

# The natural history of antibiotic-treated cellulitis: data derived from a randomized trial of cellulitis of over 400 patients.



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## Background

Despite being a common condition the natural history of cellulitis is poorly described. This makes it difficult to determine recovery at different time points and to give the patient a likely duration of the condition. We have used data collected as part of a clinical trial on the treatment of limb cellulitis to describe the day-by-day changes in physiology, pain, blood parameters and limb measurements. We have used these variables to estimate severity, and relate this to time to recovery.

## Methods

At entry into the trial patients had routine observations, limb measurements and blood tests. Pain (VAS) and well-being scores were also recorded. The patients were followed up with 2 subsequent face-face visits and a telephone questionnaire up to 40 days after entering the study. Patients kept a record of pain and other features.

## Results

410 patients from 20 centers, entered the study. The actual follow-up days varied from patient to patient so data was available from recruitment for every day up until 15 days for 20 variables and up until 40 days for well-being and physical activity. Plots were constructed for each variable both from the onset of local features and from the start of antibiotic therapy. In general, limb swelling increased over the first few days before starting to decrease at 6 days, erythema was still evident at 10 days and pain decrease uniformly. Baseline severity and age was correlated to the likelihood of prolonged disability.

## Significant findings

- Local features of cellulitis may progress for the first few days despite other parameters improving and should not be used to influence antibiotic therapy.
- IV antibiotics do not lead to better outcomes and short duration of antibiotic therapy is as good as long duration.
- The severity of cellulitis at diagnosis is the feature most strongly predictive of time to recovery.
- Significant deterioration in renal function does occur but is not common and, if it does, it appears reversible within a few days.
- Mild and transient increases in liver enzymes may occur within the first week.
- Older age is strongly associated with delayed return to normal activities at Day 30

## THERMAL IMAGING



### THE TRIAL PROVIDED FIVE TYPES OF DATA:

- Systemic observations e.g. heart rate, blood pressure
- Blood tests e.g. neutrophil count, CRP
- Limb measurements e.g. affected area, swelling
- Subjective e.g. pain scores, quality of life scores
- Antibiotic usage related to time of symptoms onset

### PATIENTS WERE SEEN OR REVIEWED AT:

- Baseline; the time of recruitment (Day 1).
- Day 5; on average 4 days after Baseline
- Day 10; on average 9 days after Baseline
- A telephone follow up was also made at the Day 30 follow up which collected subjective data from the patient

### ANTIBIOTIC THERAPY

Of 410 patients with a record of their antibiotic therapy, 121 patients had some IV antibiotics recorded, the remainder only having PO antibiotics. The mean duration of either IV or PO antibiotics was 7.2 days.

31% patients on antibiotics for less than 24 hours prior to recruitment, had some IV therapy compared with 56% patients on antibiotics for 24 hours or more (OR 2.85, 95% CI: 1.66 to 4.88,  $p < 0.00$ ).

### IV THERAPY, DURATION AND OUTCOMES

Patients on oral therapy were as likely as those on IV therapy to have improved at Day 5 or to be back to their normal activities at Day 10:

84% patients on oral therapy alone achieved primary outcome compared with 78% patients who had some IV therapy (OR 0.46, 95% CI: 0.25 to 0.86,  $p = 0.020$ ).

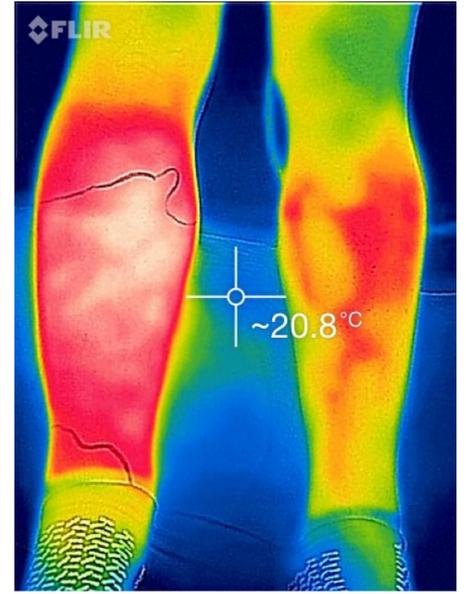
60% patients on oral therapy alone were back to normal activities at Day 10 compared with 48% patients who had some IV therapy (OR 0.56, 95% CI: 0.36 to 0.97,  $p = 0.052$ ).

There was no association between duration of therapy and outcome as measured at Day 10: 56% patients had antibiotics for > 5 days were back to normal activities at Day 10 compared with 53% patients who had antibiotics for 5 days or less (OR 1.13, 95% CI: 0.61 to 2.09,  $p = 0.824$ ).

### STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study uses a wide range of data from a controlled clinical trial
- The data is available over 10+ days
- There was no control group with other limb skin or soft tissue disorders

## THE WAY FORWARD

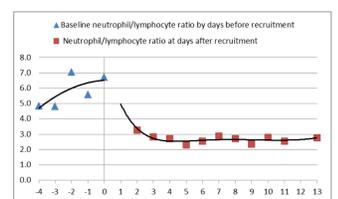
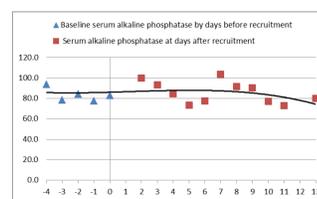
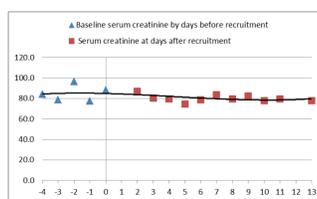
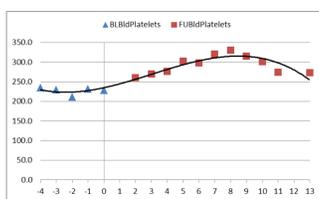
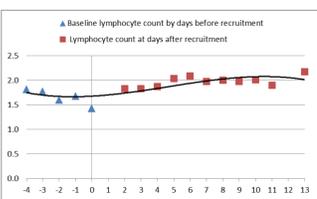
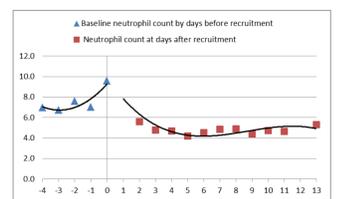
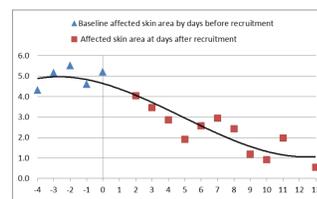
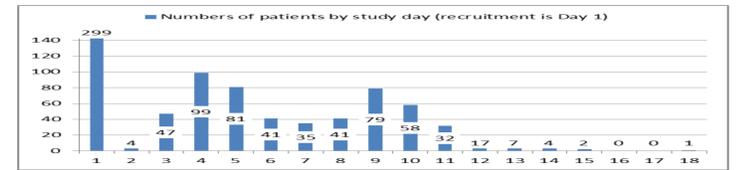
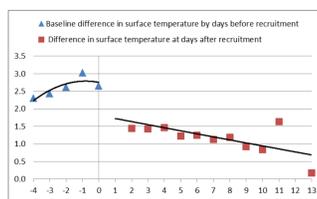
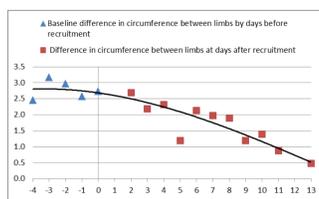
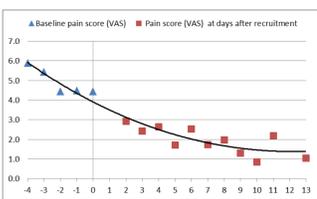


## Limb measurements, pain scores and blood results for the whole study population with any follow up values

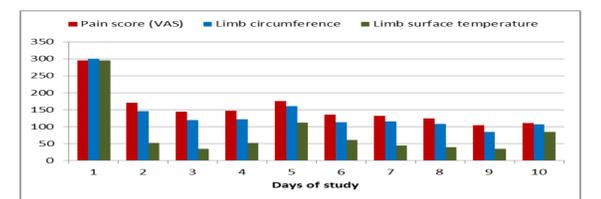
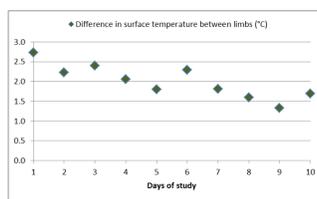
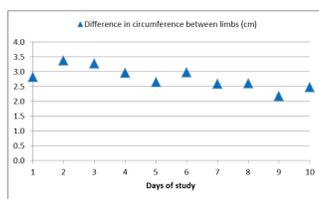
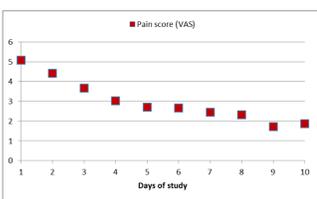
Blue triangles are values at recruitment (0 on these charts) broken down by day of onset of local features

e.g. -4 means the patients had local features of cellulitis 4 days before being recruited.

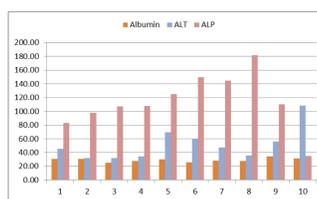
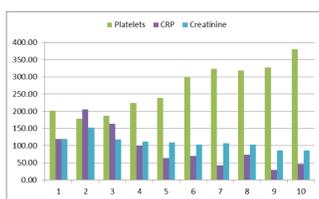
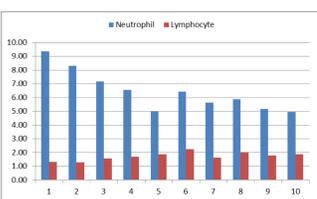
Red squares are values at each day of follow up (integer of days post first dose of study drug).



## Pain (visual analog scale), swelling (difference in circumference) and redness (difference in skin surface temperature) scores from patient logs – filled in by the patient (or study nurse if an inpatient or attending a visit). By follow up study day (Day 1 is first day of study on these charts).



## Blood results from a subgroup of 33 patients (mostly inpatients) followed over 10 days with approximately alternate day sampling day (Day 1 is first day of study on these charts)



## Baseline characteristics of the whole population and the sub-group

	Number	Age (mean)	Male (%)	Temperature (°C) (mean)	% affected skin area (median)	Neutrophil (10 <sup>9</sup> /L) (median)	CRP protein (mg/L) (median)
Whole study	336	50.8	68	36.9	4	6.8	37
Sub-population	33	60.5	64	37.3	8	7.0	105

