An algorithm for the management of acute bacterial cellulitis

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Acute bacterial cellulitis is a common infection seen by family physicians; it is usually caused by beta-hemolytic streptococci and/or *Staphylococcus aureus*. Cellulitis following bite wound injuries from animals and humans requires antibiotics directed at the mouth microflora characteristic of the biting animal. Depending on the severity and the rapidity of the progression of the infection, as well as patient compliance with oral therapy, intravenous antibiotics may be required for treatment, and this may often be accomplished with an outpatient administration program. In addition to intravenous and subsequent oral step-down antibiotic therapy, special attention needs to be applied to reducing or eliminating predisposing factors such as pre-existent edema and local fungi, or other forms of dermatitis. With effective antibiotic therapy, the erythema generated by acute cellulitis may resolve quickly or slowly, but usually does so progressively. Patients with persistent skin inflammation and swelling must be examined carefully for subcutaneous abscess formation.

Key Words: *Antibiotic therapy; Care pathway; Cellulitis algorithm*

Algorithme pour le traitement de la cellulite bactérienne aiguë

RÉSUMÉ : La cellulite bactérienne aiguë est une infection que voient couramment les médecins de famille. Elle est habituellement causée par des streptocoques bêta-hémolytiques et (ou) par le staphylocoque doré. La cellulite consécutive à la morsure d'un animal ou d'un être humain requiert des antibiotiques qui agiront contre la microflore buccale caractéristique de l'agresseur. Selon la gravité et la rapidité de la progression de l'infection, ou selon la fidélité du patient à son traitement oral, des antibiotiques intraveineux peuvent se révéler nécessaires et il est possible de les administrer par l'entremise d'un programme ambulatoire. En plus de l'antibiothérapie séquentielle, d'intraveineuse à orale, on accordera une attention spéciale à la réduction et à l'élimination des facteurs prédisposants, par exemple un œdème pré-existant, une mycose locale ou d'autres formes de dermatite au moyen de l'antibiothérapie. L'érythème causé par la cellulite aiguë peut se résorber rapidement ou lentement, mais la résorption est en général progressive. Il faut surveiller la formation possible d'un abcès sous-cutané chez les patients dont l'inflammation et l'œdème cutanés persistent.

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Cellulitis is technically any inflammation of soft tissue but by convention usually refers to a bacterial infection of skin and superficial connective tissue (1). There are two types: those referred to as idiopathic, in which no portal of entry can be identified on careful physical examination, and those that develop from a recognizable break or lesion in the skin. The microorganisms generally responsible for cellulitis are beta-hemolytic streptococci, usually group A, and *Staphylococcus aureus*, although other bacteria can cause cellulitis – for example, *Haemophilus influenzae* (in children) or marine vibrios. By far, the majority of infections will be staphylococcal or streptococcal. Initial empirical therapy of cellulitis should be targeted at beta-hemolytic streptococci and *S aureus* unless otherwise directed by specific exposure or trauma history, or results of Gram-stained lesion material (which is usually nonexistent). If there is an open lesion, staphylococci are fairly common in conjunction with streptococci, whereas in marginated spreading cellulitis without an open lesion, which is similar to the classic syndrome described as erysipelas, the infection is usually streptococcal. A prominent predisposing condition for cellulitis, especially secondary to streptococci, is leg or arm edema. This is particularly true for lymphedema as might occur in patients who have undergone an axillary lymph node resection for breast cancer or in patients who have had saphenous vein removal for use in coronary bypass grafting (2). Patients with these factors may have recurrent cellulitis. Another often unappreciated predisposing factor is dermatophyte fungal in-

fection, which can cause skin fissures and alterations in local bacterial flora (3,4). Control of these cofactors may be as important as the antimicrobial treatment of the acute infection itself in the overall management of cellulitis.

The clinical presentation of patients with cellulitis may vary. There may be marked toxicity with fever, rigors and even delirium, or there may be only localized erythema and some mild tenderness. Severe excruciating pain and tenderness in the area of the cellulitis must raise the question of necrotizing fasciitis or myofasciitis, which require emergency surgical consultation. The presence of a generalized erythematous rash should raise suspicions of streptococcal or staphylococcal toxic shock syndrome. Both of the latter conditions are beyond the scope of this discussion. Obviously, the physician's assessment of the severity of the patient's illness will be the primary determining factor about admission to hospital. If hospitalization is not considered necessary and oral therapy is not feasible or appropriate for the degree of illness, then outpatient intravenous antibiotic therapy may be required. In one retrospective review, cellulitis in inpatients was managed effectively but inefficiently (5). Home intravenous antibiotic therapy for cellulitis has been proven to be as effective as and less costly than inpatient management for eligible patients (6).

Different methodologies have been adopted to deliver parenteral antibiotic therapy for cellulitis – home-based treatment (6,7) and emergency room treatment (8) – both with effective results. Drug choices for extending the plasma half-life

Figure 1) Algorithm for the management of cellulitis by an outpatient intravenous antibiotic therapy. IV Intravenous

