Results. Echos from 29 KD, 30 IKD, 28 febrile, and 27 healthy patients were reviewed. The initial echo of 41% of KD and 43% of IKD groups met echo criteria for diagnosis of IKD and 55% and 57%, respectively, had CA dilation or aneurysm. Among febrile patients, 7 (25%) had an abnormal CA size of which 4 (14%) met echo criteria for IKD. In the healthy patients, four (15%) had abnormal CA of which two (7.4%) met echo criteria for IKD. Among patients with a positive read, the median number of readers who read a CA as a dilated was similar for each group. Furthermore, of all patients meeting echo criteria for IKD, 90% had aneurysmal CA dilation.

Conclusion. Although CA abnormalities diagnostic of KD were commonly present at time of diagnosis in patients with KD or IKD, these findings were also present in some healthy and some febrile patients. Diagnosis of IKD in febrile children using echo criteria may result in an over-diagnosis of KD.

Disclosures. All authors: No reported disclosures.

644. How Antibody Isotype Affects Anti-Capsular Antibody Protection Against Carbapenem-Resistant Klebsiella pneumoniae Infection
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Background. New monoclonal antibodies (mAb) are being developed against infectious disease. However, antibody isotype is an important consideration, as different IgG variants interact different with Fc receptors and differ in avidity due to Fc structural differences. Our recent anti-capsular murine IgG, mAb 17H12 was shown to mediate protection against clone 2 72K carbapenem-resistant Klebsiella pneumoniae (Kp). However, our previous studies showed an IgG, mAb to perform better than an IgG, mAb in mediating infection against a carbapenem-sensitive Kp isolate. Therefore, we sought to determine whether differences in antibody isotype contribute to differences in protection against CR-Kp infections.

Methods. We treated IgG, producing 17H12 parent hybridomas with LPS and IL-4 to generate isotype variants which were subcloned by sib selection. This yielded an IgG, producing clone which was sequenced and compared with the complementarity-determining region (CDR) sequence of the parent. We then compared binding kinetics of the two mAbs to CR-Kp capsular polysaccharide by ELISA. Opsonophagocytosis by macrophages was compared between CR-Kp strains pre-opsonized with the IgG1 or IgG2 mAb. Finally, mice were infected intratracheally with CR-Kp pre-opsonized with either IgG1 or IgG2 mAbs and organ burdens were compared after 24 hours.

Results. Sequence analysis showed the IgG2 antibody sequence to be identical to the 17H12 IgG1 parent. Interestingly, the IgG2 antibody bound at nanomolar affinity, but 10-fold less than the parent, suggesting loss of affinity or avidity. IgG1-opsonized CR-Kp phagocytized by macrophages 40-60% less than IgG2-opsonized CR-Kp. However, both antibodies performed comparatively in vivo, reducing bacterial burden in the lung, liver and spleen of intratracheally infected mice by an average of 3 log.

Conclusion. The IgG2 isotype variant of mAb 17H12 appears to have inferior binding and in vitro efficacy when compared with its IgG1 parent, despite having the same CDR region. However, in vivo efficacy is unaffected in our model. Future studies plan to further analyze the differences in binding kinetics between these two antibodies, as well as their ability to bind pro and anti-inflammatory Fc Receptors and mediate the host response to CR-Kp infection.

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645. Mucosal-Associated Invariant T Cells in Renal Tissue From Patients With Recurrent Urinary Tract Infections
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Background. Mucosal associated invariant T (MAIT) cells are innate-like T cells involved in the antibacterial and fungal response by recognizing riboflavin metabolites produced by these organisms. MAIT cells are present in blood and are highly abundant in the mucosa of the liver, lungs and intestines. In murine models of urinary tract infection (UTI), MAIT cells appear to play a role in the antibacterial response to UTI. MAIT cells remain in renal tissue in a quiescent state. However, in some samples more tissue resident phenotype than MAIT cells in rejection kidneys. These findings may suggest that MAIT cells play a role in the first-line defense in the kidney and that after RUTI, MAIT cells remain in renal tissue in a quiescent state.

Methods. The mean percentage of MAIT cells within the lymphogate was higher in RUTI kidneys (2.24%) compared with the rejection kidneys (0.14%) and the consurgically removed because of renal cell carcinoma (adjacent nontumorous tissue) (0.05).

Results. The mean percentage of MAIT cells within the lymphogate was higher in RUTI kidneys (2.24%) compared with the rejection kidneys (0.14%) and the consurgically removed because of renal cell carcinoma (adjacent nontumorous tissue) (0.05).

Conclusion. MAIT cells are present in renal tissue that is or has been subjected to an immunologic response. MAIT cells in RUTI kidneys display a more quiescent and in some samples more tissue resident phenotype than MAIT cells in rejection kidneys. These findings may suggest that (I) MAIT cells play a role in the first-line defense in the kidney and (II) that after RUTI, MAIT cells remain in renal tissue in a quiescent state.

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646. Activated Macrophages as Pathogenesis Factors in Ebola Virus Disease in Humans
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Background. Ebola virus disease (EVD) is associated with elevated cytokine levels that are more pronounced in fatal cases. This type of hyperinflammatory state is reminiscent of other inflammatory disorders, such as macrophage activation syndrome (MAS) or hemophagocytic lymphohistiocytosis (HLH). These are both part of a spectrum of rheumatologic phenomena characterized by both macrophage and T-cell activation. These disorders can be secondary to infection, malignancy, underlying rheumatologic disorder, or, paradoxically, immune deficiency.

