AN IMPACT OF AGING ON RESPIRATORY SYNCYTIAL VIRUS INFECTION IN AIR-LIQUID-INTERFACE CULTURE BRONCHIAL EPITHELIIUM

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Background Elderly people are known to be vulnerable to virus infection. However, this has not been appropriately tested in vitro studies due to a lack of appropriate virus infection models. The aim of this study was to investigate the impact of age on respiratory syncytial virus (RSV) in pseudotratiﬁed air-liquid-interface (ALI) culture bronchial epithelium, which more closely mimic human airway epithelium morphologically and physiological, than submerged cancer cell line cultures.

Methods RSV A2 was inoculated apically to the bronchial epithelium, and time-proﬁles of viral load and inﬂammatory cytokines were analysed in donors with different ages and genders (8 donors).

Results RSV A2 replicated well in ALI-culture bronchial epithelium. The viral peak day and peak viral load were similar between donors at <60 years old (n=4) and >65 years old (n=4) (elderly group), but virus clearance was impaired in the elderly group, and there was a good positive correlation between basal p21 expression and viral load or RANTES (AUC).

AUCs of RANTES and dsDNA (cell damage marker) were statistically higher in the elderly group, also the elderly group showed a trend of higher AUC of CXCL8, CXCL10 and mucin production. The gene expression of p21 (cellular senescence marker) at baseline was also higher in the elderly group, and there was a good positive correlation between basal p21 expression and viral load or RANTES (AUC).

Conclusion Age would be a key factor affecting viral kinetics and biomarkers post virus infection in an ALI-culture model.

Please refer to page A288 for declarations of interest related to this abstract.

S129 AN IMPACT OF AGE ON RESPIRATORY SYNCYTIAL VIRUS INFECTION IN AIR-LIQUID-INTERFACE CULTURE BRONCHIAL EPITHELIIUM

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Methods RSV A2 was inoculated apically to the bronchial epithelium, and time-proﬁles of viral load and inﬂammatory cytokines were analysed in donors with different ages and genders (8 donors).

Results RSV A2 replicated well in ALI-culture bronchial epithelium. The viral peak day and peak viral load were similar between donors at <60 years old (n=4) and >65 years old (n=4) (elderly group), but virus clearance was impaired in the elderly group. Furthermore, area under the curve (AUC) analysis, calculated from viral load peak to the end of sample collection (Day 3 to 10 post inoculation), revealed statistically higher live viral load (PFU assay) and viral genome copies (PCR assay) in the elderly group, and a positive correlation between viral load and age was observed. In addition, the AUCs of RANTES and dsDNA (cell damage marker) were statistically higher in the elderly group, also the elderly group showed a trend of higher AUC of CXCL8, CXCL10 and mucin production. The gene expression of p21 (cellular senescence marker) at baseline was also higher in the elderly group, and there was a good positive correlation between basal p21 expression and viral load or RANTES (AUC).

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infections made up 4% of infections in this peak. The months with the highest number of medical admissions did not entirely correlate with the peaks of the positive viral results, with the greatest number of admissions in January.

**Discussion**

Respiratory viruses are a significant burden on hospitals every year. During the winter of 2022–2023, North Bristol Trust had two peaks, driven by SARS-CoV-2, and then Influenza A combined with SARS-CoV-2. The rise in hospital admissions did not completely follow this, which may represent admissions with post-viral illnesses, but more data would need to be collected to investigate this. This data should help hospitals plan for future peaks in respiratory viral infections, highlighting the importance of strong infection control measures, and preparation for the seasonality of viral infections impacting hospital admissions each year.

Despite anti-viral drugs and vaccines, influenza viruses are still poorly controlled and pose a threat to those who suffer chronic diseases such as COPD and asthma. The most dangerous influenza symptoms are caused by damage to the lung tissue, and repairing this damage is essential for survival. Lung repair is driven by activation of epithelial progenitor cells, but their exact role is not well understood. We infected mice with influenza virus and studied the behaviour of epithelial progenitors and consequent effects on the cellular composition of the recovering lung. We found that the epithelial composition of the lung is changed during the peak and recovery phases of influenza. There is a loss of ciliated and alveolar cells at day 6 post infection, but by day 10 these populations are restored. This recovery correlates with increased activation and proliferation of progenitor cells. Using differential expression and pathway analysis, we found lung basal cells activation and proliferation is fuelled by a switch from lipid metabolism to high energy yield oxidative phosphorylation. Our findings confirm that lung epithelial precursor activation occurs during recovery from influenza, and the reshaping of the lung after infection is fuelled by a change in progenitor metabolism. We suggest a careful balance is struck by lung progenitors after infection: they assist in clearing the infection in the short term, while also preparing to recover the damaged epithelium in the long term.