Host Susceptibility to Post-Influenza Secondary Bacterial Infections

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ABSTRACT

Both female and male Balb/c mice were bred at the Montana State University Animal Resource Center in Bozeman, Montana. The mice enrolled in experiments ranged in age between the ages of 6-13 weeks old.

Mice were infected with 500 pfu (plaque forming units) of mouse-adapted influenza A virus PBS strain on day 0 and/or challenged with 1x10^6 cfu (colony forming units) of Staphylococcus aureus (USA300 LAC strain) on day 3. Mice were monitored daily and body weights and temperatures were recorded. At the time of sacrifice lungs were isolated, processed and plated on TSA plates to determine lung bacterial burden.

RESULTS

Figure 5. No difference in bacterial burden between secondary infection and S. aureus alone. Mice were infected as described in Fig. 3. The temperature and lung bacterial burden was evaluated 8 days post-influenza infection. Results show no significant differences in the lung bacterial burden between mice infected with Flu only and super-infection with the S. aureus on day 3. Data represent mean bacterial burden.

Figure 6. Low concentrations of S. aureus resulted in similar body weight loss as mice infected with influenza alone. Mice were infected with 500 PFU of influenza virus on Day 0, followed by the challenge with one of the three different concentrations of S. aureus on Day 3. The concentrations include 1x10^5 (Red), 1x10^4 (Blue) and 1x10^3 CFU (Green). The average body weights show that when mice are given a secondary infection of S. aureus at day 3, all of the “low” concentrations result in a similar body weight loss as mice infected with Flu only. Data represent mean body weight.

CONCLUSIONS

• The mice infected with a concentration of 1x10^6 CFU of S. aureus showed decreased weight and temperature when mice were infected with influenza.
• At Day 3 post-influenza, super-infections with lower concentrations of S. aureus (1x10^5, 1x10^4, or 1x10^3 CFU) resulted decreased body weight and temperature compared to mice that received a larger dose of S. aureus (1x10^6 CFU).
• Higher bacterial burden occurred in mice that received the lower doses of S. aureus (1x10^4 and 1x10^3 CFU).

FUTURE WORK

Future research involving secondary bacterial infections post-influenza has a very wide range of possibilities. We will further investigate why a higher concentration of S. aureus is less of a burden, compared to a lower concentration. Additionally, we will also determine how the introduction of a triple infection involving S. pneumoniae, at Day 7, will affect the host’s susceptibility.

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INTRODUCTION

Over the past century the human population has witnessed several well-documented pandemics that have impacted not only the United States, but also the world. With the 1918 Spanish Flu, over 500 million people were infected, which resulted in over 50 million deaths. Within these 50 million individuals, approximately 95% resulted from secondary bacterial infections with either Staphylococcus aureus or Streptococcus pneumoniae. Pandemics also occurred in 1957, and 1968 and were caused by the H2N2 and H3N2 influenza viruses, respectively. Although during these times, a decrease in mortality rates were seen due to the advancements in technology and medicine that the antibiotic antibiotics secondary bacterial infections with either Staphylococcus aureus (1957) or Streptococcus pneumoniae (1968) were still prevalent. The most recent pandemic called SARS-CoV-2 in 2009 was caused by a influenza H1N1 strain that underwent an antigenic shift in swine. Even with today’s advancements, it is still difficult to determine the mortality rate globally, though it is estimated that the pandemic caused approximately 200,000 deaths, mainly due to respiratory issues. The Most common organisms found during the 2009 pandemic were Staphylococcus aureus and S. pneumoniae. These studies demonstrate that bacterial super-infections were associated with higher morbidity and mortality during the pandemics in the last century, thus signifying the importance is determining how to prevent them.

HYPOTHESIS

Our previous research demonstrated that at day 3 post-influenza virus infection, susceptibility to secondary bacterial infections decreased compared to the increased susceptibility found at day 7 post-influenza. Therefore, we hypothesized that susceptibility to secondary bacterial infections 3 days after influenza virus infection would allow the host to establish an immunological environment that would protect mice from increased susceptibility to S. pneumoniae super-infection on day 7.

METHODS

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Mice were infected with 500 pfu (plaque forming units) of mouse-adapted influenza A virus PBS strain on day 0 and/or challenged with 1x10^6 cfu (colony forming units) of Staphylococcus aureus (USA300 LAC strain) on day 3. Mice were monitored daily and body weights and temperatures were recorded. At the time of sacrifice lungs were isolated, processed and plated on TSA plates to determine lung bacterial burden.

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