A New Term: The Point of Pathogenicity

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Infection in chronic wounds proceeds along a continuum from contamination to colonization and eventually to systemic infection. All open wounds are contaminated with bacteria; however, in this state, the bacteria are harmless: they do not compete with host cells for oxygen and nutrients or injure the tissue. Over time, bacteria will colonize a chronic wound. The colonizing bacteria replicate in the wound bed. They may compete with host cells for nutrients, which in turn impedes wound healing, but they do not invade host tissues. At a subsequent stage, the bacteria begin to produce proteases (virulence factors) that break down host tissue, allowing the bacteria to invade deeper into the wound bed. Unchecked local and eventually systemic infection will ensue.

In the past, the term "critical colonization" loosely described the transition from colonization to infection. However, this is a misnomer. Once the bacteria in the wound progress from a colonized state to invasive microorganisms, the term "colonization" is no longer appropriate. At this stage, the bacteria actively produce virulence factors that degrade host tissue, delay wound healing, and increase the risk for systemic infection.

A recently completed multicenter randomized clinical trial[1] conducted at seven centers in the US evaluated a diagnostic designed point-of-care test to detect the presence of bacterial protease activity (BPA) in chronic wounds. The trial demonstrated that in 39% of chronic wounds BPA increases prior to any signs or symptoms of infection. Therefore, I suggest the term *point of pathogenicity* to describe this stage of the continuum, rather than *critical colonization*. It is the point at which bacteria begin producing proteases that break down host tissues leading to infection. In the absence of treatment, ulcers reaching the point of pathogenicity will proceed to active infection.

The clinical signs and symptoms of infection in chronic wounds lag behind the production of harmful proteases or may never materialize despite active infection. In previous clinical trials, 25% of wounds had active infection in the absence of clinical signs and symptoms.[1–3] The signs and symptoms of infection may not appear until the patient is suffering from systemic limb and life-threatening infection. In the aforementioned large study (266 patients),[1] 6 patients had ulcers with elevated BPA prior to the development of observable clinical signs or symptoms of infection. This group developed sepsis and underwent amputation of the affected extremity. The data strongly suggest that the early discovery of elevated BPA, at the point of pathogenicity, would have led to earlier intervention and perhaps obviated the need for amputation.

In conclusion, the evidence suggests that there is a point at which bacteria transition from colonization to active invasion. This is heralded by the production of bacterial proteases that do not immediately lead to clinical signs and symptoms of infection in chronic wounds. I suggest the term *point of pathogenicity* for this phase in the infection continuum. Failure to recognize and treat patients at this stage can have serious consequences, such as amputation and sepsis. The advent of testing for BPA in chronic wounds may result in early detection of infection at the point of pathogenicity and decrease the incidence of infectious complications.

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