Use of Prophylactic Antibiotics in Patients with Lymphedema

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Cellulitis and erysipelas are infections and inflammation of the skin and subcutaneous soft tissues caused almost exclusively by -hemolytic streptococcus and to a lesser extent staphylococcus aureus. Although erysipelas and cellulitis vary slightly in their clinical features, most experts consider them different presentations of the same illness and both may be grouped under the general heading of cellulitis.

The clinical spectrum of cellulitis ranges from mild inflammation to rare cases of life-threatening illness. Most people with cellulitis are not seriously ill and have a low risk of severe complications. Cellulitis is believed to be extremely common and its frequency appears to be increasing, although there are few published studies on its incidence. In recent years there is concern over a corresponding increase in infections caused by antibiotic resistant strains, such as methicillin-resistant staph aureus (MRSA).

Research data on risk factors for development of cellulitis is scant, and most studies have focused on lower extremity infection. Some studies indicate that risk factors for cellulitis in the lower extremities include disruption of the skin barrier, for instance by ulceration, surgical wound, or athlete’s foot, as well as lymphedema, obesity and venous insufficiency. In fact, lymphatic abnormalities and/or lymphedema were found to be an especially important risk factor for development of acute and recurrent cellulitis. Studies have also reported a high incidence of cellulitis in lymphedematous upper extremities after treatment for breast cancer.

Persons with lymphedema frequently suffer more prolonged bouts of cellulitis and longer duration and severity of inflammatory symptoms than those without lymphedema, possibly due to impaired elimination of bacterial components that trigger local and systemic inflammatory responses. In addition, cellulitis may further damage already impaired lymphatics resulting in greater stagnation of lymph and reduced clearance of bacteria, thus initiating a vicious cycle of infection and lymphatic dysfunction.

As a result, many persons with lymphedema who have suffered an initial episode of cellulitis subsequently suffer recurrent episodes, sometimes with alarming frequency and severity. Some patients may require hospitalization several times a year for IV antibiotic therapy, while others are treated with repeated course of oral antibiotics at home.

Treatment of acute cellulitis is covered elsewhere in this issue, but prevention of recurrent cellulitis in those patients who continue to experience infection has become an important and somewhat controversial issue for patients and their healthcare providers. Prevention of recurrent cellulitis is a reasonable objective, especially given the risk of further damage to the lymphatic system from repeated bouts of infection, as well as the patient distress and healthcare costs associated with cellulitis. However, it is important to balance the risks and benefits of any intervention undertaken in medicine, and this article is intended to provoke thoughtful assessment of risks and benefits regarding use of antibiotic prophylaxis (AP) in lymphedema rather than provide definitive answers.

There is some evidence that Complete Decongestive Therapy (CDT) may reduce the frequency and severity of recurrent cellulitis in patients with lymphedema and this finding is supported by anecdotal evidence and expert opinion. However, further studies are needed to confirm this. Controversy arises over the use of chronic long-term AP for patients with lymphedema who suffer recurrent bouts of cellulitis. Unfortunately, little literature exists to guide us in making evidence-based decisions in this arena. On a positive note, a large multicenter trial on “Prophylactic Antibiotics in the Treatment of Cellulitis at Home” (PATCH I and II) is currently in progress.

Traditionally those who suffer at least three bouts of cellulitis in a year have been considered candidates for long-term prophylactic antibiotic therapy. The mainstay of prophylaxis of recurrent cellulitis in lymphedema has been long acting benzathine penicillin injections monthly, but chronic daily oral penicillin or penicillin derivatives and other antibiotics have probably been utilized more frequently in recent years. However, in practice no clinical consensus exists with regard to effectiveness, timing, dosage or duration of long-term prophylactic antibiotics in patients with lymphedema. At least one study showed no benefit of long-acting benzathine penicillin in preventing recurrent lower extremity cellulitis in persons with lymphedema. Another study proposed a self-medication strategy in which patients begin self-administration of oral antibiotics at the first sign of cellulitis. Very little published evidence comparing outcomes in patients with and without AP exists. At this point decisions are made by individual practitioners based on anecdotal experience, individual patient factors, and local practice norms.