Methods. Two cohorts of EVD patients were evaluated with respect to common plasma markers of HLH/MAS. Immunohistochemistry was used to evaluate tissue macrophages and viral antigens in various tissues from fatal cases of EVD.

Results. Neither fibrinogen nor soluble IL-2 receptor were significantly different between fatal and nonfatal cases. However, elevated levels of triglycerides, ferritin and noreactivity for CD163 cells in host tissues was observed in fatal cases, predominantly in areas of extensive immunostaining for EBOV antigens.

Conclusion. These data suggest that host macrophage activation contributes to EVD pathogenesis and that directed anti-inflammatory therapies could be beneficial in the treatment of EVD.

Disclosures. All authors: No reported disclosures.

647. Characterization and Development of Human Monoclonal Antibodies to Pneumococcal Serotype 3
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Results. Echos from 29 KD, 30 IKD, 28 febrile, and 27 healthy patients were reviewed. The initial echo of 41% of KD and 43% of IKD groups met echo criteria for diagnosis of IKD and 55% and 57%, respectively, had CA dilation or aneurysm. Among febrile patients, 7 (25%) had an abnormal CA size of which 4 (14%) met echo criteria for IKD. In the healthy patients, four (15%) had abnormal CA of which two (7.4%) met echo criteria for IKD. Among patients with a positive read, the median number of readers who read a CA as a dilated was similar for each group. Furthermore, of all patients meeting echo criteria for IKD, 90% had aneurysmal CA dilation.

Conclusion. Although CA abnormalities diagnostic of KD were commonly present at time of diagnosis in patients with KD or IKD, these findings were also present in some healthy and some febrile patients. Diagnosis of IKD in febrile children using echo criteria may result in an over-diagnosis of KD.

Disclosures. All authors: No reported disclosures.
648. Urinary Tract-Associated Escherichia coli Bacteremia Strains Are Genetically More Virulent than Those Originating From Non-urinary and Neutropenic Infective Foci

Methods. We sorted individual PPS3-specific memory B cells from PBMCs isolated on days 0 and 7 post-vaccination from pneumococcal polysaccharide (PPS3)-based vaccine (Pneumovax or Prevnar13) recipients using fluorescently labeled PPS3. Immunoglobulin heavy (lgH) and light (lgL) chains were sequenced, cloned into IgH and k or a vectors, and expressed in HEK-293 cells. PPS3 specificity was confirmed using ELISA.

Results. Here, we report the first PPS3-specific humAbs isolated: 5 used lambda light chains and two used kappa light chains. Six of these humAbs used variable heavy 3 (VH3) IgH gene elements. Kappa humAbs used VH3-30 or VH3-37, while lambda humAbs used VH3-3, VH3-72 or VH3-23. Sequence analysis revealed somatic mutations in complementary determining as well as framework regions. Initial studies show that some humAbs aggregated in vitro in a V-region dependent manner ongoing to identify specific determinants of PPS3 binding and biological efficacy against ST3 in vitro and in vivo.

Conclusion. The results of this study provide further understanding of the biology of PPS3 antibodies and may facilitate design of adjunctive immunotherapy to treat and prevent ST3 disease.

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649. The Clinical Significance of Sequence Type 17 of Vancomycin-Resistant Enterococcus faecium

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Background. Streptococcus pneumoniae is the main bacterial cause of pneumonia in the United States and globally. Although pneumococcal conjugate vaccines are highly effective against invasive pneumococcal disease, they are less effective against pneumococci, particularly in the elderly and those with immunity deficiency. Given the additional challenge of antibiotic resistance, immunotherapy holds promise for treatment of pneumococcal pneumonia. The current PCV13 vaccine is less effective against serotype (ST-3), which carries a higher risk of mortality than other vaccine-included STs. Our group has previously identified murine monoclonal antibodies (mAb) to ST3 capsular polysaccharide (PPS3) that are protective in experimental models of sepsis and pneumonia. The aim of the present study is to isolate and develop PPS3-specific human monoclonal antibodies (humAbs) as adjunctive immunotherapy for pneumonia.

Methods. Structure-function relationship studies are used to define the diversity to ensure adequate coverage of strains associated with site-specific disease.

Results. Enterococcus faecium more prevalent amongst strains associated with UTI-foci vs. non-UTI-foci amongst immunocompetent patients. UTI-foci vs. non-UTI-foci in immunocompetent patients. Hence, for every unit increase in VF score, the odds of a bacteremia strain originating from UTI-foci increased 1.01–1.46, \( P < 0.0001 \) and recurrence was included in each cohort. There were six cases and 10 cases of subsequent bacteremia in cohorts ST17 and non-ST17, and 1-year VREF bacteremia free rates were 85.9% and 90.2%, respectively. There was no significant difference of subsequent bacteremia (\( P = 0.28 \)) and recurrent urinary tract infection/urinary tract infection (OR 1.21, 95% CI, 1.32–12.29, \( P = 0.015 \)). Of 16 patients who had developed to subsequent VREF bacteremia, 12 VREF blood isolates could be analyzed. Only six cases (50%) of rectal and blood isolates had identical ST, whereas all available ST17 VREF cases (four cases) had identical ST and PFGE pattern (Figures 1 and 2). Patients who had identical ST isolates had shorter time difference than those who had non-identical ST isolates (\( P = 0.041 \)).

Conclusion. In our study, ST17 VREF was risk factors of subsequent bacteremia and the strain that showed strong concordance between rectal and blood isolates. Further study is needed to improve clinical outcome of patients carrying VREF using genotype data of rectal VREF isolates.

Figure 1: Rectal isolates Blood isolates

Figure 2: Blood isolate not collected

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