Conclusion. During the acute phase of infectious disease with severe inflammation, iron levels were immediately decreased due to enhanced production of hepcidin-25. Understanding of host iron status may be essential for effective use of siderophore cephalosporin, with a unique mechanism of action involving the use of bacterial iron uptake systems.

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637. B-Lactam (BL) Antibiotics Promote an IL-1β Response in Patients with *Staphylococcus aureus* Bacteremia (SaB)

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Background. BL therapy has been associated with reduced SaB duration compared with non-BL therapy. It has been shown that patients with SaB who fail to generate increased serum IL-1β are at risk for prolonged SaB (> 4 days duration), a predictor of mortality. This suggests a major role for the IL-1β host response in prompt clearance of SaB. Furthermore, BL result in reduced peptidoglycan cross-linking, reduced peptidoglycan O-acetylation, and increased alpha-toxin expression, all of which have independently been shown to enhance IL-1β release. This study aims to show that BL therapy results in a more robust IL-1β host response compared with non-BL therapy to explain, in part, more rapid SaB clearance.

Methods. Fifty-nine patients (47 MRSA and 12 MSSA) with diverse SaB sources, including endovascular, extravascular (e.g., pneumonia), and catheter-related infections were included. In the first 48 hours, patients were treated with either BL, including oxacillin, ceftaroline, or cefazolin (n = 24), vs. non-BL vancomycin or daptomycin (n = 35). IL-1β concentrations were determined by ELISA on serum samples obtained on Days 1, 3 and Day 7 after bacteremia onset and compared between groups by Mann–Whitney U test.

Results. Patients in BL and non-BL groups had similar IL-1β concentrations on Day 1 of bacteremia (median BL 6.1 pg/mL vs. non-BL 2.8 pg/mL, P = 0.090). BL-treated patients had significantly higher IL-1β serum concentrations on Day 3 (median 7.54 mg/mL vs. 1.9 pg/mL; P = 0.007) and Day 7 (12.52 pg/mL vs. 1.56 pg/mL, P = 0.016) when compared with non-BL-treated patients. BL therapy resulted in 23% and 105% increase in IL-1β at Days 3 and 7, respectively, while non-BL treatment resulted in 32% and 44% reduction in IL-1β. The median duration of SaB was similar between BL and non-BL-treated patients (2.5 vs. 2.0 days, respectively, P = 0.590).

Conclusion. Given that a lack of inflammasome-mediated IL-1β production is associated with prolonged SaB, the significant increases in IL-1β levels in patients treated with BL has important therapeutic implications. Previously observed reduced duration of MRSA bacteremia with the addition of BL to vancomycin may have its basis on enhancing IL-1β release. A therapeutic regimen of vancomycin or daptomycin in combination with BL to treat MRSA bacteremia and use of BL therapy in MSSA bacteremia is strongly advised to improve outcomes based on these results.

Disclosures. **G. Sakoulas**, Allergan: Consultant and Speaker, Consulting fee and Speaker honorarium. Sunovion: Speaker, Speaker honorarium. The Medicines Company: Speaker, Consulting fee. Paratek Pharmaceuticals: Consultant, Consulting fee. Cidara Therapeutics: Scientific Advisor, None. Arsanis Pharmaceuticals: Scientific Advisor, None. **W. Rose**, Merck: Grant Investigator, Research grant.

638. CMV-Specific T-Cell Immune Responses in Older vs. Younger Kidney Transplant Recipients

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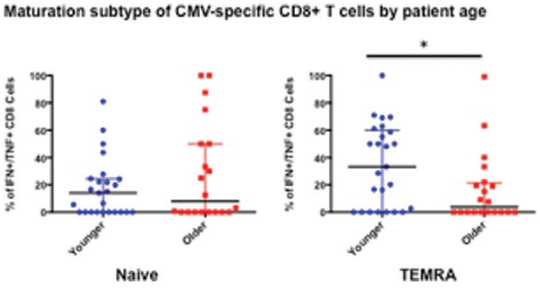
Background. Compared with younger patients on similar immunosuppression regimens, older solid-organ transplant recipients experience increased rates of infection and death, but decreased rates of rejection. The mechanism behind these differences has yet to be defined, but may be related to ÒinflammagingÓ driven by CMV infection. The objective of this study was to evaluate older vs. younger solid-organ transplant recipients for CMV-specific T-cell immune responses.

