Ionic Modulation of Bacterial Virulence and Its Role in Surgical Infection.
Authors: Alverdy JC

Abstract
Background: Bacterial virulence is a dynamic property of pathogens that is expressed in a context-dependent manner. For a bacterial pathogen, the expression of virulence is a tradeoff, as there is an energy cost that can disturb other functions. As a result, virulence is activated only when bacteria sense the need for it. Methods: Recent work from our laboratory has identified many of the local cues in the environmental context that activate bacterial virulence during surgical injury, resulting in bacterial invasion, tissue inflammation, and, in some cases, lethal sepsis. Results: After surgical injury, cytokines, opioids, and end-products of ischemia can activate bacterial virulence circuits, such as the quorum-sensing signaling system, directly. However, when key ions are present, such as phosphate and iron, certain pathogenic bacteria become insensitive to these incoming host cues. Conclusion: In this review, we provide molecular insight into the process by which certain surgical infections may be prevented by ionic modulation of the local microenvironment.

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Oral Polyphosphate Suppresses Bacterial Collagenase Production and Prevents Anastomotic Leak Due to Serratia marcescens and Pseudomonas aeruginosa.
Authors: Hyoju SK, Klabbers RE, Aaron M, Krezalek MA, Wiegerinck M, Hyman NH, Zaborina O, Van Goor H, Alverdy JC

Abstract
OBJECTIVE: The objective of this study was to determine the effect of polyphosphate on intestinal bacterial collagenase production and anastomotic leak in mice undergoing colon surgery.
BACKGROUND: We have previously shown that anastomotic leak can be caused by intestinal pathogens that produce collagenase. Because bacteria harbor sensory systems to detect the extracellular concentration of phosphate which controls their virulence, we tested whether local phosphate administration in the form of polyphosphate could attenuate pathogen virulence and prevent leak without affecting bacterial growth.
METHODS: Groups of mice underwent a colorectal anastomosis which was then exposed to collagenolytic strains of either Serratia marcescens or Pseudomonas aeruginosa via enema. Mice were then randomly assigned to drink water or water supplemented with a 6-mer of polyphosphate (PPI-6). All mice were sacrificed on postoperative day 10 and anastomoses assessed for leakage, the presence of collagenolytic bacteria, and anastomotic PPI-6 concentration.
RESULTS: PPI-6 markedly attenuated collagenase and biofilm production, and also swimming and swarming motility in both S. marcescens and P. aeruginosa while supporting their normal growth. Mice drinking PPI-6 demonstrated increased levels of PPI-6 and decreased colonization of S. marcescens and P. aeruginosa, and collagenase activity at anastomotic tissues. PPI-6 prevented anastomotic abscess formation and leak in mice after anastomotic exposure to S. marcescens and P. aeruginosa.
CONCLUSIONS: Polyphosphate administration may be an alternative approach to prevent anastomotic leak induced by collagenolytic bacteria with the advantage of preserving the intestinal microbiome and its colonization resistance.

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