Sequential Infections with Influenza and Novel Respiratory Bacteria

To the Editor—McCullers and colleagues [1] recently reported results of their studies of influenza and Streptococcus pneumoniae infection in ferrets. The findings documented that pneumococcal transmission was enhanced in ferrets previously infected with influenza: ferrets that were infected with pneumococci after—but not before—influenza infection developed lethal secondary pneumonias and other invasive complications [1]. These findings, if generalizable to humans, have important public health policy and practice implications.

Most deaths during the 1918 influenza pandemic were caused by secondary bacterial pneumonias. The bacterial species most often implicated in fatal cases were *S. pneumonia*, *S. pyogenes*, and *S. aureus*; all are common colonizers of the nasopharynx of healthy humans [2,3]. It has been presumed that the bacteria that caused most of the secondary pneumonias in 1918 were colonizers of their victims and that previously benign carriage strains were enabled to invade the lower respiratory tract of their hosts after influenza disrupted their physical and immunologic defenses.

The findings of McCullers et al [1] suggest a different pathogenic sequence. Specifically, the life-threatening bacterial complications of influenza required sequential infections: first with an influenza virus that degraded the physical and immunologic defenses of the host’s lower respiratory tract, and then with a bacterial strain to which the host was susceptible (eg, the host lacked protective antibodies). Given this sequence, individuals infected with potentially invasive bacteria prior to infection with influenza would be at low risk of invasive disease (because intact physical barriers and immune responses would be protective). In addition, individuals would not be at risk of invasive complications from their own nasopharyngeal microflora because preexisting antibodies against them would be protective [4]. Only exposures to novel bacteria within several days after influenza infection would threaten to cause lethal pneumonias and other invasive complications.

This pathogenic sequence is consistent with observations in military groups during the 1918 pandemic.
During influenza epidemics at United States (US) Army mobilization camps in the fall of 1918, soldiers in their first weeks of service were at much higher risk of fatal secondary bacterial pneumonias than their more seasoned counterparts [3]. Undoubtedly, during influenza epidemics at training camps in the fall of 1918, many and diverse bacterial strains cocirculated with influenza virus in crowded barracks, dining facilities, clinics, and hospital wards. Hence, prior to their exposures to pandemic influenza, seasoned soldiers were likely exposed to, and gained natural immunity against, many of the circulating bacterial strains; in contrast, recent arrivals to the camps were likely immunologically susceptible to many circulating bacterial strains.

Among Australian soldiers deployed in Europe during the fall of 1918, influenza illness rates among persons in medical occupations were similar to, but influenza-related mortality rates were much lower than, those among persons in other military occupations [5]. Prior to infection with pandemic influenza, medical workers were likely exposed to and naturally immunized against numerous and diverse respiratory bacterial strains. Soldiers in nonmedical occupations were likely exposed—while being treated for influenza—to many bacterial strains to which they were not immune.

On US troop transport ships, the permanently assigned naval crewmen (who were likely exposed to numerous and varied respiratory bacteria) had rates of influenza illness that were similar to, but pneumonia and mortality rates that were lower than, those among the soldiers who were in transit [3]. During shipboard influenza epidemics, the crewmen were likely protected from death (but not influenza illness) because of preexisting naturally acquired immunity to diverse bacterial strains. The soldiers who had been recently congregated on the crowded ships were at risk of death from secondary pneumonias caused by bacterial strains to which they were newly exposed and immunologically susceptible.

In summary, we hypothesize that in 1918, previously healthy and immunologically competent influenza-affected hosts were at risk of life-threatening bacterial complications because they had influenza-mediated degradation of the physical and immune defenses of their lower respiratory tracts and no preexisting protective antibodies against respiratory bacterial strains to which they were newly exposed. If so, then during future pandemics, previously healthy individuals with influenza-like illnesses should avoid persons, locations, and settings that would expose them to new or diverse respiratory bacteria. Thus, for example, otherwise healthy individuals with, or recovering from, influenza should avoid crowded public settings (eg, buses, airports, and athletic events), places where acutely ill individuals congregate (eg, medical clinics and hospitals), and other locations that may increase the risk of exposure to bacteria to which they are immunologically susceptible.

The findings of McCullers et al [1] should be validated and extended to further elucidate the relationships between influenza, respiratory bacteria, and host immune defenses. A primary objective of influenza-related research should be the identification of safe, effective, and inexpensive lifesaving countermeasures against pandemic influenza.

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References


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