ASSOCIATIONS BETWEEN SERUM C3 CONCENTRATIONS AND CLINICAL OUTCOMES IN PEDIATRIC ACUTE RESPIRATORY DISTRESS SYNDROME (PARDS)

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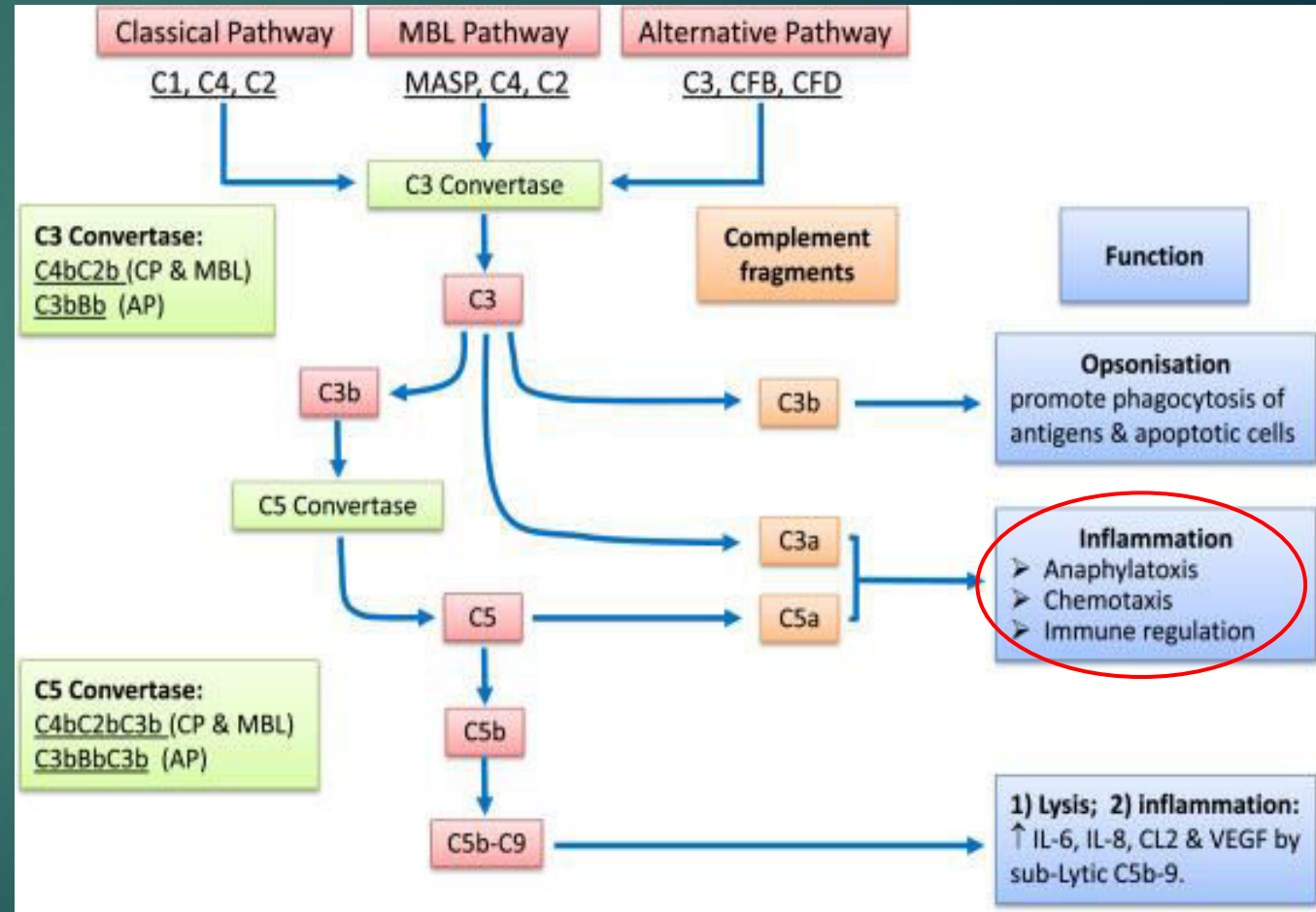
PEDIATRIC CRITICAL CARE FELLOW, PGY-5

Background

- Pediatric Acute Respiratory Distress Syndrome (PARDS) is commonly regarded as one of the most difficult conditions to manage in the pediatric intensive care unit

- Characterized by acute lung injury that occurs within 7 days of either a direct (pulmonary) or indirect (extrapulmonary) insult, which triggers an inflammatory cascade, leading to alveolar edema and subsequent hypoxemic respiratory failure

- The complement system has been shown to play a pivotal role in the innate immune and inflammatory responses and there have been several studies evaluating the role of complement in acute respiratory distress syndrome (ARDS)

- There have been conflicting results regarding complement activation as being protective versus harmful in the ARDS cohort

- No pediatric specific studies evaluating this relationship in ARDS currently exists

Study Objective and Hypothesis

- Objective:
  - To evaluate associations between serum C3 concentrations and various clinical outcomes in a critically ill pediatric cohort with PARDS

- Hypothesis:
  - Lower day 1 serum C3 concentrations, consistent with increased complement system activation, are associated with worse clinical outcomes, specifically, worse illness severity scores, the development of acute kidney injury (AKI), longer duration of mechanical ventilation, longer ICU stays and increased mortality

Targeting the Complement System for the Management of Retinal Inflammatory and Degenerative Diseases, (Heping, et al, EJP, 2016)

Study Design and Methods

▶ Data were collected from a multicenter observational study of pediatric intensive care unit (PICU) patients across 5 PICUs from 2008 to 2016

▶ 234 pediatric patients aged 1 month to 18 years old and meeting the American European Conference Consensus (AECC) criteria for ARDS

▶ Using Wilcoxon rank sum test, Spearman's rank order correlation coefficient, univariable and multivariable logistic regression modeling, we evaluated associations between serum C3 concentrations measured within 24 hours of ARDS diagnosis (day 1) and:

  ▶ 60-day mortality

  ▶ Pediatric Risk of Mortality III (PRISM-III) Score

  ▶ Pediatric Logistic Regression (PELOD) Score

  ▶ Duration of mechanical ventilation

  ▶ ICU length of stay

  ▶ Indirect vs. direct ARDS

  ▶ Presence/absence of day 3 AKI

Preliminary Results

▶ No statistically significant associations observed between day 1 serum C3 concentrations and 60-day mortality, PRISM-III and PELOD scores, duration of mechanical ventilation, ICU length of stay, and indirect vs. direct ARDS

▶ **Lower day 1 serum C3 concentrations were associated with the development of day 3 AKI (p=0.01)**

  ▶ Patients <u>with</u> day 3 AKI:

    ▶ Day 1 serum C3 concentration – <u>80 (20, 250) mg/dl</u> (median [IQR])

  ▶ Patients <u>without</u> day 3 AKI:

    ▶ Day 1 serum C3 concentration – 100 (20, 390) mg/dl (median [IQR])

▶ **These findings suggest that lower initial serum C3 concentrations, consistent with increased complement system activation, may play a pathogenic role in AKI development in the setting of critically ill PARDS patients**

THANK YOU

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