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 rhodamine-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, 0.365 ± 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.

Disclosures. All authors: No reported disclosures.

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 RSV pathology in mouse airways. 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 (2 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 cell activity. Patients who went on to develop 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.
630. Identification of a Depressed Mucosal Immune Environment in HIV Infection
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Background. Among patients with human immunodeficiency virus (HIV), pulmonary complications are a common cause of morbidity and mortality. Emerging evidence suggests that respiratory viruses contribute to this disease burden. Although HIV is known to alter other mucosal surfaces including the GI tract and vagina, its effect on the upper respiratory mucosa, the primary target of respiratory viruses, has not been well described. We sought to characterize the effect of HIV on the upper respiratory mucosal immune environment.

Methods. Ten HIV-infected patients and 10 sex-matched uninfected controls were enrolled. Subjects were ages 18–49, non-smokers, and otherwise healthy. HIV-infected subjects had complete viral load suppression for at least 6 months prior to participation. Subjects provided serum samples and underwent nasal mucosal sampling procedures—epithelial lining fluid (ELF) collection, nasal lavage (NLF) and nasal biopsies. Serum, ELF, and NLF were analyzed using ELISAs targeted at pro-inflammatory cytokines. NLF was analyzed by flow cytometry for nasal-specific immune cells.

Results. T-cells in NLF including both CD8 and CD4 populations, were significantly decreased in HIV-infected compared with uninfected subjects. We also found decreased numbers of neutrophils. Additionally, we identified diminished levels of IL-16 in ELF, a T-cell chemoattractant in HIV-infected subjects; however, all other cytokines and chemokines were similar between the two groups. These findings were in contrast to an earlier study we had done in six HIV-infected men with variable levels of HIV control and age-matched control subjects which also demonstrated decreased levels of other pro-inflammatory cytokines, including IL-1β, IL-8, and IL-5 in those with HIV.

Conclusion. The mechanism underlying the morbidity and mortality of respiratory viruses in HIV-infected patients is unclear. However, we identified that HIV infection does result in relative upper respiratory immune suppression, including in both CD4 and CD8 T-cell populations, despite otherwise excellent systemic control of HIV. We hypothesize that this suppression persists in viral infection leading to an impaired immune response and prolonged respiratory virus replication, contributing to the observed burden of disease in this population.

Disclosures. All authors: No reported disclosures.

631. Markers of Immune Response in Patients with Acute, Chronic and Fatal Infection with Chikungunya Virus in Colombia During the 2015 Epidemic
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Background. After 2014 Chikungunya virus (CHIKV) became in public health problem in west world with disability and deterioration in the quality of life that it generates and fatal complications. The objective of this study was, to determine the markers of immune response in patients with acute, chronic and fatal infection by CHIKV in Colombia, during the epidemic in 2015.

Methods. Cross-sectional study, carried out in serological samples of patients with laboratory-confirmed diagnosed for acute cases (AC), chronic cases (CC) and fatal CHIKV cases (FC). The samples were supplied by the virology laboratory of the National Health Institute and through commercial kit 13 cytokynes were processed

Results. One hundred sixty-four samples were analyzed. 50 from patients with AC, 25 from FC due to CHIKV and 89 from patients with CC. The average age was 48.2 years ± 24.4 SD. AC were more prevalent in the extreme ages of life (<10 years and >70 years), and the CC in young adults and intermediate adults (20–60 years) (P < 0.05). The median time taken for the sample was 4.2 [IQR3:75] for AC. Ten plasma cytokines (INF-gamma, IL-10, IL-13, IL-17a, IL-2, IL-4, IL-5, IL-6, TGF-a, TNF-a) were significantly elevated in patients deceased compared with patients with acute infection (P < 0.005). In patients with FC, IL-6 was the pro-inflammatory cytokines with the highest median value and among the anti-inflammatory cytokines, IL-10. Exception of GM-CSF and IL-12, the comparison of medians between FC and patients with CC (INF-gamma, IL-10, IL-13, IL-17a, IL-2, IL-4, IL-5, IL-6, LT-α/TNF-β, TGF-α, TNF-a) presented statistically significant results.

Conclusion. This is the first study conducted in Colombia, which provides evidence on cytokine levels in the acute, fatal and chronic outcome of patients with CHIKV. AC had an increase in IFN-γ, IL-2, IL-4, IL-10, IL-17a and TNF-a cytokines, which if persisted elevated for more than 3 months with some decreased levels of IFN-γ and IL-6, maybe progression to chronic phase. If in addition of acute phase cytokines, IL-2, IL-4, IL-13, LT-α/TNF-β, TGF-α, increase the disease maybe move to a chronic or fatal. Cytokines, especially IL-6, is becoming a tool for monitoring, evolution and prognosis of CHIKV disease.

Disclosures. C. Arteta-Acosta, National Health Institute, Universidad del Norte: Collaborator, Research support. J. Acosta-Reyes, National Health Institute, Universidad del Norte: Collaborator, Research support.

632. Recurrent Pneumococcal Meningitis in Adults
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Background. Recurrent pneumococcal meningitis is uncommon in adults. Underlying disorders include humoral immune deficiency, cerebrospinal fluid (CSF) leaks, asplenia or cochlear implants. We evaluated two women who each had two separate episodes of Streptococcus pneumoniae meningitis. Both had histories of systemic lupus erythematosus (SLE).

Methods. Immune evaluations were negative except for occasional Howell-Jolly bodies on their blood smears. Immunoglobulin levels were normal. SLE patients were tested for their post vaccine responses to pneumococcal polysaccharide vaccine-23 (Pneumovax 23). Complement levels: C3, C4 and CH50 were normal. Lab but not clinical markers of SLE were present. In both patients, the spleen was anatomically present. In both, there was near absent splenic function on a heat damaged tagged RBC TC 99 m spleen scan. A literature search was carried out using Medline/PubMed and Google.

Results. Streptococcus pneumoniae infections make up about 6–18% of all bacterial infections in SLE; most are pneumonia. Although several cases of pneumococcal sepsis/shock have been reported in such patients, we could not find similar cases of recurrent pneumococcal meningitis in patients with inactive, untreated SLE.

Conclusion. Recurrent pneumococcal meningitis is uncommon in adults and is usually associated with humoral immune deficiency, CSF leaks or cochlear implants. Complement deficiency (primary) is rarely found. Sickle cell disease and other hemoglobinopathies have also been associated with pneumococcal sepsis and meningitis. SLE and other autoimmune connective tissue disorders are associated with functional asplenia, even when clinically inactive. These patients are at increased risk for invasive pneumococcal disease. Functional asplenia in adult patients is often overlooked in patients with severe or recurrent infections caused by polysaccharide encapsulated bacteria. We report on two patients with recurrent pneumococcal meningitis and SLE. Functional asplenia and complement deficiency are the primary factors when such patients develop invasive or recurrent infections. Demonstration of a poorly functional spleen by a TC 99 heat denatured RBC spleen scan when the spleen is anatomically present confirms the diagnosis.

Disclosures. All authors: No reported disclosures.

633. HIV-1 Vpu Immune Correlates in a Narrow-Source Infection Cohort: Impact of ADCC and KIR-Associated Pressure
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Background. We investigated vpu diversity and immune correlates of sequence variation in a unique cohort of former plasma donors (FPDs) from rural China who were infected with a very narrow range of clade B HIV-1 strains.