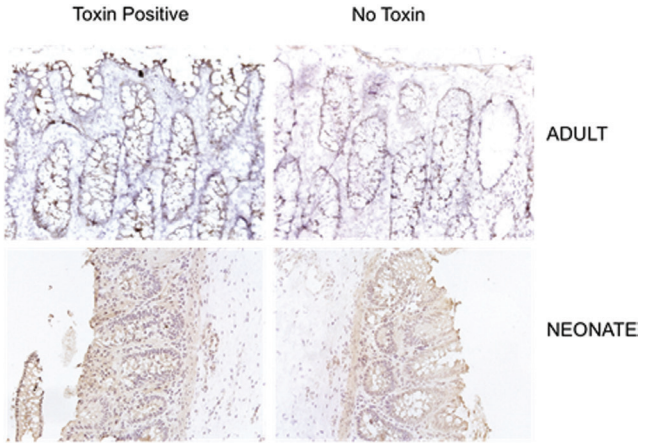
Methods. Tissue from infants (<6 months) and adults > 21 years were studied. Toxin A binding was assessed using an indirect staining method, which included incubation with toxin A (List Labs) and detection with a rabbit polyclonal anti-sera (Lee Labs). A trained pediatric pathologist assessed the extent of staining in a blinded fashion. In other studies, toxin A was labeled with rhenium-188 and incubated with albumin-blocked tissue sections (four-infant and six-adult) for 1 hour. After washing, gamma counts were measured and the average percentage of retained radiolabeled toxin A calculated. Fisher exact tests and ANOVA were used for analyses. All studies were done in compliance with our institutional IRB.

Results. Six of 13 (46%) adult specimens were found to have reactivity on both the apical epithelial surface as well as crypt staining. Another six had reactivity localized only to the basal and lateral surface of the crypts. One specimen demonstrated no reactivity at all. For neonates ($n = 15$), no specimens were found to have reactivity localized to the apical epithelial surface, though four specimens had reactivity at the basal epithelial surface (P value for comparison of apical staining 0.0046) (see figure). Average percentage of retained counts for control (no tissue), infant and adult colon sections were, 0.318 ± 0.147, 0.305 ± 0.079 and 0.48 ± 0.114, respectively ($P = 0.051$).



Conclusion. Immunohistochemistry and radiolabelling studies indicate that neonatal colon section binds *C. difficile* toxin A less strongly and in a different distribution pattern (i.e., without apical staining) when compared with adult colon sections. These findings are consistent with previous animal studies and support the paradigm that a lack of toxin receptors in the infant colon contributes to immunity against *C. difficile* colitis. Additional studies are needed to define the presence of specific receptors and determine if a similar phenomenon applies to toxin B binding.

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628. Short-Term Water-Pipe (Shisha) Smoke Exposure Worsens Lung Inflammation in Mice Infected with Respiratory Syncytial Virus

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Background. Water-pipe smoking (WPS) is becoming popular all over the world and among various populations despite the growing concern about the associated deleterious health effects. Chronic cigarette smoke exposure enhances respiratory syncytial virus (RSV) pathology in mouse airways. However, the effects of exposure to WPS on the course of RSV are not known. Here, we examined the impact of short-term WPS exposure on the course of RSV in a mouse model.

Methods. BALB/c mice were exposed to nose-only mainstream WPS for 30 min/day for 4 consecutive days. Control mice were exposed with the same regimen to air only. At the end of the exposure period, WPS-exposed and control mice were intranasally inoculated with RSV A2 strain. The mice were sacrificed on selected days post-infection. Several endpoints including body weight, markers of inflammation (tumor necrosis factor-α [TNF-α] and interleukin 1β [IL1β]) and oxidative stress (superoxide dismutase [SOD]), histopathology and lung viral copies were evaluated.

