Bacterial respiratory tract colonization prior to catching the flu may protect against severe illness

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Many studies have shown that more severe illness and even death are likely to result if you develop a secondary respiratory infection after developing influenza. Now, however, a team of researchers based at The Wistar Institute has determined that if you reverse the order of infection, the bacteria *Streptococcus pneumoniae* (often called pneumococcus) may actually protect against a bad case of the flu.

The researchers discovered that the bacterial protein pneumolysin, which is described as a bacterial virulence factor, might protect macrophages—a type of immune system cell—in the lungs. Their findings, performed in a mouse model of influenza infection, appear in the August issue of the journal *Virology*, available online now.

"Influenza remains a major killer, and there is a preponderance of evidence, both scientific and historical, to show how secondary bacterial infections can be fatal," said Jan Erikson, Ph.D., professor at The Wistar Institute. "However, pneumococci often colonize the respiratory tract asymptomatically, particularly in children, leading us to consider how pre-colonization would impact a subsequent influenza infection."

"Our studies showed that prior colonization offered a protective effect against severe disease in mice," Erikson said, "and we were able to point to the bacterial virulence factor pneumolysin in mediating this protection."

In their investigations, Erikson and her colleagues found that mice who were colonized by Streptococcus pneumonia ten days prior to exposure to influenza were significantly less likely to develop severe disease or pneumonia than mice who were not colonized by the bacteria. In contrast, disease symptoms were exacerbated in mice that were exposed to the flu prior to a secondary pneumococcal infection.

"Mice that were first exposed to pneumococci exhibited less inflammation in the lungs following influenza infection. Virus infection wasn't blocked but the response to it was changed such that the mice no longer showed signs of illness," Erikson said.

The researchers then went about investigating how this might occur. Using mutant strains of pneumococcus that lacked certain proteins, Erikson and her colleagues were able to single out one bacterial protein, pneumolysin, which was necessary to generate the protective effect of pneumococcus. While the exact mechanisms by which pneumolysin lessens the severity of disease remain unknown, Erikson and her colleagues were able to show how alveolar macrophages were less likely to recruit inflammation-causing immune cells to the lungs. Less inflammation would mean less chances of developing pneumonia, which

is a major source of flu deaths, Erikson says.

According to Erikson, her results suggest that one factor contributing to the highly variable response to influenza virus infection and severity of disease observed in humans is the presence of specific respiratory tract microbes. "It remains to be seen what lessons we can learn from pneumococcus in lessening flu infections," Erikson said, "but I would be interested in seeing if we could get the benefit of pneumococcal colonization without the associated risks."

Provided by The Wistar Institute