

# Management of impetigo and cellulitis

## Simple considerations for promoting appropriate antibiotic use in skin infections

Lynette Kosar MSc Tessa Laubscher MBChB CCFP FCFP

For years health care providers have been encouraged to judiciously use antibiotics in their practices. It is an important message, and programs have been developed to focus solely on promoting appropriate antibiotic use. While these initiatives are valuable, simple steps without a formalized program can have a positive effect on rational antimicrobial use. This article will review the evidence on antibiotics for the treatment of impetigo and cellulitis, and answer questions about the role of topical antibiotics, if antibiotics are required after incision and drainage of an abscess, and when empiric coverage for community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is recommended.

### Case 1

Charles is a 6-year-old boy seen in the clinic with “infected” mosquito bites on his face and limbs. He has no fever and feels well. He has no medical history of note and no known allergies. On examination he looks well; there are numerous excoriated papules on all his limbs and 5 discreet small patches of erythematous skin covered with yellow crusting on his chin and arms that he reports are itchy.

### Bringing evidence to practice

Impetigo, the most common skin infection in young children, can occur when there is a disruption in the skin due to minor trauma (eg, insect bites, scratches).<sup>1</sup> Yellow- or honey-crust lesions are a classic sign of nonbullous impetigo, which accounts for 70% of impetigo cases.<sup>1,2</sup> Nonbullous impetigo is most often caused by group A streptococcus, but might also be caused by *S aureus* or a combination of both.<sup>2</sup>

**Can topical antibiotics be used to treat impetigo?** Clinical practice guidelines recommend a topical antibiotic for 5 to 7 days when treating uncomplicated impetigo infections with limited and localized lesions.<sup>2-4</sup> A 2012 Cochrane review, which included 68 randomized controlled trials

(RCTs) and 5578 patients, compared various treatment options for impetigo.<sup>5</sup> The authors concluded that topical antibiotics (eg, mupirocin, fusidic acid) were as effective as oral antibiotics (eg, cephalosporins, macrolides), based on 22 RCTs involving 884 patients.<sup>5</sup> Topical mupirocin was slightly superior to oral erythromycin (relative risk of 1.07, 95% CI 1.01 to 1.13) in 10 of these studies, with 581 patients.<sup>5</sup> It was noted that studies were lacking in individuals with more extensive impetigo.<sup>5</sup> There was also no evidence to support the combined use of a topical and an oral antibiotic for impetigo.<sup>5</sup> One small RCT with 49 patients compared a topical antibiotic with a topical antibiotic plus an oral antibiotic and failed to show a benefit with dual therapy.<sup>5</sup> Regarding which topical antibiotic to use, mupirocin and fusidic acid had similar efficacy based on 4 RCTs with 440 patients.<sup>5</sup>

In addition to being as effective as oral antibiotics, topical antibiotics have less systemic absorption and therefore less risk of adverse events.<sup>1</sup> Topical therapy also reduces the risk of antimicrobial resistance compared with oral therapy<sup>1</sup>; however, resistance still occurs with overuse, and topical antibiotics should be reserved for skin infections, like impetigo, and not for noninfectious scratches or rashes.

### Back to Charles

You prescribe a topical antibiotic for Charles because his impetigo lesions are limited and localized to the face and arms. You select 2% mupirocin ointment to be applied sparingly to the lesions 3 times daily for 5 days, as you are not aware of any local resistance to this antibiotic. You explain to his mother that the crusts do not need to be removed before applying the antibiotic<sup>4</sup>; however, you advise her that removing the crusts by soaking in warm water or using warm compresses might relieve skin itch. You encourage Charles to avoid scratching the lesions to minimize spreading the infection and to wash his hands frequently. You also instruct his mother to cover the lesions with bandages if he continues to scratch.

Two weeks later Charles returns to the clinic. The impetigo lesions initially resolved, but he is still scratching mosquito bites and his mother noticed new infected areas of skin yesterday. He now has several new patches of impetigo on his arms and legs with a 4×6-cm area of cellulitis on the dorsum of his left forearm. He is afebrile and looks well. His current weight is 25 kg.



