Wound infection criteria: What is the level of awareness among researchers and clinicians?

CONTRIBUTORS

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For approximately two millennia, the criteria of the Roman Celsus have been used to diagnose infection: redness, swelling, heat, and pain. These criteria have been employed for all infections, regardless of the tissues involved. Each criterion relates to the inflammatory response and, therefore, may be regarded as "limited" insofar as other, non-inflammatory signs and symptoms of infection are excluded.

The diagnosis of infection is one of the most challenging aspects of wound management. The implications of underdiagnosis include inappropriate treatment and increased morbidity and even mortality. Over- or mis-diagnosis can expose the patient to unnecessary treatments and, more broadly, compromise the efficacy of available antibiotic therapies. The emphasis must be to "get it right".

In 1994, Cutting and Harding published what many regard as a seminal article: *The diagnosis of wound infection*. In the two decades since its publication, various articles clarifying and validating the criteria contained therein – particularly in chronic wounds – have been published (Cutting, 1994; 1997; 1998; Gardner et al, 2001a; b; Cutting and White, 2004; 2005).

However, there are strong indications that the criteria of Celsus are still the most widely used. Can this be regarded as "best practice"? What is being taught to students and post-registration clinicians? Is enough being done to improve diagnosis and avoid misdiagnosis?

Richard White

Despite the fact that changes in practice usually take time to become "standard", is it not time that Cutting and Harding (1994) be regarded as *the* criteria for the diagnosis of wound infection?

KC: Fifteen to twenty years is the average lag time for changes or innovations to be accepted into practice, so the adoption of the 1994 criteria into standard practice is apposite. At the time of its publication, the 1994 criteria provided a clear breakthrough in our understanding of the clinical signs of infection and afforded the opportunity to take us to a level beyond that given to us by Celsus.

The Cutting and Harding (1994) criteria comprise "traditional" and "additional" sets of clinical criteria. The traditional signs align closely with the Celcian signs of redness, swelling, heat, and pain, which have proved to be reliable markers of inflammation for over 2000 years. These traditional signs are representative of an acute wound infection process. It is recognised there is a problematic vagueness encompassing definitions of acute or chronic wound status (Wolcott et al, 2010.). The additional set of criteria would appear to be more relevant to chronic wound infection in the absence of the classical (acute) Celcian signs. These additional signs are characterised by their subtleness. Their subtlety is the key to their value in wound infection diagnostics, but also represents a stumbling block to their acceptance in clinical practice. Whereas the Celsian signs are obvious, these subtle signs of infection require a deeper acuity on the part of the clinician. Therefore, education and training are required at both the theoretical and clinical level. I would not be surprised to find that, in due course, these subtle signs of infection are aligned with biofilm (sub-clinical) infection.

BAL: The criteria proposed by Cutting and Harding (1994) almost 20 years ago were based on their clinical experience and a review of the literature available to them at that time. Their criteria include several that were subtler than the classic findings of inflammation. Subsequent to the publication of their article, several studies have been conducted that purport to support the value of these "secondary" findings in defining infection of various types of wounds.

In one study, Cutting (1998) asked ward nurses to decide if wounds were infected, then classified their diagnoses as "correct" or otherwise based on Cutting's own conclusions (the 1994 criteria and the results of cultures of the wound). The nurses agreed with Cutting in only 47.5% of cases. The author then compared his opinions on whether or not the wound was infected to the findings on wound swab cultures, as interpreted by a microbiologist (who presumably did not see the patient). In all but one case, the author stated that his opinions were supported by the microbiology result.

In addition to the problems associated with using swab (as opposed to tissue) specimens for culture, there is no definition of what specific culture results were considered to be true infection, as opposed to colonisation, and we have no information about how many patients may have had

false negative cultures because of antibiotic therapy. While the author concluded that the criteria had a high degree of validity, I do not think it is possible to adequately interpret the results of this study.

A second study cited to support these criteria was that of Gardner et al (2001b). This cross-sectional study compared the presence of 12 clinical findings in 31 patients with various types of chronic wounds against the "gold standard" – defined as the results of quantitative tissue cultures. The authors concluded that the signs specific to secondary wounds were better indicators of chronic wound infection than the classic signs, with a mean sensitivities of 0.62 and 0.38, respectively.

While the authors are to be applauded for using tissue cultures, there are no data to support quantitative microbiology in chronic wounds as being a criterion standard for infection. Of note, almost no clinical microbiology laboratories do quantitative microbiology on clinical samples. Furthermore, their primary conclusion that "the only subject variable to be associated with wound infection status was systemic antibiotic therapy" demonstrates the problem with defining infection by a positive culture, which is obviously less likely to occur in the face of antibiotic treatment.

More recently, these authors published another study of clinical signs of infection, comprising 64 patients with diabetic foot ulcers (Gardner et al, 2009). Among the 39% who had $>10^6$ organisms/gram of tissue, no individual sign significantly predicted high microbial load. While they concluded that these signs did not predict infection, I would argue that defining infection by microbial load fails to correlate with the clinical findings of inflammation.

With specialisation being common in wound management, should clinical specialists now be using the Cutting and White (2005) criteria, based on Cutting and Harding (1994), the as standard?

