Brothers in arms

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Influenza, or flu, is an unpleasant affair with fever, cough, as well as head and body ache. When this illness is further complicated by a bacterial pneumonia, a harmful super-infection develops. Until now, researchers thought that the flu facilitates an infection with pneumonia bacteria because it leads to a decrease of immune cells in the blood and thus impairs the body's defenses.

A joint venture from researchers from the Helmholtz-Centre for Infection Research (HZI) in Braunschweig, the Otto-von-Guericke-University in Magdeburg, and the Karolinska institute in Sweden have taken an in-depth look at the connection between flu infection and pneumonia. Their results, recently released in the scientific journal "*PLoS One*", have disproven a common theory about flu-like pneumonia.

Some viral infections trigger a decrease of immune cells in the blood - a so-called "lymphopenia". The reasons behind it and whether this is the case with influenza are unknown. To investigate the latter, HZI researchers infected mice with flu viruses and measured the amount of immune cells in the animal's blood every day. Some days later, flu-infected mice received a dosage of pneumonia bacteria usually harmless for healthy mice. While the flu-infected mice did develop a superinfection & subsequently died, surprisingly, they were not suffering from lymphopenia. The healthy, non-flu-infected mice defeated the bacteria successfully and recovered.

To discover whether a lack of immune cells encourages an infection with pneumonia bacteria in general, an artificial drug-induced lymphopenia was established in the mice. Without infecting these lymphopenic mice with flu viruses, they received pneumonia bacteria. Despite a severe lack of immune cells, the mice recovered completely.

With these results, the researchers could show that influenza facilitates and intensifies an infection from pneumonia bacteria, while disproving the common idea that this is caused by a lack of immune cells. "This result was an enormous surprise for us because it directly contradicts widespread assumptions", says Sabine Stegemann, researcher in the groups "Immune regulation" at the HZI and "Molecular Immunology" at the Otto-von-Guericke-University in Magdeburg.

"Now we want to understand the reasons for the increased susceptibility", says Matthias Gunzer, head of the group in Magdeburg. "It could be interplay of weakened mucous membranes and scavenger cells that induce ideal conditions for pneumonia bacteria to create a deadly lung infection. Another reason may be a reaction of the host immune system: It disables hyperactive flu-fighting immune cells to inhibit destruction of healthy lung tissue. "The immune system keeps itself under control and that makes it easy for pneumonia bacteria to infect the lung", says Gunzer.

More information: Stegemann S, Dahlberg S, Kröger A, Gereke M, Bruder D, et al. 2009 Increased Susceptibility for Superinfection with Streptococcus pneumoniae during Influenza Virus Infection Is Not Caused by TLR7-Mediated Lymphopenia. *PLoS ONE* 4(3): e4840. doi:10.1371/journal.pone.0004840

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