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## Bringing evidence to practice

Most of the limited evidence on impetigo focuses on uncomplicated infections.<sup>2</sup> Based on clinical experience, clinical practice guidelines suggest oral antibiotics for the following<sup>2-4</sup>:

- lesions that are unresponsive to topical antibiotics (ie, no improvement after 24 to 48 hours);
- recurrent or widespread (ie, numerous or large) lesions;
- infections that occur during an outbreak;
- patients with constitutional symptoms suggesting bacteremia or a fever;
- patients with lymphadenopathy, with valvular heart disease, or who are immunocompromised; and
- patients who are younger than 1 month old.

## Back to Charles

Topical antibiotic therapy was appropriate when Charles first presented. However, with spreading of the infection, more extensive lesions, and cellulitis, an oral antibiotic is now preferred. You prescribe 325 mg of cephalexin 4 times daily (50 mg/kg daily), which will empirically cover group A streptococcus, the most common pathogen in impetigo and nonpurulent cellulitis.

As noted above, Charles does not have any medication allergies. However, if his mother reported a nonsevere penicillin allergy (eg, delayed rash during or after use of amoxicillin), cephalexin would still be an appropriate option. If the penicillin reaction was severe (eg, anaphylaxis), erythromycin or clindamycin could be used. Clinical response to erythromycin or clindamycin should be monitored owing to potential resistance concerns.<sup>3,4</sup> The RxFiles document on  $\beta$ -lactam allergies is available from **CFPlus**.\*

## Case 2

Mark is a 28-year-old man who presents with pain and swelling of his left lower leg. This evolved after scraping his leg while moving equipment at the local gym a few days ago. Mark is generally healthy; he takes no medications and has no allergies. He is mildly febrile with a temperature of 37.8°C; his pulse is 90 beats/min and his blood pressure is 122/68 mm Hg. On examination you note moderate swelling of his left lower leg and a small scabbed lesion on the lateral calf with surrounding skin erythema, warmth, and induration. Beneath the lesion is an area of fluctuation suggestive of an abscess about 3 cm in diameter.

\*The RxFiles document on  $\beta$ -lactam allergies, the trial summary, and the newsletter on antibiotics for skin infections are available at [www.cfp.ca](http://www.cfp.ca). Go to the full text of this article online and click on the **CFPlus** tab.

## Bringing evidence to practice

Whereas group A streptococcus is the predominant causative bacteria in nonpurulent skin infections, purulent skin infections (eg, cutaneous abscess, purulent cellulitis) are often caused by *S aureus*.<sup>2</sup> Categorizing skin infections as purulent versus nonpurulent helps tailor antibiotic therapy to the most likely organisms.<sup>2</sup> Consideration of empiric coverage for CA-MRSA is primarily limited to purulent skin infections<sup>2</sup> (**Table 1**).<sup>6,7</sup>

### Are antibiotics needed after incision and drainage of an abscess?

Incision and drainage is recommended for all abscesses,<sup>2-4</sup> as antibiotics penetrate pus poorly. Studies have shown that at least 75% of uncomplicated abscesses resolve after incision and drainage without antibiotics.<sup>8,9</sup> A 2014 meta-analysis of 4 RCTs involving 589 patients found no difference in clinical cure rates when incision and drainage plus antibiotics was compared with incision and drainage alone (88.1% vs 86%, odds ratio of 1.17, 95% CI 0.7 to 1.95).<sup>9</sup> More recently, an RCT of 1265 patients who underwent incision and drainage for uncomplicated skin abscesses compared high-dose (2 double-strength tablets twice daily) trimethoprim-sulfamethoxazole (TMP-SMX) for 7 days with placebo.<sup>8</sup> The median abscess size was 2×2.5 cm, and approximately 45% of the *S aureus* isolates were methicillin-resistant *S aureus* (MRSA).<sup>8</sup> The investigators found a modest improvement in clinical cure rates with the antibiotic (80.5% vs 73.6%, 95% CI 2.1 to 11.7) at days 14 to 21, which resulted in a number needed to treat of 14.<sup>8</sup> The number needed to harm for antibiotic-related gastrointestinal adverse events was 15.<sup>8</sup> There was no difference in the rate of invasive infections.<sup>8</sup> The RxFiles trial summary of this study is available from **CFPlus**.\*

Clinical practice guidelines suggest using an oral antibiotic for abscesses that are “complicated”<sup>2-4</sup>—for example, abscesses<sup>2-4</sup>

- that are large (ie, greater than 5 cm) or not resolving;
- with extensive cellulitis or rapid progression;
- in areas where incision and drainage is difficult (eg, face, hands, genitalia);
- in patients with systemic symptoms; or
- in patients with substantial comorbidities, immunosuppression, or extremes of age.