Similar controversies and varying practices arise around the question of whether to prescribe prophylactic antibiotics prior to invasive dental procedures in patients with lymphedema.
lymphedema and/or a history of cellulitis. The practice is based on historical use of antibiotic prophylaxis for these procedures in persons with certain cardiac conditions or history of joint replacements to prevent infective endocarditis (IE) or late prosthetic joint infections, (LPJI) both of which may cause devastating and even life-threatening consequences.

The rationale for dental prophylaxis in these situations is the belief that bacteria from the mouth enters the bloodstream during many dental procedures and may cause serious joint or heart infections. Even here, scientific evidence for the practice is lacking, and studies have shown that similar levels of bacteria enter the bloodstream routinely after daily activities such as tooth brushing, flossing, chewing, and use of toothpicks and water-picks. Many feel that good oral hygiene and access to regular dental care are likely to be far more effective in reducing the risk of IE than AP for isolated procedures.

The American Heart Association in 2008 substantially reduced the number of conditions for which antibiotic prophylaxis is recommended and stated that “In patients with... highest risk of adverse outcome from IE... prophylaxis is reasonable, even though we acknowledge that its effectiveness is unknown.” The American Academy of Orthopedic Surgeons has reversed its position twice in the last 8 years on the question of dental prophylaxis for persons with artificial joints. Their latest information paper in July 2009 was, by their own admission “based on the opinions of the authors” and recommends “antibiotic prophylaxis for all total joint replacement patients prior to any invasive procedure that may cause bacteremia”, even though there is no credible evidence linking LPJI with dental procedures. Interestingly, in one survey 24% of infectious disease specialists who “usually” or “always” recommended antibiotic prophylaxis prior to dental procedures volunteered that they did so for medicolegal rather than scientific reasons.

In patients at risk for cellulitis associated with lymphedema, a far less catastrophic infection than endocarditis or prosthetic joint infection, to my knowledge there is even less (in fact no) published scientific rationale for prophylactic antibiotics prior to dental procedures.

With regard to both long-term AP and the use of AP for dental procedures, the possible but as yet unproven benefit of preventing infection in at-risk persons must be balanced against the very real risks associated with antibiotic use. In patients with prosthetic joints, for instance, risk analysis has demonstrated that the risk of death from anaphylaxis, especially with penicillins, far outweighs the risks of developing LPJI. Other adverse effects of antibiotics include C. difficele colitis, other gastrointestinal symptoms, skin reactions ranging from rashes to (rarely) life-threatening Stevens-Johnson syndrome, and many others. In addition, an increasing number of antibiotic-induced adverse medication interactions are being reported. Perhaps most important, there is grave concern about the emergence of resistant organisms caused by widespread and often inappropriate use of antibiotics. Lastly, in an era of escalating and unsustainable healthcare spending, the cost of antibiotic use without adequate scientific rationale cannot be ignored.

In summary, patients with lymphedema are at high risk of developing cellulitis, and many suffer recurrent episodes that may cause further lymphatic impairment, increased swelling, and a vicious cycle of repeated infections. Long-term prophylactic antibiotics are sometimes prescribed for patients with recurrent cellulitis. However, antibiotic prophylaxis is not without risk.

A reasonable initial approach to the patient at risk for cellulitis would be adequate CDT (repeated as necessary), careful self-management after CDT, meticulous skin and oral hygiene, prompt treatment of athlete’s foot and other skin breakdown, and rapid treatment of acute infections with appropriate and targeted antibiotics.

In the small number of patients who suffer severe and repeated infections in spite of all the above measures, a careful assessment of the risks and benefits of long-term antibiotic prophylaxis should be made by the patient and their healthcare provider. If AP is initiated, appropriate attempts should be made to eventually discontinue antibiotic prophylaxis if possible.

With regard to use of prophylactic antibiotics for dental procedures, it is this author’s opinion based on available evidence that this should not be routine, and