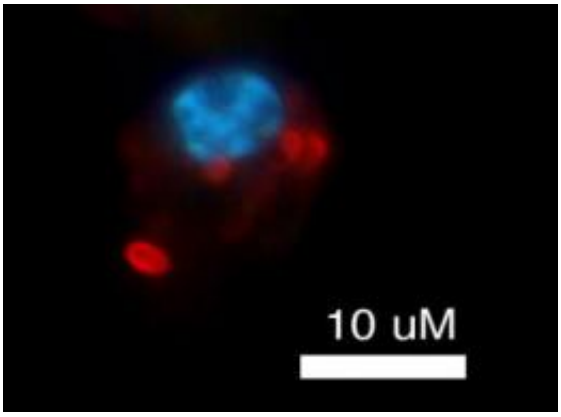
'Good' bacteria keep immune system primed to fight future infections

January 27 2010



This is bacteria (*Streptococcus pneumoniae*, red) under attack by a neutrophil (blue). Credit: Jeffrey Weiser, PhD, University of Pennsylvania School of Medicine

Scientists have long pondered the seeming contradiction that taking broad-spectrum antibiotics over a long period of time can lead to severe secondary bacterial infections. Now researchers from the University of Pennsylvania School of Medicine may have figured out why.

The investigators show that "good" bacteria in the gut keep the immune system primed to more effectively fight infection from invading pathogenic bacteria. Altering the intricate dynamic between resident and foreign bacteria - via antibiotics, for example -- compromises an animal's immune response, specifically, the function of white blood cells

called neutrophils.

Senior author Jeffrey Weiser, MD, professor of Microbiology and Pediatrics, likens these findings to starting a car: It's much easier to start moving if a car is idling than if its engine is cold. Similarly, if the immune system is already warmed up, it can better cope with pathogenic invaders. The implication of these initial findings in animals, he says, is that prolonged antibiotic use in humans may effectively throttle down the immune system, such that it is no longer at peak efficiency.

"Neutrophils are being primed by innate bacterial signals, so they are ready to go if a microbe invades the body," Weiser explains. "They are sort of 'idling', and the baseline system is already turned on."

Weiser and first author Thomas Clarke, PhD, a postdoctoral fellow in the Weiser lab, published their findings last week in Nature Medicine.

"One of the complications of antibiotic therapy is secondary infection," Weiser explains. "This is a huge problem in hospitals, but there hasn't been a mechanistic understanding of how that occurs. We suggest that if the immune system is on idle, and you treat someone with broad-spectrum antibiotics, then you turn the system off. The system is deprimed and will be less efficient at responding quickly to new infections."

The findings also provide a potential explanation for the anecdotal benefits of probiotic therapies because keeping your immune system primed by eating foods enhanced with "good" bacteria may help counteract the negative effects of sickness and antibiotics.

Researchers have for many years understood that most bacteria in the body are not "bad." In fact, humans (and mice) have a symbiotic relationship with their resident microbes that significantly impacts,

among other things, metabolism and weight homeostasis. As shown in this study, microbes also affect the innate immune response, via the cellular protein Nod1.

Present within neutrophils, Nod1 is a receptor that recognizes parts of the cell wall of bacteria. Weiser and his colleagues found that neutrophils derived from mice engineered to lack Nod1 are less effective at killing two common pathogens, *Streptococcus pneumoniae* and *Staphylococcus aureus*, than neutrophils from mice that do express the receptor.

In addition, neutrophils from mice that were raised in a germ-free environment or on antibiotics were likewise diminished in their immune responses, but this effect was not permanent: Re-exposure of these mice to a conventional environment (that is, one containing normal bacteria) restored immune function.

The team provided evidence for a potential mechanism for these observations by showing that bacterial cell wall material could be detected in the blood of normal mice, and that it influences neutrophils in the bone marrow. Finally, the team demonstrated they could improve immune function by treating both antibiotic-treated mice and human neutrophils with the Nod1 ligand - a finding that suggests it may be possible to counter the adverse consequences of antibiotics in humans.

Provided by University of Pennsylvania School of Medicine