KC: Cutting and White (2005) developed infection criteria according to six wound types. This method – infection criteria by indication – avoided the catch-all approach of the 1994 criteria and was the product of a Delphi study where 54 international experts contributed to the process. The mantra "by specialists for specialists" would seem to be appropriate. However, it is important to note that, whereas the 1994 criteria benefit from two validation studies, the 2005 criteria are yet to undergo external validation.

BAL: All clinicians involved in the care of patients with wounds should be reading from the same script (i.e. using the same criteria for identifying infection). This applies to specialists, whether physicians or nurses, as well as to general practice clinicians.

The problem we have currently, however, is a lack of agreement on how to define infection. This is a crucial issue because this diagnosis leads to the decision about whether or not to prescribe antimicrobial therapy. With the worsening crisis of antibiotic-resistant organisms, combined with a "dry pipeline" for new antimicrobial agents, clinicians must be careful stewards of these precious and limited agents.

I think that we need to consider what is important in diagnosing infection. First, we want to halt the progressive spread of a clinically obvious infection, as this can lead to loss of a limb, or even a life. Second, we want to reduce distressing symptoms, both local and systemic, associated with infection. Third, we want to promote healing of the wound, which will not happen in the presence of active infection. We need to seek a definition of infection that supports these goals.

Has the reliance on Celsus' infection criteria led to our apparent overuse of antibiotics and topical antimicrobials?

KC: I am not sure it is as simple as that. Whereas antibiotics have undoubtedly been abused, topical agents, such as antiseptics, continue to play a valuable role in managing wound infection, either on their own or in conjunction with antibiotics. There is a profound need to increase our understanding of how topical agents work, their impact on pathogens (this can vary according to the vehicles used to deliver them), and most importantly, when to stop them. For example, not all honey dressings are the same, neither are the various preparations of silver or iodine.

An extensive misunderstanding has been demonstrated regarding topical agents. In the VULCAN trial by Michaels et al (2009), topical silver was used to treat venous leg ulcers that were not necessarily infected and where different forms of silver (ionised, nanocrystalline, silver sulphadiazine) were used, as were different carrier dressings. The bold conclusion was made that "there was no evidence to support the routine use of silver-donating dressings beneath compression for venous ulceration".

No dressing, medicated or otherwise, should be used routinely. All topical applications should be prescribed according to individual circumstances and the needs of the patient.

BAL: In his encyclopaedic work, *De Medicina*, the first century Roman writer Aulus Cornelius Celsus is credited with recording the cardinal signs of inflammation: calor (warmth), dolor (pain), tumor (swelling), and rubor (redness or hyperaemia). His remarkable text – largely ignored by his contemporaries – was rediscovered by Pope Nicholas V and, in 1478, was among the first medical works to be published after the introduction of the printing press. Almost one-and-a-half millennia after they were written, the value of these findings was clearly apparent to medieval physicians.

Are we now prepared to discard Celsus' paradigm that has served clinicians for over half a millennium? Or, worse yet, as the question implies, attribute the certain overuse of antibiotics that has

been occurring in our generation on the diagnostic criteria used for infection? To do so would, I think, be a clear case of blaming the messenger for the message. To the extent that the classical signs and symptoms are now found wanting, it is because they may be absent in the presence of infection (i.e. with peripheral vascular disease or neuropathy). If anything, this would lead to an underuse of antibiotic therapy in infected, but apparently benign, wounds. One could argue, however, that clinicians, realising the insensitivity of the classic findings, are treating clinically uninfected wounds with antibiotics because they fear they may miss unrecognised infections.

If more widely adopted, would the criteria of Cutting and Harding be likely to reduce morbidity associated with wound infection?

KC: Undoubtedly!

BAL: Again, I think the focus should not be on the potential value of this one set of criteria, but on determining which criteria actually define a clinical situation that requires antimicrobial therapy. The mere presence of organisms in a wound is not an indication for such therapy, while a progressive, inflammatory process with tissue destruction does. The difficulty is in the intermediate state; namely, a wound that lacks the classical signs of inflammation, purulence, deep tissue gas, bone destruction, or manifestations of the systemic inflammatory response, which, despite treatment, fails to heal.

The presence of peripheral neuropathy, arterial insufficiency, or immunosuppression can mask (or mimic) some of the classical signs of infection and, in these individuals, we need to be especially vigilant. We may need to use evidence of systemic inflammation (e.g. erythrocyte sedimentation rate or C-reactive protein), or of local inflammation or destruction only visible with advanced imaging procedures (e.g. magnetic resonance imaging, SPECT/computed tomography, positron emission tomography; Aslangul et al, 2013).

Furthermore, modern molecular microbiological techniques are now allowing us to quickly identify the presence of specific genes associated with virulence, as well as antibiotic resistance (Sotto et al, 2012). These techniques, when widely available, may well allow more accurate identification of wound infection (Lipsky et al, 2013).

What can be done to increase the awareness and clinical usage of modern wound infection criteria?

KC: Education, education, education.

BAL: The first step would be to improve the definition of wound infection, as discussed previously. Nothing will deter the use of any diagnostic tool faster than clinicians finding that their efforts do not consistently correlate with the outcomes they are seeking. Clinicians and patients (as well as their family and carers) must also be educated to be watchful for signs or symptoms suggestive of wound infection. Making it easy for clinicians to diagnose infection (i.e. rapid molecular techniques using easily obtainable specimens) will also encourage diagnosis and correct treatment. WUK

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