“I know it when I see it . . .,” as Justice Potter Stewart famously said of hard-core pornography. Would that this were the case with cellulitis. In principle, cellulitis is simply defined as an acute infection with inflammation of the skin involving the dermis and subcutaneous tissues. In practice, because of the overlapping signs and symptoms of skin infections, the terminology has become burdened with terms such as erysipelas, purulent cellulitis, nonpurulent cellulitis, nonsuppurative cellulitis, cellulitis with drainage, cellulitis with ulcer, cellulitis with abscess, abscess with surrounding cellulitis, and necrotizing cellulitis (to name a few), in an effort to parse differences in microbiology, severity, and prognosis that may impact therapy and management. At the semantic other extreme is International Classification of Diseases, Ninth Revision coding, which lumps cellulitis and abscess together, even though these 2 entities would appear to be easily differentiated clinically and microbiologically. Clearly, an abscess is a collection of pus often in association with pain, swelling, and inflammation. Whatever cellulitis is, it is not an abscess, as there is no collection of pus, which, if there were, the lesion would be an abscess and not cellulitis.

Presence of a collection of pus affords the clinician great comfort, diagnostically and therapeutically. It is abscess defining, and culturing it permits a precise microbiological diagnosis. By far the most common cause of skin abscesses (barring unusual exposures or injury such as brackish water or bites) is *Staphylococcus aureus*, and pus and abscess formation are its modus operandi. Treatment is quite straightforward: Drain the pus, all of it. If an antimicrobial is needed (a topic that is well beyond the scope of this editorial), a narrowly defined microbiology allows for specific, pathogen-directed antimicrobial therapy against both methicillin-susceptible and methicillin-resistant strains of *S. aureus*.

With respect to cellulitis, lack of clarity about the microbiology is a problem. If blood culture is the gold standard for microbiological diagnosis, then β-hemolytic streptococci cause the majority of cases of cellulitis (57%–75%) and *S. aureus* causes only 14% [1]. However, blood cultures are negative in ≥90% of cases [1–3]. In blood culture-negative cases, serological testing with anti-streptolysin O and anti-DNase-B indicates that β-hemolytic streptococci account for 70% of these infections [3]. If culture of the skin by various means, including punch biopsy, aspirate, or swab, is deemed the gold standard, then these proportions are essentially reversed. *Staphylococcus aureus* is isolated in 50%–82% of cases in which a culture is positive and β-hemolytic streptococci in only 9%–28% [4, 5]. If prevalent in the community, a substantial proportion of the *S. aureus* isolates are methicillin-resistant *S. aureus* (MRSA) [4, 6–8]. Pus, an ulcer, or other purulent drainage is invariably the material that has been cultured for cellulitis from which MRSA has been isolated [4, 6, 8]. As with blood cultures, cultures of skin specimens are usually negative and in the range of 72%–84% of all cellulitis cases [4, 5]. The study by Ells et al [9] of nasal colonization in patients with cellulitis and negative blood and skin cultures suggests that cellulitis is unlikely to be due to *S. aureus*. Staphylococcal colonization tracks very closely with concomitant infection and these investigators found that rates of colonization for cellulitis and uninfected controls were similar and neither was different from that expected for a general population [9]. Considering all of the available data, a skin infection with pus, either an abscess or purulent drainage, is strongly associated with isolation of by *S. aureus*, whereas infection without pus is not. In the latter instance, β-hemolytic streptococci are very likely the cause of the infection.
This analysis notwithstanding, an uncertain microbiology has fostered angst and insecurity, a sort of existential crisis, for the treating physician faced with deciding whether or not MRSA should be covered in the patient with cellulitis. Fortunately and at last, the study by Pallin et al published in this issue of Clinical Infectious Diseases provides some guidance based on an absence-of-pus approach and a logically inferred absence of S. aureus, MRSA in particular. This high-quality, randomized, double-blind, placebo-controlled clinical trial compared the effectiveness of cephalexin plus placebo to cephalexin plus trimethoprim-sulfamethoxazole in adults and children with uncomplicated cellulitis without abscess with the idea that, if occult MRSA were present, then patients treated with the cephalexin plus trimethoprim-sulfamethoxazole combination would do better. Operationally, the approach seemed to work, although not quite as expected because the outcomes were about the same, based on the results of this small but important study. Clinical cure rates were similar, 82% for cephalexin alone and 85% for cephalexin plus trimethoprim-sulfamethoxazole, and progression to abscess occurred in only 5% in each group. That cephalexin plus trimethoprim-sulfamethoxazole did not improve outcome is unlikely to be explained by a low prevalence of MRSA in Boston, where community MRSA is endemic and prevalent. These results indicate that it is not necessary to cover MRSA in otherwise generally healthy outpatients with uncomplicated cellulitis, and the data provide hard evidence in support of the Infectious Diseases Society of America treatment guidelines that a penicillinase-resistant semisynthetic penicillin or a first-generation cephalosporin should be used as first-line treatment of cellulitis [10].

Notably, there were a number of exclusions in this study, including hospitalization, diabetes, renal insufficiency (even mild), immunodeficiency broadly defined, and cellulitis associated with peripheral vascular diseases. Although purulence of the cellulitis was not an exclusion, 87% did not have it at all and, of those who did, a volume >1 mL by report or observation was cause for exclusion. Further clinical trials are needed to determine whether these results are generalizable to other outpatient populations. Confirmatory data from other studies also will be critical for increasing physicians’ confidence that they know cellulitis when they see it and that MRSA coverage is unnecessary in uncomplicated cases in outpatients.

Notes

Financial support. This work was supported by the National Institutes of Health, National Institute of Allergy and Infectious Diseases (contract number HHSN272200700031C) and the US Public Health Service (grant number AI100291). Potential conflicts of interest. Author certifies no potential conflicts of interest. The author has submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References