Results. On Day 3 post-infection, mice exposed to WPS and infected with RSV exhibited significant weight loss in comparison to control mice ($P = 0.002$), Figure 1. Lung infection with RSV was also associated with increased albumin in bronchoalvelar lavage fluid, a biomarker that distinguishes infection-induced lung injury from WPS-induced lung injury, Figure 2. Other biomarkers of inflammation (TNF-α and IL1β) and oxidative stress (SOD) increased in both types of injuries. In mice exposed to WPS and infected with RSV, the intensity of inflammatory infiltrates (mainly lymphocytes), the size of damage to the distal airway spaces and the size of involved area were clearly higher than in control mice. Despite the increased disease, lung viral load was not significantly affected by exposure to WPS.

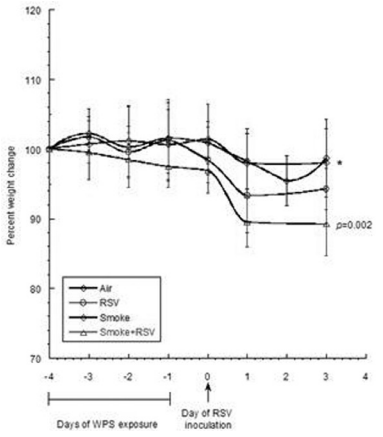

Figure 1. Body weight changes in mice following short-term nose-only water-pipe smoke or air (control) exposure with or without RSV infection. Data (mean ± SD) are percentages of daily weights divided by the starting weight for each condition. The shown p value denotes comparison between (WPS exposed + RSV infected) and (Air exposed only) groups; * indicates the comparison group.

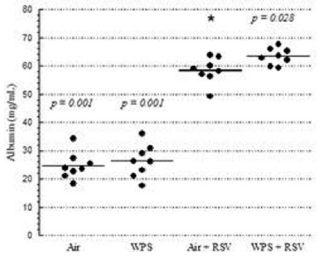

Figure 2. Concentrations of albumin in bronchoalveolar lavage fluid of mice following short-term nose-only water-pipe smoke or air (control) exposure, with or without RSV infection (day 3 post-infection). The shown p values denote comparison between each indicated group and (Air exposed RSV infected) group; * indicates the comparison group.

Conclusion. In this model, short-term water-pipe smoke exposure resulted in severe RSV disease (increased weight loss) and worsened pathology.

Disclosures. **All authors:** No reported disclosures.

629. Blood Transcriptome Variations Predict Infection and Rejection in the Older Kidney Transplant Recipient

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. Compared with younger patients on similar immunosuppression regimens, older solid-organ transplant recipients experience increased rates of infection and death, but decreased rates of rejection. Our previous findings demonstrated increased T-cell immunosenescence and pro-inflammatory monocytes in older patients. This study sought to define the implications of transcriptome alterations for clinical outcomes. The objective of this abstract is to evaluate older vs. younger solid-organ transplant recipients for differential patterns of gene expression associated with infection and rejection.

Methods. Peripheral blood mononuclear cells were isolated from 23 older (≥age 60) and 37 matched younger (ages 30–59) kidney transplant recipients at 3 months after transplantation. RNA extraction was performed on banked PBMCs. Isolated RNA was converted to fluorescent cRNA and hybridized to Illumina Human HT-12 v4 BeadArrays. Gene expression values were quantile-normalized and log2-transformed for mixed effect linear model analyses to identify differential expression as a function of age, adjusted for induction type, donor type, and sex. Statistical analysis was performed using R software.

Results. Genes differentially expressed in older patients revealed an over-representation of pro-inflammatory genes and a down regulation of genes associated with the CD8 immune response. Patients who went on to develop infection demonstrated an increase in IRF transcription factor activation and plasmacytoid dendritic cell activity. Patients who developed rejection demonstrated an increase in myeloid lineage immune cell activity.

Conclusion. Differential patterns of gene expression were observed in patients who developed infection in the first year after kidney transplantation. These findings were distinct from the gene expression changes associated with development of rejection. These findings may explain the mechanism behind vulnerability to infection in older transplant patients. In addition, monitoring of changes in gene expression may provide an avenue for patient monitoring after transplantation as well as individualization of immune suppression after solid-organ transplantation.

Disclosures. **All authors:** No reported disclosures.