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The Gastrointestinal Tract: A Friend or Foe to Listeria monocytogenes?

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Listeria monocytogenes is a gram-positive bacillus and is the causative agent of listeriosis. Approximately 2500 cases of listeriosis and 500 deaths are reported each year, making it the deadliest food borne pathogen [1]. The CDC has reported that the incidence of L. monocytogenes has decreased by 36% between 1996 and 2006. However, outbreaks still occur, making it a cause for concern among the medical and food industries.

During its infection cycle, L. monocytogenes is subjected to a variety of elements that are in place by the host to combat infections. The bacterium enters the body through ingestion of contaminated food (most likely) and must then resist the dangerous environments encountered throughout the gastrointestinal tract. Some of these stressors are acidic environment of the stomach, intracellular states within intestinal epithelial cells and macrophages, reduced oxygen content, and bile. Bile is composed of a multitude of components, of which bile salts have been shown to provide protection against pathogenic bacteria [2]. It has been proposed that resistance to high concentrations of bile salts is critical to the establishment of listeriosis [3]. Studies have found that L. monocytogenes replicates extracellularly within the lumen of the gallbladder, where bile salt concentrations can be as high as 15% or more [4, 5]. It is surprising that this facultative intracellular pathogen chooses to grow extracellularly in this potentially harmful environment. It has been proposed that L. monocytogenes grows extracellularly in the gallbladder in order to be more efficient at spreading throughout the gastrointestinal tract.

Recently, it was found that bile actually enhanced the ability of L. monocytogenes to form biofilms [6]. The study was conducted using 0.3% bile salts, which is a concentration similar to that found in the small intestine. It was proposed that this might allow for enhanced colonization by Listeria in the intestines. Therefore it is possible that the cells are forming biofilms in the intestines, but the gallbladder provides a location for the cells to replicate before establishing an invasive infection.

Findings from our lab suggest that pathogenic strains may be more resistant to high concentrations of bile salts than avirulent strains [7]. We found that extensive surface deformities were present on an avirulent strain and were not observed in a virulent strain following exposure to high concentrations of bile salts (20%). The cell width of the virulent strain increased, while the width of the avirulent strain actually decreased [7]. We proposed that bile salts alter the cell membrane of both virulent and avirulent strains, but the effect is much more severe in the avirulent strain. The compromised membrane then allows for the influx of bile salts, which then target the DNA and induce ds breaks, leading to cell death.

Even though these findings have contributed significantly to our understanding of how bile resistance influences the establishment of invasive infections, much work is still needed in this area in order to determine mechanisms involved in bile resistance in enterics. Many "bile resistance genes" have been found in L. monocytogenes, but it is unlikely that these genes are the only means for bile resistance since they are also found in bile sensitive strains [7]. Therefore, studies are needed that analyze the global expression patterns presented by enterics in these stressful environments.

Recently, it was found that exposure to the acidic environment of the stomach preconditions L. monocytogenes to be more invasive [8]. They found that L. monocytogenes treated with acid or salt prior to infections were better equipped to grow within Caco-2 epithelial cells.

Another study also found that exposure of L. monocytogenes to acid selects for acidtolerant bacteria, which in turn were more virulent than wild-type strains [9]. These (and other) studies suggest that the sequential exposure of L. monocytogenes to the stressors encountered throughout the gastrointestinal tract may actually increase resistance to downstream stressors, 3 thus making the bacterium more virulent. Research is needed to determine whether exposure to bile salts also precondition bacteria for intracellular infections or even biofilm formation and whether this preconditioning might be dependent upon the pathogenic potential of the bacterium.

In conclusion, many studies suggest that bile tolerance is a major contributor to the infection cycle of L. monocytogenes and other enterics as well. The gastrointestinal tract exposes L. monocytogenes to varying concentrations of bile salts, which could possibly result in bacteria better adapted to survive within the gastrointestinal tract. Deciphering the mechanisms utilized to tolerate these environments will help develop methods to circumvent enteric diseases.

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