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<tr><td>Study/Reference</td><td colspan="2">Chen AE, Carroll KC, Diener-West M, Ross T, et. al. Randomized Controlled Trial of Cephalexin Versus Clindamycin for Uncomplicated Pediatric Skin Infections. Pediatrics. 2011: 127(3); e573-80.</td></tr>
<tr><td>Purpose</td><td colspan="2">Authors investigate the clinical outcomes of children with uncomplicated purulent staph-soft-tissue infections (SSTI) who were randomly assigned to receive treatment with cephalexin (a traditional antistaphylococcal antibiotic without activity against MRSA) or clindamycin (an antibiotic with high clinical activity against CA-MRSA).</td></tr>
<tr><td rowspan="3">Study Design/ Methodology</td><td colspan="2">This study was a single-center, randomized, double blind, controlled trial funded by a research grant from National Institute of Health and an award supported by Thrasher Research Foundation.</td></tr>
<tr><td>Primary Outcome(s):</td><td>Secondary Outcome(s):</td></tr>
<tr><td>The primary outcome was clinical improvement at 48 to 72 hours after initiation of treatment, <u>defined as</u> improvement in at least 1 of the measured parameters:
• Overall improvement (according to subject or parent/ guardian)
• Fever
• Erythema
• Pain
• Tenderness
• Drainage
**Without worsening of any said parameters.</td><td>The secondary outcome was resolution of disease at 7 days, <u>defined as</u> overall improvement according to subject or parent in addition to resolution of all symptoms.</td></tr>
<tr><td rowspan="2">Population</td><td>Inclusion criteria:</td><td>Exclusion Criteria:</td></tr>
<tr><td>o Patients ages 6month-18yrs
o Presented to outpatient center and outpatient management was anticipated
o Purulent SSTI
▪ Abscess (w/ or w/o surrounding cellulitis)
▪ Furuncle
▪ Carbuncle</td><td>• Anyone hospitalized upon the initial visit or those who had been previously hospitalized in the last 14 days
• Hypersensitivity to either study drug or chemically related compound
• Those having an immunocompromised states (such as HIV infection, uncontrolled diabetes mellitus, congenital immunodeficiency);
• Those having a skin infection that could be related to surgical wounds or hardware
• Current use of antibiotic therapy</td></tr>
<tr><td>Size</td><td colspan="2">Enrollment occurred between September 2006 and May 2009 at the John Hopkins ED or Harriet Lane Clinic.
It was estimated a sample size of 178 (88 per group) needed to detect a 15% difference between improvement in the clindamycin and cephalexin groups with a power of 80% and a 2-sided significance level of 5%.
<u>Authors increased the planned sample size by ~10% to 100 per group to account for subjects lost to follow-up.</u></td></tr>
<tr><td>Treatment Groups</td><td colspan="2">Subjects were randomized to receive oral cephalexin 40 mg/kg per day in divided doses 3 times per day for 7 days or oral clindamycin 20 mg/kg per day in divided doses 3 times per day for 7 days.</td></tr>
<tr><td>Intervention</td><td colspan="2">Clinical data was collected during the initial encounter, and then during repeat visits or by telephone follow-up at 2 to 3 days, 1 week, and 3 months.
In addition to the 3-month follow-up, hospital medical records were reviewed to capture any visits for repeat infections.
Wound specimens were obtained for culture and susceptibility tests were performed on all samples.
The disk-diffusion induction test (D test) was employed to detect inducible clindamycin resistance in erythromycin resistant, clindamycin-susceptible staphylococcal isolates.
All S. aureus isolates were subjected to pulsed-field gel and evaluated for strain relatedness.
The first 20 isolates and all subsequent isolates not identical to USA300 strain were tested by PCR for the presence of the genes implicating the Panton-Valentine leukocidin toxin.</td></tr>
<tr><td>Statistics</td><td colspan="2">Chi square or Fisher’s exact test were used to compare proportions of outcomes or characteristics according to study drug assignment. Analysis was performed using an intent-to-treat basis.</td></tr>
<tr><td>Results</td><td colspan="2">General Results</td></tr>
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<tr><td>(Efficacy/ Safety)</td><td colspan="2">

