

Double trouble: Bacterial super-infection after the flu

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Current research suggests that the flu may predispose to secondary bacterial infections, which account for a significant proportion of mortality during flu pandemics. The related report by Lee et al, "A mouse model of lethal synergism between influenza virus and *Haemophilus influenzae*," appears in the February 2010 issue of The *American Journal of Pathology*.

Influenza affects between three and five million people annually, causing up to 500,000 deaths worldwide. While most people will recover in one to two weeks, others will develop life-threatening conditions such as pneumonia or bronchitis. High-risk groups for seasonal influenza include the very young and old, people with compromised immune systems, and pregnant women. However, during influenza pandemics, mortality may be significant in previously healthy young adults.

A common complication of flu infection is a secondary "superinfection" by bacteria, which greatly increases the morbidity and mortality of the disease. The most common bacterial agents found following flu pandemics have been *Streptococcus pneumoniae*, *Haemophilus influenzae*, Group A *Streptococcus*, and <u>Staphylococcus</u> <u>aureus</u>. Furthermore, reports of infection with antibiotic-resistant strains have been increasing in recent years.

To explore the mechanisms governing the increased pathogenesis of flu upon super-infection, a group led by Dr. Sally R. Sarawar of the Torrey Pines Institute for Molecular Studies, San Diego, California confirmed



that otherwise nonlethal influenza and *H. influenzae* infections cause high mortality rates in mice when flu infection precedes *H. influenzae* infection. Their data confirm a restricted time period for this heightened susceptibility and highlight that excessive bacterial, and not viral, growth is associated with increased lethality. The fact that this increased mortality was observed in both immunocompromised and immunocompetent mice suggests that even normal healthy people are at increased risk for complications following bacterial super-infection.

Lee et al suggest that the "lethal synergy between influenza virus and the bacterial respiratory pathogen, *H. influenzae*, is mediated by innate immunity. They observed that severe damage to the airways was an early event in the co-infected mice, eventually leading to death. This underscores the need for early antiviral and antibiotic treatment to combat severe disease in human patients and highlights the importance of vaccination and effective hygiene measures to prevent secondary bacterial infections during influenza infection. This new model will be useful for further investigating the mechanisms underlying severe disease caused by the interaction between influenza virus and bacteria, which may have resulted in numerous deaths during influenza pandemics and continues to constitute a significant clinical problem in susceptible individuals." Currently ongoing studies suggest that this model may also be useful for identifying target molecules for the development of novel therapeutic agents and strategies.

More information: Lee LN, Dias P, Han D, Yoon S, Shea A, Zakharov V, Parham D, Sarawar SR: A mouse model of lethal synergism between influenza virus and Haemophilus influenzae. Am J Pathol 176: 800-811

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