Olszewski WL (1996) Episodic dermatolymphangiodenitis (dla) in patients with lymphoedema of the lower extremities before and after administration of benzathine penicillin: a preliminary study. *Lymphology* 29(3): 126–32
- Sjoblom AC, Eriksson B, Jorup-Ronstrom C, Karkkonen K and Lindqvist M (1993) Antibiotic prophylaxis in recurrent erysipelas. *Infection* 21(6): 390–3
- Société Française de Dermatologie. Conference (2001) Erysipelas and necrotizing fasciitis: management. *Ann Dermatol Venereol* 128: 307–482
- Soo JK, Bicanic WA, Heenan S, Mortimer PS (2008) Lymphatic abnormalities demonstrated by lymphoscintigraphy after lower limb cellulitis. *Br J Dermatol* 158: 1350–3
- Vignes S, Dupuy A (2006) Recurrence of lymphoedema-associated cellulitis (erysipelas) under prophylactic antibiotherapy: a retrospective cohort study. *J Eur Acad Dermatol Venereol* 20: 818–22
- Woo PCY, Lum PNL, Wong SSY, Cheng VCC, Yuen KY (2000) Cellulitis complicating lymphoedema. *Eur J Clin Microbiol Infect Dis* 19: 294–7

### Key points

- ▶▶ The audit studied whether national consensus guidelines on the management of patients with cellulitis in lymphoedema were being followed and whether these were effective.
- ▶▶ Despite the publication of consensus guidelines, most patients were treated with antibiotics different from those recommended as first line and for a shorter duration.
- ▶▶ There was no evidence from this audit that the type and duration of antibiotic received affected the outcome.