Cephalexin<sup>3</sup> and cloxacillin<sup>3,4</sup> are considered first-line options for purulent skin infections caused by methicillin-susceptible *S aureus* (**Table 1**).<sup>6,7</sup> The Infectious Disease Society 2014 guideline on skin and soft tissue infections recommends 5 days of antibiotics, but notes therapy should be extended if the infection has not improved within this time period (strong recommendation, high level of evidence).<sup>2</sup> The recommendation is based on a small RCT of 121 patients with uncomplicated cellulitis that compared 5 versus 10 days of antibiotic therapy.<sup>10</sup> The rate of clinical success was the same for both treatment arms (98%) at 14 and 28 days after study enrolment.<sup>10</sup>

**Table 1.** Empiric antibiotic selection for nonpurulent and purulent cellulitis

ANTIBIOTIC	USUAL ADULT DOSE	PEDIATRIC DOSE
<b>Nonpurulent cellulitis</b>		
Empiric therapy for group A streptococcus		
• Cephalexin	500 mg orally, 4 times daily	50-100 mg/kg orally, divided 4 times daily
Empiric therapy for group A streptococcus and MRSA		
• Cephalexin and 1 of the following: -TMP-SMX* or -doxycycline <sup>†</sup>	500 mg orally, 4 times daily, and 1 of the following: • 1 to 2 DS TMP-SMX tablets orally, twice daily, <sup>‡</sup> or • 100 mg of doxycycline orally, twice daily	50-100 mg/kg orally, divided 4 times daily, and 1 of the following: • 8 to 12 mg/kg of TMP-SMX orally, divided twice daily, or • 4 mg/kg of doxycycline orally, divided twice daily
<b>Purulent cellulitis</b>		
Empiric therapy for MSSA		
• Cephalexin	500 mg orally, 4 times daily	50-100 mg/kg orally, divided 4 times daily
• Cloxacillin	500 mg orally, 4 times daily	50 mg/kg orally, divided 4 times daily
Empiric therapy for community-associated MRSA		
• TMP-SMX*	1 to 2 DS tablets orally, twice daily <sup>‡</sup>	8-12 mg/kg orally, divided twice daily
• Doxycycline <sup>†</sup>	100 mg orally, twice daily	4 mg/kg orally, divided twice daily

DS—double strength, MRSA—methicillin-resistant *Staphylococcus aureus*, MSSA—methicillin-sensitive *Staphylococcus aureus*, TMP-SMX—trimethoprim-sulfamethoxazole.

\*Do not use TMP-SMX in infants younger than 1 mo old.

<sup>†</sup>Avoid using doxycycline in children younger than 9 y of age.

<sup>‡</sup>Consider using 2 DS TMP-SMX tablets twice daily in individuals with body mass index of 40 kg/m<sup>2</sup> or greater.<sup>6,7</sup>

## Back to Mark

In view of Mark's fever, clinical signs and symptoms of purulent cellulitis, and absence of CA-MRSA risk factors (**Box 1**), you prescribe 500 mg of cephalexin 4 times daily for 5 days. In addition, you perform incision and drainage of the abscess. You instruct him to return if he does not see improvement within a

few days, if he has ongoing fever, or if he notes rapid progression with reaccumulation of pus or worsening redness or pain in his calf. You also provide him with a medical certificate to stay home from work and emphasize the importance of elevating his left lower leg to optimize wound healing.

### Box 1. Risk factors for community-associated MRSA

Factors that increase the risk of community-associated MRSA include the following:

- history of MRSA colonization or recent MRSA infection
- previous hospitalization for a skin and soft tissue infection
- age younger than 2 y or older than 65 y
- antibiotic use in the past 6 mo
- recent invasive procedures (eg, dialysis)
- intravenous drug use
- penetrating trauma
- being an athlete, particularly one who plays contact sports
- men who have sex with men
- living in a correctional facility
- being military personnel
- homeless persons
- residing in an endemic area for community-associated MRSA

MRSA—methicillin-resistant *Staphylococcus aureus*.

