Unconventional Immunity

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If Someone Sneezes on a Plane, Will Everyone Else Get Sick?

In the wake of the 1918 "Spanish Flu" pandemic, a series of experiments was carefully designed to model human transmission of influenza using U.S. Navy volunteers. The ethics of these experiments seem questionable, and one can only hope that the volunteers knew what lay in store for them. Acutely sick patients were asked to cough, sneeze or breathe on more than 150 well volunteers, who were monitored for development of flu-like symptoms. The results: not a single patient showed symptoms of illness. In additional experiments, the nostrils of sick patients were rinsed with saline and the resulting solution was aerosolized and sprayed into the eyes, noses and throats of well volunteers. Again, not a single volunteer became ill. A much more recent 2003 review found no studies in the English-language literature delineating person-to-person transmission of influenza.

The influenza A virus, cause of the seasonal flu and the subject of ongoing pandemic pandemonium, presents an interesting challenge to our conventional wisdom. The basic assumption with most infectious diseases is that they are transmitted in a serial chain from sick to well, and influenza virus is no exception. But when we take a closer look at how influenza is propagated within human populations, numerous discrepancies begin to arise.

For example, when we are cooped up in an airplane with a coughing, sneezing, miserable passenger, whom we all suspect is going to make us sick (as we eye them with unveiled disdain), why doesn't *everyone* on the plane get sick? A reasonable answer would be that the people who do get sick are being exposed to this variant of the virus for the first time — they've had no previous exposure. By contrast, the lucky passengers who sat right next to the sneezing passenger and never developed a sniffle must have been granted immunity to the virus from some previous exposure — possibly to a milder form of the virus.

This is a good guess, but not completely correct. Remember those 1918 experiments, where all of the volunteers remained well, showing no symptoms of flu after being blasted in the face by sneezings from acutely sick patients? It turns out that all of them tested seronegative for Spanish Flu, which means that there was no record of previous exposure to this flu virus. These patients had not developed antibodies against the Spanish Flu. But without the protection of antibodies, why did they not fall acutely ill?

The answer, and a piece of the complex puzzle of influenza transmission, lies in the mechanics of our immune system. Human immunity can be divided into two parts: adaptive immunity and innate immunity. Most of us are familiar with adaptive immunity. We are exposed to some foreign material, our bodies recognize this material as non-self and mount an attack against it, including the raising of antibodies — small molecular tags that label the foreign material for destruction. The next time we encounter this same foreign material, our bodies are ready for it. This is the basis of the wonderful protection from disease granted through vaccination. Innate immunity is easy to overlook, as it protects us from invading bacteria, fungi and viruses through seemingly mundane — but absolutely critical — features, like skin and mucous membranes.

Part of our innate immunity is conferred by a class of molecules known as antimicrobial peptides (AMPs), small chains of amino acids with catalytic activities, which line our skin, nostrils and lungs. AMPs drill through the cell membranes of invading bacteria, and destroy the integrity of invading viruses like influenza. Innate immunity grants us protection in the absence of previous exposure. It turns out that vitamin D is a critical building block of AMPs. On top of this, most of us do not obtain the required amount of vitamin D directly through our diets. Rather, we generate vitamin D from dietary precursors in a reaction that requires exposure to sunlight.

This connection between innate immunity and patterns of sun exposure fits with previous observations regarding seasonal outbreaks of influenza. Spending more time indoors during "flu season" doesn't so much increase our contact with infected individuals as decrease our exposure to the already attenuated winter sunlight. This results in lowered production of vitamin D and therefore a weakened barrier of AMPs to protect us from novel flu variants. (And beyond influenza, recent studies show that vitamin D is vital for many immune system functions.)

This is still not the complete picture: several details remain obscure regarding the erratic transmission patterns of influenza. However, these established links between flu outbreaks, solar radiation, seasonality and innate immunity do allow us to make a better predictive model of flu transmission. And a clearer understanding of influenza transmission is essential for implementing more effective prevention of influenza outbreaks, both seasonal and pandemic.

Kurt Williamson received his Ph.D. from the University of Delaware. His research focuses on the ecology of naturally occurring viruses in soil and freshwater ecosystems, and the co-evolution of viruses with their hosts. In the fall of 2009, Professor Williamson will be teaching a course in virology — a course that has been missing from the biology curriculum for eight years.

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