Letter to the Editor

Letter to the Editor: Editor's Spotlight/Take 5: Is Single-stage Revision According to a Strict Protocol Effective in Treatment of Chronic Knee Arthroplasty Infections

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Since World War II, with the beginning of the extensive use of antibiotics, mankind has been in an arms race against bacteria. Each new antibiotic seems to be met

by a new mechanism to overcome our best efforts. From efflux pumps to biofilms—all would have to agree we are fighting a worthy adversary.

Although the complication infection rate for primary total joint arthroplasty is low at 1% to 2% and 7% for revisions [3], those involved in treating these infections know they can be devastating to the individual patient, especially staphylococcal infections. The recently published study by Haddad and colleagues [4] examined single-stage revision versus two-stage involving highly selected patients. The use of highly selected patients was also addressed in the study's accompanying Editor's Spotlight [6]. Clearly, though, if the patients in this series were highly selected, there must be a group of other patients whose needs are not met with the one-stage approach, and we need other options for treating them.

Treatments focusing on factors related to cellular pH may offer an angle that has not been fully exploited. Cellular pH may vary across different bacterial pathogens and may vary in the host in the presence of infection [2]. The pH level, intracellularly and

extracellularly, is controlled by cellular pumps, channels, and transporters in the cell membrane. The function of these pumps may be genetically driven, but it can be influenced by hormones, medications, and other factors any or all of which might offer therapeutic opportunities. Human cellular pumps, channels, and transporters are probably similar, but not exactly the same as those of bacteria. Modifying the machinery of the cellular pumps in pathogenic bacteria might influence cell wall channels, efflux pumps, and antibiotic neutralizing enzymes.

Many bacterial infections have associated biofilms making eradication more difficult. In short, the biofilm allows the bacteria to control the environment like a bio-dome. We now know that at least some biofilms can be impacted by pH [5]. Perhaps this is a vice versa situation with each having the ability to impact the other.

There is some indirect evidence that bone may be more sensitive to pH than has previously been appreciated [7, 9]. This notion makes sense since two important enzymes in bone are

(RE: Leopold S. Editor's Spotlight/Take 5: Is Single-stage revision according to a strict protocol effective in treatment of chronic knee arthroplasty infections? *Clin Orthop Relat Res*. [Published online ahead of print November 1, 2014]. DOI: [10.1007/s11999-014-4034-7](https://doi.org/10.1007/s11999-014-4034-7).)

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alkaline phosphatase and acid phosphatase in osteoblasts and osteoclasts (by names alone they are suggestive of possible pH involvement). Some cytokines like IL-1B, which are known to be active in bone, are also sensitive to pH changes [8]. According to Wolff's Law, bone is deposited and reinforced in areas of greatest stress [1]. Perhaps a mild pH change is induced in the stressed area causing a slow change.

We need to better understand the bacterial versus the human cellular pumps, channels, and transporters. Once we gain a better understanding, we can develop treatments that might partially reduce the effectiveness of the bacterial cell membranes versus the human cell membranes (ie, cellular pumps, channels, and transporters). However, because both bacteria and humans have so many different types of cellular pumps, channels, and transporters, partially blocking just one type may only invoke a mild difference or none at all. Since redundancy

is built into most life forms, blocking combinations should be developed in order to be considered effective.

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