Excess dietary manganese promotes staph heart infection

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Too much dietary manganese—an essential trace mineral found in leafy green vegetables, fruits and nuts—promotes infection of the heart by the bacterium *Staphylococcus aureus* ("staph").

The findings, reported this week in the journal *Cell Host & Microbe*, add to the evidence that diet modifies risk for infection. The discovery also suggests that people who have excess levels of tissue manganese, including those who consume dietary supplements with high concentrations of the metal, may be at increased risk for staph infection of the heart.

"The human body does a wonderful job of regulating nutrient levels, and a traditional Western diet has plenty of minerals in it. The idea of super-dosing nutrients needs to be given careful consideration," said Eric Skaar, Ph.D., MPH, Ernest W. Goodpasture Professor of Pathology and senior author of the current study.

Skaar and his colleagues studied the impact of dietary manganese on staph infection in a mouse model. Most of the mice that consumed a high manganese diet—about three times more manganese than normal—died after infection with staph. The investigators discovered that the animals on the high manganese diet were particularly susceptible to staph infection of the heart, which was a surprise, said Skaar, who is also professor of Pathology, Microbiology and Immunology and director of the Vanderbilt Institute for Infection, Immunology and Inflammation.

"We know very little about how manganese is moved around and regulated. It's a mystery why high manganese affects staph infection of a single organ," he said.

The researchers found that excess manganese inactivates a key line of defense against pathogens: the innate immune system's reactive oxygen burst. Normally, in response to staph, "neutrophils pour into the site of infection and blast the bacteria with reactive oxygen species," Skaar explained. The excess manganese counters this blast.

"It's striking that a single dietary change can inactivate one of the most powerful branches of innate immune defense and lead to fatal infection ," Skaar said.

The protein calprotectin—another line of defense—usually acts as a "sponge" to mop up manganese and other metals. Keeping nutrients away from pathogens is known as "nutritional immunity." For reasons that are not clear, however, calprotectin is completely ineffective in the high manganese hearts, Skaar said.

Staph is the leading cause of bacterial endocarditis (infection of the inner lining of the heart chamber and heart valves) and the second most frequent cause of bloodstream infections.

Interestingly, some populations of people have both increased risk for staph infections, particularly endocarditis, and higher than normal levels of tissue manganese, Skaar noted. These populations include intravenous drug users, patients with chronic liver disease and patients on long-term intravenous diets.

In ongoing studies, Skaar and his colleagues are working to understand how manganese is transported and regulated in vertebrates and why the heart is particularly susceptible to fatal staph infections when manganese

levels are high. They are also exploring the impact of other nutrient minerals and vitamins on infection.

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