## Bringing evidence to practice

**When is empiric coverage for CA-MRSA recommended?** In 2015, approximately 20% of *S aureus* isolates in Canada were MRSA, and fewer than half of these were community-associated strains.<sup>11</sup> However, there are regional differences across the country, and health care providers are encouraged to be familiar with their local resistance patterns.<sup>11,12</sup> Based on the latest Canadian Antimicrobial Resistance Surveillance System report, three-quarters of the MRSA isolates were nonblood isolates and approximately half of these were from skin and soft tissue infections.<sup>12</sup> Skin infections often respond to antibiotics that do not cover MRSA, even if the patient has risk factors for CA-MRSA (**Box 1**).<sup>4</sup> Thus, empiric therapy with a  $\beta$ -lactam is reasonable; however, coverage for CA-MRSA should be considered if the patient does not respond to the  $\beta$ -lactam or develops systemic symptoms (eg, fever), or if you have high suspicion of CA-MRSA.


If MRSA coverage is required for skin infections, the preferred antibiotics are TMP-SMX and doxycycline.<sup>3,4</sup>

Depending on local antibiogram data, clindamycin is often considered a third-line agent owing to concerns with group A streptococcus and MRSA resistance to clindamycin from overuse,<sup>3,4,7\*</sup> and owing to potential inducible resistance in MRSA from macrolide use.<sup>2</sup> According to the 2015 Canadian Antimicrobial Resistance Alliance, 12% of CA-MRSA isolates were resistant to clindamycin, while 100% of isolates were sensitive to TMP-SMX and doxycycline.<sup>11</sup> Clindamycin has also been associated with a 4-fold increased risk (relative risk of 3.92, 95% CI 1.15 to 136.43) of community-acquired *Clostridium difficile* diarrhea.<sup>13</sup> In a small RCT of 524 patients with uncomplicated skin infections (which included purulent cellulitis and abscesses), there was no statistically significant difference in clinical cure rates between TMP-SMX and clindamycin, which was assessed 7 to 10 days after the end of treatment.<sup>14</sup> Approximately one-third (32%, n=167) had a positive culture for MRSA, of which 4% were resistant to clindamycin (3.5% in the TMP-SMX group and 4.5% in the clindamycin group).<sup>14</sup> All abscesses underwent incision and drainage.<sup>14</sup>

**How would the approach to empiric treatment change if Mark were a member of a competitive wrestling team and resided in a community known to have high rates of CA-MRSA?** Initial treatment with incision and drainage of his abscess and antibiotic therapy would remain unchanged; however, it would be beneficial to send a wound swab to assess for MRSA.<sup>4</sup> It would be appropriate to select an antibiotic with activity against CA-MRSA, such as TMP-SMX or doxycycline.<sup>3,4</sup> Clindamycin should be reserved for individuals with allergies to these agents. If there were concern about a mixed group A streptococcus and *S aureus* infection, treatment could be initiated with cephalexin plus TMP-SMX or doxycycline.

## Conclusion

Integrating simple considerations for the management of skin infections into practice can facilitate judicious antibiotic use. Topical antibiotics are recommended for limited and localized uncomplicated impetigo. If the lesions are itchy, educating the patient and caregiver on measures to reduce scratching might help reduce the spread of impetigo. For cellulitis, stratification of treatment based upon the presence or absence of purulence, and subsequently the most likely pathogen, will assist with antibiotic selection. Empiric coverage for both group A streptococcus and *S aureus* is not required. Limit antibiotics with CA-MRSA coverage to patients with risk factors for CA-MRSA and, if required,

consider TMP-SMX or doxycycline over clindamycin owing to resistance and safety concerns. All abscesses should be incised and drained, and uncomplicated abscesses might not require antibiotics. 

**Ms Kosar** is Information Specialist for the RxFiles Academic Detailing Program for the Saskatoon Health Region in Saskatchewan and Assistant Clinical Professor in the College of Pharmacy at the University of Saskatchewan in Saskatoon. **Dr Laubscher** is Clinical Associate Professor of Academic Family Medicine at the University of Saskatchewan.

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### Correspondence

**Ms Lynette Kosar**; e-mail [lynette@rxfiles.ca](mailto:lynette@rxfiles.ca)

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