ASPIRES tidbits:

Skin and Soft Tissue Infections (SSTIs): Recognizing and Treating Infections

Cellulitis, a superficial infection of skin and skin structures, is frequently seen in clinical medicine and is a common reason to prescribe antibiotics. Here are a few things to consider in immunocompetent patients with presumed cellulitis:*

1. **Not all red legs (or arms) are due to cellulitis:**
   Venous stasis and arterial insufficiency, as well as a number of other conditions can mimic cellulitis. Some strategies that can be used to distinguish between non-infectious from infectious skin conditions include:

   Table 1. Clinical presentation of non-infectious skin syndromes versus infectious cellulitis

Favours non-infectious cause	Favours infectious cellulitis
Changes colour with positioning (e.g. blanches when limb is elevated)	Remains red in different positions
Symmetrical discolouration ("bilateral cellulitis")	Asymmetric discolouration
Does not blanch with pressure	Blanches with pressure
Cooler temperature (compared to other side or proximal areas of same limb)	Warm temperature (compared to other side and proximal areas of same limb)
Distal spreading	Streaking/spreading proximally (especially along lymphatic tracts)
Brown or other colouration	Red colour
Not usually associated with other systemic symptoms of infection	Associated with systemic signs/symptoms (e.g. fevers, chills, and malaise)

   On history, patients can often describe if there has been a significant change in symptoms in an area with a pre-existing chronic skin conditions. Pain alone is not diagnostic of infection since arterial insufficiency (and other conditions) may often result in significant pain.

2. **The cause of non-purulent (i.e. spreading) cellulitis is almost always due to streptococci (e.g. Group A *Streptococcus*); gram-negative organisms rarely cause cellulitis and should not be covered with empiric therapy:**
   Cellulitis that is characterized by superficial spreading, without areas of purulence or abscess, are generally caused by streptococci which are best treated with beta-lactam agents that have good gram-positive coverage (e.g. cephalexin and cefazolin). Alternative agents in patients with beta-lactam allergies include clindamycin and vancomycin.

3. **The cause of purulent cellulitis is almost always due to *Staphylococcus aureus*; gram-negative organisms rarely ever cause cellulitis and should not be covered with empiric therapy:**
   Purulent cellulitis is a skin structure infection that is associated with abscesses or collections. Abscesses without surrounding cellulitis require drainage only; antibiotics are only indicated for treatment if there is cellulitis around an abscess. The initial therapy of choice should include coverage for methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) in patients who are at risk of carriage. First generation cephalosporins (e.g. cephalexin and cefazolin) are first choice agents for MSSA, while oral agents

* Excludes complicated SSTIs (e.g. diabetic foot infections or chronic ulcers)

such as trimethoprim-sulfamethoxazole, doxycycline and clindamycin should be considered for MRSA. Patients with signs of SIRS (such as tachycardia, hypotension, etc.) should be started on IV MRSA therapy (i.e. vancomycin), rather than oral therapy and be stepped down once improving clinically.

4. **Very broad-spectrum agents should <u>not</u> be used for cellulitis:**
   Broad-spectrum agents with gram-negative activity (e.g piperacillin-tazobactam) do not add any benefit to skin and soft tissue infections, but put patients at risk for side effects including *Clostridium difficile* infection and disruption of the normal microbiome. Likewise, use of ceftriaxone is not preferred, because of its broader Gram-negative spectrum; treatment with earlier generation cephalosporins (e.g. cephalexin and cefazolin) is recommended. While some agents have official Health Canada labeling to treat skin and soft tissue infections, they should avoided as they have unnecessarily broad activity and do not add anything to standard therapies. Specifically, once daily dosed medications (e.g. ertapenem, daptomycin) should not be used for treatment of common skin infections based on convenience since they should be reserved for multi-drug resistant pathogens.

5. **Streptococcal infections often appear to worsen in the first 48 hours:**
   Initial therapy, especially with beta-lactam antibiotics which are rapidly bacteriocidal, results in bacterial death which causes an initial inflammatory response to the dying bacteria. Typically, cellulitis appears to get worse in the first few days of treatment in that it tends to spread past its initial area and may appear redder. This is not a sign of clinical failure, but rather one of success. Peeling and puckering of the skin may often occur. In contrast, signs of failure would include worsening of systemic symptoms and/or increasing pain.

6. **All ulcers will grow bacteria when cultured, but few are actually infected:**
   Many patients with skin lesions due to chronic conditions (e.g. venous stasis) develop ulcers due to mechanical pressure, resulting in skin break-down. These ulcers will inevitably be colonized by multiple bacterial species which can be easily cultured, but these represent colonization and not infectious agents. Ulcers should not be routinely cultured, and cultures from ulcers should not be assumed to represent the pathogen in a presumed infection. Signs of an infected ulcer are similar to those described in Table 1. If further expertise is required, Infectious Diseases (ID) or wound clinic consultation can be helpful.

7. **Failure of therapy requires further investigation and consultation:**
   There are several reasons for clinical failure, which include sequestered infection, inadequate dosing, antibiotic resistance, or an alternative diagnosis. If there is no sign of clinical improvement by 72 hours, consider all of the following actions:
   i. Consult ID or other appropriate medical service;
   ii. Increase spectrum of gram-positive coverage (e.g. cover for MRSA if not already targeted);
   iii. Culture blood or the leading edge of the lesion by saline injection/withdrawal or biopsy;
   iv. Image the area to look for underlying collections; and/or
   v. Perform skin biopsy for pathological examination to rule out an alternative diagnosis.

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