demographic and infection characteristics were collected. A 10-multiplex TH1/TH2 cytokine analysis was performed using electrochemoluminescence with the MesoScale Discovery platform analyzed by Mann–Whitney U.

Results. Patients’ median values were significantly elevated and above the normal range in CF for IL-1β (P = 0.029), IL-10 (P = 0.018), TNF-α (P = 0.042), and IL-6 (P = 0.006) (figure). Epidural abscess source was associated with CF; but no other host or pathogen characteristics correlated to outcome. Patients infected with isolates with \( \text{VAN MIC} = 2 \text{mg/L} \) (by Etest and broth dilution) had lower concentrations of IL-1β and IL-10 (P = 1.5 mg/L). In ROC analysis, IL-1β, IL-10, TNF, and IL-6 were higher sensitivity and specificity predictors of CF (AUC 0.65–0.71; 0.006).

Conclusion. A suboptimal host immune response to SAB at presentation predicts adverse clinical outcomes. IL-10, TNF-α, and IL-6 serum concentrations appear to reflect immunopathology in patients with SAB. These predictive markers may be considered in therapeutic clinical decision-making, such as escalation of alternative therapies in high-risk patients and/or de-escalation treatment in low-risk patients. These data offer steps toward further refining therapeutic precision for patients with SAB beyond the standard clinical or microbiological metrics that are employed in current practice.

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413. Differences in Inflammatory Mechanisms in Pseudomonas aeruginosa and Staphylococcus aureus Infections in Cystic Fibrosis Melissa S. Phuong, BHSc; Rafael E. Hernandez, MD, PhD; and Subash Sad, PhD; \(^1\)University of Ottawa, Ottawa, ON, Canada; \(^2\)University of Washington, Seattle, Seattle, Washington

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Background. Chronic bacterial lung infections are the primary cause of morbidity and mortality in cystic fibrosis (CF). The most common CF pathogens, Pseudomonas aeruginosa (P. aeruginosa) or Staphylococcus aureus (S. aureus), are common commensal or environmental organisms that adapt to the CF lung. We sought to investigate whether adaptation from early lung colonizer to chronic pathogen alters the bacterial effects on host inflammation.

Methods. P. aeruginosa (\( n = 25 \)) and S. aureus (\( n = 25 \)) isolates from CF patients with early and chronic infections were acquired from Seattle Children’s CF Environmental (\( n = 8 \)) and clinical, non-CF P. aeruginosa (\( n = 8 \)) isolates were obtained from the University of Ottawa. P. aeruginosa reference strain PA14 and PA14 transposon mutants for TSS and flagellin were used to observe the relationship between cell death and cytokine production. We infected THP-1-derived macrophages (PMA differentiated) \( \text{in vitro} \) for 3 hours with various MOIs. We subsequently measured cell death of THP-1-derived macrophages using neutral red assay and cytokine production using ELISAs.

Results. Infections with PA14 mutants and non-CF P. aeruginosa isolates demonstrated that rapid cell death of THP-1-derived macrophages caused a reduction in cytokine production relative to strains that did not cause as much cell death. At 10 MOI, early P. aeruginosa isolates from CF patients induced more THP-1-derived macrophage cell death compared with chronic isolates (\( P < 0.001 \)). Chronic P. aeruginosa isolates induced greater production of TNF, IL-8, and IL-6 (\( P < 0.01, P < 0.001 \), and \( P < 0.001 \), respectively) compared with early strains. No difference in IL-1β production was observed. When controlling for cell death between the two groups by using heat-killed bacteria, only the difference maintained was in TNF production (\( P < 0.01 \)). Between early and chronic S. aureus isolates, the one difference observed was greater IL-8 production among early isolates (\( P < 0.01 \)).

Conclusion. Chronic P. aeruginosa isolates from CF patients induce less cell death compared with TNF, IL-8, and IL-6 production compared with early isolates. This suggests that P. aeruginosa producing chronic infections induce inflammatory signals that may contribute to increased morbidity among CF patients.

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414. Developing Digital Phenotypes of Primary Immune Deficiencies Using Machine Learning on a Large Electronic Health Record Database Leo Meister, MSc; Christie Zerbo, MSc; Luigi D. Notarangelo, MD; \(^5\)Mandeep S. Kadri, MD, MSc; \(^6\)D. Rebecca Prevots, PhD; and Emily Ricotta, PhD, ScM; \(^1\)National Institute of Allergy and Infectious Diseases, National Institutes of Health, Rockville, Maryland; \(^2\)Laboratory of Clinical Immunology and Microbiology, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland; \(^3\)NIH Clinical Center, Bethesda, Maryland; \(^4\)National Institutes of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

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Background. More than 350 genetic disorders cause immune deficiencies; given the rarity of these conditions, in-depth study of infections associated with primary immune deficiencies (PID) requires extremely large sample sizes from broad populations. Using a large electronic health record (EHR) dataset, we linked clinical and microbiologic data to develop digital phenotypes for PID.

Methods. Using the Cerner Health Studies EHR dataset from 2009 to 2017 we extracted clinical and microbio logic data for hospitalizations from patients <18 years old with ICD9/10 PID diagnoses and ≥1 positive culture for infection. Machine learning models were used to identify key features to predict PID diagnosis. Features included patient and hospitalization characteristics; infectious agent and infection site; and selected comorbidities. Model validation was done using the area under the receiver operating characteristic (AUC) curve.

Results. Overall 3136 patients with a PID were identified (Table 1). The 10 most common pathogens identified by PID are listed in Table 2. The models classified DiGeorge syndrome (positive predictive value 49%), functional disorders of polymorphonuclear neutrophils (PMN) (PPV 43%), and common variable immunodeficiency (CVID) (PPV 47%) better than combined immunodeficiency (CID) (PPV 20%); the overall true positive rate was 47% with an AUC of 0.73. Predictive features for each PID were as follows: CVID—having enteritis, hypertension, and pneumonia (Figure 1a); PMN—having hypoxia and hypertension (Figure 1b); DiGeorge syndrome—having congenital deformities and not having hypertension (Figure 1c); CID—finding Staphylococcus aureus in a wound or Escherichia coli in the blood were predictive of CID (Figure 1d).

Conclusion. Early models demonstrate some discrimination, specifically for more common PIDs (CVID) and those with highly identifying factors (DiGeorge syndrome). These models can be improved by including a wider array of clinical data, and they provide a first look at a new methodology to digitally phenotype PIDs for future diagnostic use.

Table 1. Patient counts by PID diagnosis

| PID Diagnoses                                | Number of Patients | Percentage of Patients |
|----------------------------------------------|--------------------|------------------------|
| Common Variable Immunodeficiency             | 450                | 39.3%                  |
| DiGeorge Syndrome                           | 447                | 35.6%                  |
| Functional Disorders of Polymorphonuclear Neutrophils | 307                | 24.6%                  |
| Combined Immunodeficiency - Unspecified      | 182                | 13.8%                  |
| Total                                        | 1544               | 100%                   |

**Table 2: Most frequent infections per PID diagnosis**

| Diagnosis                                                                 | Isolated (%) | Number of Patients | Percentage of Patients |
|--------------------------------------------------------------------------|--------------|--------------------|------------------------|
| *Staphylococcus aureus*                                                  | 63.2%        | 262                | 13%                    |
| *Escherichia coli*                                                        | 22.8%        | 177                | 9%                     |
| *Pseudomonas aeruginosa*                                                 | 14.5%        | 115                | 6%                     |

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