Methods. Peripheral blood mononuclear cells were isolated from 20 older (^{3} age 60) and 25 matched younger (ages 30–59) kidney transplant recipients at 3 months after transplantation. Eight recipients were high risk by CMV serology (D+/R−) and 37 were intermediate risk (D−/R+). Overlapping CMV peptide pools were used for stimulation. Intracellular staining to determine cytokine stimulation was performed by multiparameter flow cytometry. Statistical analysis was performed using Jmp Pro 11 software.

Results. There was no association between patient age and CMV risk status (P = 0.728). There was no difference between older and younger kidney transplant recipients in release of IFNγ, TNFα, or IL-2 from CD4+ or CD8+ T cells in response to CMV antigen stimulation. However, Older recipients had similar frequencies of CD8+ naive cells but decreased frequency of CD8+ terminally differentiated effector memory CD45RA+ (TEMRA) T cells releasing both IFNg and TNFa (P = 0.037) (figure). Interestingly, development of CMV viremia was associated with a weaker CMV-specific immune response: Patients who had a history of CMV viremia had a decreased frequency of CD8+ TEMRA cells releasing both IFNγ and TNFα (P = 0.041).

Conclusion. Older kidney transplant recipients demonstrated a decreased frequency of CMV-specific polyfunctional CD8+ TEMRA T cells. This impaired memory T-cell response to CMV suggests a possible mechanism for the increased vulnerability of older recipients to CMV infection or reactivation, which may in turn worsen age-related immune dysfunction. Furthermore, patients with subsequent CMV viremia had a decreased frequency of CMV-specific polyfunctional CD8+ TEMRA T cells. This finding may explain patient vulnerability to CMV viremia despite modern protocols for antiviral prophylaxis.



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

639. Indoleamine 2,3 Dioxygenase, Age, and Chronic Immune Activation in HIV Patients

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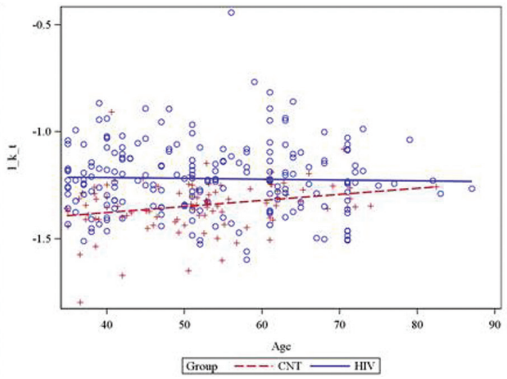
Background. Immune activation complicates HIV despite antiretroviral therapy (ART). Indoleamine 2,3 dioxygenase (IDO) catabolizes tryptophan (T) to kynurenine (K), regulating immune activity. IDO activity increases in HIV patients and non-HIV patients with age. This study examines the relationship of IDO activity, bacterial translocation, and ageing in HIV patients on ART. We hypothesize that increased IDO activity caused by bacterial translocation is a factor in inflammation during aging.

Methods. Samples and data from virologically suppressed HIV patients on ART in specific age strata were obtained from the Centers for AIDS Research Network of Integrated Clinical Systems. Samples and data from age and sex-matched healthy controls were obtained from the Multicenter AIDS Cohort Study and the Women's Interagency HIV Study. The ratio of K to T (K/T) and neopterin were used as indicators of inflammation; 16S ribosomal DNA (16S rDNA) and lipopolysaccharide (LPS) served as markers of bacterial translocation. Log transformation, chi-square tests, t-tests with Satterthwaite adjustment for continuous data, ANOVA, and ANCOVA homogeneity of slopes model were used.

Results. Samples and data from 205 HIV patients and 99 matched controls were analyzed. HIV patients had higher K/T values across all ages. Younger HIV patients had greater K/T values than older healthy controls. Age, sex or race was not associated with differences in K/T. Current CD4 count or CD4 nadir had no association with K/T ratio. For HIV patients, there was an inverse relationship between LPS detection and K/T. For controls, there was no association between LPS and K/T. There was no association between PCR detection of 16S rDNA and K/T ratio in HIV patients or controls. Both groups had positive association between K/T ratio and neopterin.

Conclusion. HIV patients have elevated K/T, even at younger ages, despite virologic control. The main hypothesis that K/T increases with advancing age was not supported in this cohort. Also, unlike other published literature, CD4 nadir, LPS, and 16S rDNA did not correlate with K/T ratio. This study suggests there may be an alternative driver of immune inflammation in well-controlled HIV patients other than bacterial translocation.

Figure 2. Age and K/T ratio.



Disclosures. **A. Mellor**, NewLink Genetics: Consultant, Consulting fee and Licensing agreement or royalty.