Centenario de la Gripe Española de 1918. La peor pandemia en la historia contemporánea mundial: lecciones para el futuro

Centenary of the 1918 Spanish Influenza, the Worst Pandemic in the Recent History of the World: Lessons for the future

Madrid, 27 y 28 de septiembre / September 27-28 2018

ABSTRACT

Local and systemic distortion of microbiota homeostasis by influenza A virus infection gives rise to bacterial super infection

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During the 1918 Spanish influenza more than half of the patients died of bacterial superinfections. Despite development of efficient antibiotics we still encounter bacterial pneumonia as a major complication following viral infections of the upper and lower respiratory tract until today. This affects primarily high risk groups of patients in hospital settings, among them elderly, immune compromised and children. Rise of bacterial resistance against the vast majority of available antibiotics is a major threat to public health and limits treatment options of clinicians for bacterial pneumonia. Secondary bacterial infection is mainly caused by three pathogens: Streptococcus pneumoniae, Staphylococcus aureus and Haemophilus influenzae. All three eventually colonize the airways of a varying percentage of the human populations as part of the natural flora. Under certain conditions these pathobionts can reach critical levels in the respiratory tract or access the more vulnerable small airways to cause bacterial pneumonia. The reasons for this outgrowth of pathobionts are still insufficiently understood and likely multi-factorial. Destruction of the epithelial barrier, induction of proinflammatory cytokines and breakdown of mucus were implicated in promoting secondary bacterial infection.

Commensal microbiota pose a natural shield against invading bacterial pathogens. Likely this is based on direct competition for nutrients, but could also be based on the release of antibacterial metabolites targeting pathogenic bacteria. Consequently, disruption of this bacterial shield, e.g. by antibiotics treatment, results in higher susceptiblity to bacterial infection. The same phenomenon can be observed in germ-free or gnotobiotic animals, harboring a lower load of commensal bacteria. We recently started a series of experiments to define the impact of acute viral infections on local (at the site of infection) and systemic microbiota using influenza A virus as a model pathogen. One aim of our study was to define whether acute viral infections weaken the natural shield of commensal bacteria, thus creating a loophole for invasion of bacterial pathogens. Indeed we found in a mouse

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model that influenza A virus transiently alters respiratory and intestinal microflora. These changes revert in parallel to viral clearance, indicating that acute infections do not permanently shape fully established, adult microbial communities. However, at the peak of viral pathogenicity we found a drastic reduction of bacterial content in the small intestine and outgrowth of Enterobacteriaceae in the respiratory tract. We could demonstrate that these changes not only coincide with increased sensitivity to bacterial infection of the lung and intestine but are also causative for better growth conditions of intestinal or respiratory bacterial pathogens.

Our data shed light on the complex ecology of commensal and pathogenic bacteria and how viral infections disturb the natural host protection against pathogens by imbalancing the microbiota.