Of 200 culture specimens, 69% grew MRSA, 19% grew MSSA, 8% grew other organisms, and 5% were sterile or unable to be collected.
93% of MRSA and 35% of MSSA isolates were identical USA 300 or related subtypes.
Panton-Valentine leukocidin was detected in 99% of the MRSA and 82% MSSA isolate.
3 MRSA isolates and 1 MSSA isolate harbored inducible clindamycin resistance (D-test positive).
Compliance with taking medications as directed was reported by subjects or parents/guardians for 84 of 96 subjects (88%) in the cephalexin arm and 81 of 95 (85%) in the clindamycin arm (p=0.66).
No serious adverse events were reported. 1 child developed mild diarrhea positive for c. difficile antigen and toxin 1 week after completing clindamycin treatment. Diarrhea resolved w/o treatment.

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<tr><td></td><td>Primary Outcome</td><td>Secondary Findings</td></tr>
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Three subjects in each study arm were lost to follow-up for this primary outcome variable.
91 of 97 (94%) cephalexin subjects and 94 of 97 (97%) clindamycin subjects showed improvement or resolution in their infection (p= .50).
Infection had worsened in 6 (all MRSA) treated with cephalexin and 3 (2 MRSA and 1 MSSA) treated with clindamycin.
7 subjects received an antibiotic that was not active against its offending organism.
2 subjects received an antibiotic with activity against the organism
Subjects aged less than 1 year and those who had fever were found to have a significantly lower rate of improvement at 48-72hrs.

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4 subjects in the cephalexin arm and 5 subjects in the clindamycin arm were lost to follow-up.
93 of 96 subjects (97%) cephalexin and 89 of 95 clindamycin subjects (94%) had clinical resolution by 7 days (p=0.33).
Only 1 subject developed a new SSTI while on therapy; this subject was infected with MRSA susceptible to clindamycin and was assigned to clindamycin treatment.
Of the MRSA infections, 100% (63 of 63) treated with cephalexin and 94% (66 of 70) treated with clindamycin had clinical resolution of disease by 7 days (p=0.12).
95% (104 of 109) of subjects who received an active antibiotic and 99% (70 of 71) who received an inactive antibiotic had clinical resolution of disease by 7 days (p=0.41). Only baseline fever was associated with a significantly lower rate of resolution at 7 days.
Four subjects were hospitalized, all within the first week after enrollment (2 were unrelated to SSTI and 2, one in each treatment group, due to worsening of initial infection (p=0.73))

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<tr><td>Conclusions</td><td>Author Conclusions</td><td>Overall Conclusions</td></tr>
<tr><td></td><td>There is no significant difference between cephalexin and clindamycin for treatment of uncomplicated pediatric STIs caused predominately by CA-MRSA. Close follow-up and thorough would care of uncomplicated SSTIs are like.ly more important than initial antibiotic choice.</td><td>Resolution of SSTI was very high whether the patient was treated with cephalexin or clindamycin and despite whether the antibiotic had in vitro activity against the offending organism. The cornerstone of uncomplicated SSTI is appropriate incision and drainage. This study helps support previous findings that antimicrobial use in uncomplicated SSTIs may not be as beneficial as once thought. Further, RCTs comparing clindamycin (or other antimicrobials active in vitro against CA-MRSA) vs. placebo are needed to truly conclude that antibiotic therapy may not have a place in the treatment of uncomplicated SSTI.</td></tr>
<tr><td>Comments</td><td>Strengths</td><td>Weaknesses</td></tr>
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Sufficient background evidence to support study purpose
Randomized controlled trial
Appropriate statistical analysis performed
Study maintained adequate power and compensated for anticipated subjects lost to follow-up to maintain an appropriate sample size.
The findings of this study are also supported in other medical literature.

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Determination of improvement in infections was not clearly defined and was subject to interpretation.
Unblinding was not assessed and the potential for unblinding was high with the study preparations used.
Majority of core outcome measurements were subjective
Much data was obtained from self-report or parent interpretation of clinical improvement.
Not all infections were attributed to MRSA and not all MRSA cultures were susceptible to clindamycin, which limits the studies ability to truly randomly compare use of antibiotics with in vitro activity to those without.

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