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TABLE 1

Suggested antibiotic therapies for cellulitis according to exposure history

Exposure history	Organism(s)	Intravenous antibiotic therapies	Therapies for patients with an accelerated penicillin allergy*	Initial oral therapy or oral step-down therapy
None ('idiopathic')	Beta-hemolytic streptococci; <i>Staphylococcus aureus</i>	Cefazolin 2 g daily plus 1 g probenecid by mouth or Cloxacillin 2 g every 5 h between 07:00 and 22:00 or Clindamycin 600 mg every 8 h	Clindamycin 600 mg every 8 h or Vancomycin 1 g every 12 h	Cephalexin 500 mg qid or Cloxacillin 500 mg qid or Clindamycin 600 mg tid
Cat bite [†]	<i>Pasteurella multocida</i> ; <i>S aureus</i> [‡]	Cefuroxime 500 mg every 8 h	Ciprofloxacin [§] 400 mg every 12 h or Levofloxacin 500 mg daily	Amoxicillin/clavulanate 500/125 mg tid or Cefuroxime axetil 500 mg bid or Doxycycline 100 mg bid or Ciprofloxacin 100 mg bid
Dog bite [†]	<i>S aureus</i> ; <i>P multocida</i> ; Gram-negative rods Anaerobes <i>Eikenella corrodens</i> [‡]		Ciprofloxacin 400 mg every 12 h plus clindamycin 600 mg every 8 h	Amoxicillin/clavulanate 500/125 mg tid or Doxycycline 100 mg bid plus clindamycin 600 mg tid or Trimethoprim/sulfamethoxazole double strength tablet bid plus clindamycin 600 mg tid
Human bite	Oral streptococci anaerobes; <i>E corrodens</i> [‡]	Cefoxitin 1 g every 8 h or Ceftizoxime 1 g every 12 h or Piperacillin/tazobactam 4.5 g every 8 h	Clindamycin 600 mg every 8 h plus ciprofloxacin 400 mg every 12 h	Amoxicillin/clavulanate 500/125 mg tid or Doxycycline 100 mg bid plus metronidazole 500 mg bid or Clindamycin 600 mg tid daily

*Indicates anaphylactoid immunoglobulin E-mediated reaction; late onset rash (later than 48 h after penicillin has been started) usually indicates immunoglobulin G-mediated allergy. In the latter reaction, cephalosporin may be given but may result in a delayed rash in 10% to 15% of patients treated; [†]Oral therapy is the preferred route if clinically appropriate; [‡]All isolates clindamycin-resistant; [§]In vitro susceptible. Minimum inhibitory concentrations against *P multocida* less than 0.03 for ciprofloxacin and 0.06 for ofloxacin (11); no controlled clinical data

of therapeutic agents have been logistically beneficial in outpatient parenteral therapy, but with the increasing use of portable computerized infusion pumps such as the CADD Ambulatory Infusion Pumps (SIMS Deltec Inc, USA), even antibiotics with short serum half-lives, such as penicillins, can be administered very conveniently for the patient.

Before initiating antimicrobial therapy, several questions have to be addressed:

- Does the patient require admission to hospital?
- Does the patient require intravenous antibiotics, or will oral antibiotics likely be effective? This decision is most often made on the grounds of the severity and the rapidity of progression of the cellulitis, the expected compliance of the patient, and the willingness and ability of the patient to buy the prescription.
- Is the patient allergic to penicillin? If so, is the history of the reaction consistent with an accelerated immunoglobulin E reaction (early onset, hives, tongue or facial swelling, or anaphylaxis) or an IgG-mediated reaction (delayed onset after several days, maculopapular rash)?
- Has the patient (if febrile) had a blood culture, a swab for Gram stain and culture, and susceptibility testing of any open lesion associated with the cellulitis?

Once this checklist has been completed, antibiotic therapy can be started. Figure 1 gives an algorithm for the empirical management of community-acquired cellulitis in adults. Table 1 lists recommended intravenous agents together with oral step-down agents (which could also be used as initial oral therapy if parenteral therapy is not required) for several types of community-acquired cellulitides.

Both cephalosporin regimens of cefazolin 2 g daily with

oral probenecid 1 g and ceftriaxone 1 g daily have been popular in outpatient parenteral antibiotic therapy of acute cellulitis. Both agents cover *S aureus* and aerobic streptococci adequately. Ceftriaxone, which is more costly, may be preferable in circumstances where parenteral therapy is required and Gram-negative rods may be implicated as a cause of the cellulitis. This may occur with cellulitis of the foot in a patient with diabetes, in which case an agent effective against anaerobes (eg, oral or parenteral metronidazole or clindamycin) would likely be added, for cellulitis in immunosuppressed patients or in the case of specific cellulitides such as those occurring after injury associated with freshwater or seawater exposure, where unusual organisms such as *Aeromonas hydrophila* (9) or *Vibrio vulnificus* (10), respectively, may be suspected. Oral therapy for the latter organisms can consist of trimethoprim/sulphamethoxazole or a fluoroquinolone such as ciprofloxacin (9).

An algorithm for following the clinical course of a patient with acute cellulitis is outlined in Figure 2. The clinical course of treated cellulitis varies. Erythema and fever may resolve within a short time after the institution of effective antibiotic treatment, but not uncommonly, there is such an intense inflammatory response that the temperature may not normalize for 72 h, especially with streptococcal cellulitis. Early signs of response are improvement in general well-being and resolution of the signs of lymphangitis. Sometimes, dusky erythema may take many days, even weeks, to resolve after an adequate 10- to 14-day course of antibiotics. These patients should be carefully examined for subcutaneous fluctuance that may indicate abscess formation. Generally, one observes progressive improvement, especially if edema is aggressively controlled.

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Figure 2) Algorithm for follow-up of treated acute bacterial cellulitis. *In an initially toxic, sick patient, the first sign of response is usually the return of general well-being despite local inflammation; †Erythema may take up to several weeks to disappear completely. As long as resolution is occurring, there is no need to treat longer than 10 to 14 days or to change antibiotics; ‡In addition to the wearing of compression stockings, long term management of chronic edema in patients who have more than one recurrence of cellulitis may be aided by Lymphopress (Global Medical Imports, Canada) treatments. The Lymphopress is a regulatable graded limb compression device that physically mobilizes edema into the vascular space. The frequency of these treatments will depend on how rapidly the edema returns

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