

## Complement Membrane Attack Complex (MAC) Level in CSF Provides Rapid Identification of Shunt Infection and Failure

James M. Johnston MD; Theresa N Ramos PhD; Anastasia A Arynchyna MPH; Tessa E Blackburn BS; John Amburgy MD; Brandon George Rocque MD, MS; Jeffrey P. Blount MD; Curtis J. Rozzelle MD; Jerry Oakes; Scott R Barnum PhD Departments of Neurosurgery and Microbiology, University of Alabama at Birmingham, Children's of Alabama



### Introduction

Shunt infection and failure are associated with significant medical costs and hospitalization days. Current practice relies on microbiology culture, which significantly delays definitive diagnosis. Complement activation in the cerebrospinal fluid (CSF) has been shown to be a reliable biomarker of meningitis but has not been evaluated in shunt infection or failure. A rapid diagnostic complement assay could aid in identifying patients with hydrocephalus-associated complications.

#### Methods

A prospective cohort of 78 pediatric neurosurgical patients with newly diagnosed hydrocephalus, shunt failure, or shunt infection were enrolled from November 2014 through July 2015 at a single tertiary-care children's hospital. CSF was acquired at the time of initial surgical intervention and, in cases of infection, serial CSF draws were performed. Complement membrane attack complex (MAC) levels in 108 CSF samples were measured by ELISA. Statistical analysis was performed using GraphPad Prism<sup>™</sup> to correlate MAC levels with culture-proven CSF infection and symptomatic hydrocephalus/shunt malfunction.

## Results

Of 78 patients, the median age was 4 years (range 0-23). Etiologies of hydrocephalus included intraventricular hemorrhage, myelomeningocele, congenital and tumor.

Three statistically distinct categories of CSF MAC levels were identified:

1) Pyogenic infection (1905 +/- 765 ng/ml, mean +/- SEM)

2) Symptomatic hydrocephalus (HCP) without infection (37 +/- 7.2 ng/ml)

3) Normal/Asymptomatic ventricular enlargement (VE)/P. acnes infection (<5.2 ng/ml at 1:7 dilution)

Infected patients had significantly higher MAC levels compared with uninfected patients with symptomatic HCP (Mann Whitney, p=0.003). In addition, infected patients undergoing serial CSF draws demonstrated progressive decrease in MAC levels over the course of antibiotic treatment.

# Results

CSF MAC Levels, Shunt Infection and Hydrocephalus



# Conclusions

Preliminary results show CSF MAC levels may help differentiate between pyogenic infection, symptomatic hydrocephalus and normal children. Importantly, P. acnes infection is not associated with increased MAC levels in CSF. We are currently expanding this study with respect to patient number and additional biomarkers to establish predictive values for a rapid assay that facilitates clinical decision making in this challenging population.

## Acknowledgements

Fran Lund, Department of Microbiology University of Alabama at Birmingham Tessa Blackburn, Shannon Stephens Children's of Alabama

### References

Cerebrospinal fluid complement activation in patients with pneumococcal and meningococcal meningitis. Mook-Kanamori BB, Brouwer MC, Geldhoff M, Ende Av, van de Beek D.J Infect. 2014 Jun;68(6):542-7. doi: 10.1016/j.jinf.2013.12.016. Epub 2014 Jan 9.

### **Learning Objectives**

By the conclusion of this session, participants should be able to:

1) Understand the biology of complement activation in the CNS and its relationship to infection and ventricular distention.

2) Discuss the potential of complement biomarker assays to improve diagnosis and management of shunt malfunction and infection