Discovery of exosome-based biomarkers of neonatal arterial ischemic stroke



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Background:

We propose that plasma exosome profiles exist that characterize AIS in the newborn. Further, this profile could be used to identify newborns with AIS *before* the seizure provoked by AIS occurs. In addition, we anticipate the pattern of exosomal RNA expression found after neonatal AIS will correlate with the inflammatory profile found in blood after AIS in neonates. Currently, no treatment for acute AIS in the newborn exists; development of such treatment will be concordant and harmonize with the American Heart Association mission to produce *longer* and *healthier* lives. These hypotheses are novel and hold promise for transformation of therapy for this very common cerebrovascular disorder of children.

Study Aims:

Aim 1:

Identify plasma-derived profiles of exosomes following MRI confirmed acute AIS in term infants using RNAseq to identify mRNAs and miRNAs.

Aim 2:

Establish the plasma inflammatory biomarker profile of AIS in the newborn and correlate it with the exosome RNA profile.

Inclusion Criteria:

- Full-term infants >37 weeks
- MRI-confirmed AIS within 24 hours

Exclusion Criteria:

- Infants with underlying genetic conditions, intracranial hemorrhage, or congenital viral infection

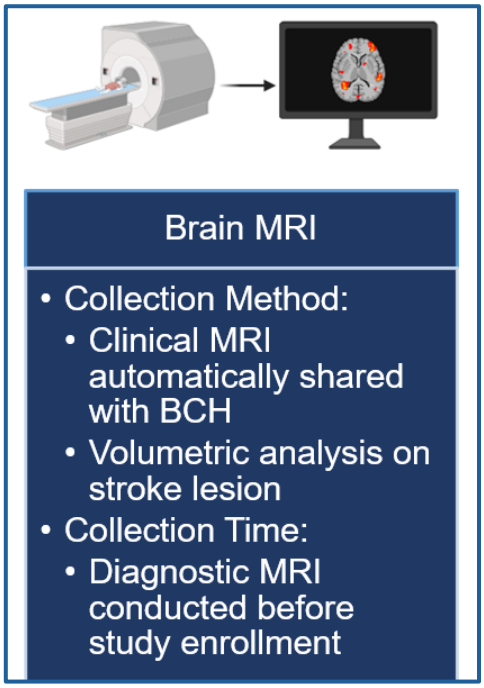
Risks:

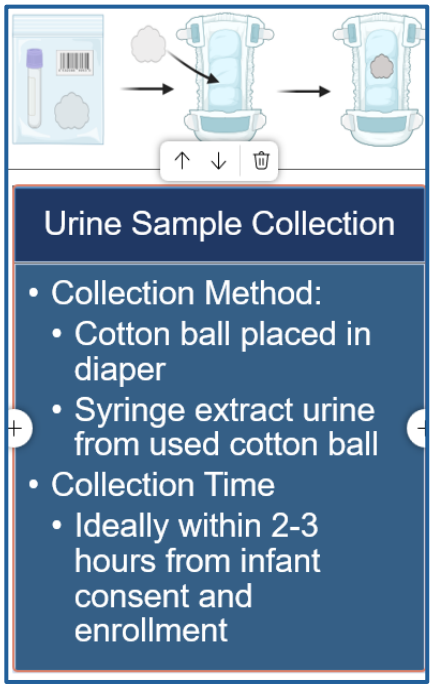
- **Risk of blood draw:** Potential for discomfort or bruising- will use standard of care pain relief with sucrose/pacifier/swaddling and attempt to align with clinical draw when possible.
- **Loss of confidentiality:** All information and specimens will be de-identified and anonymized. All data will be stored on a password, encrypted server used by the co-Principal Investigators and study team.

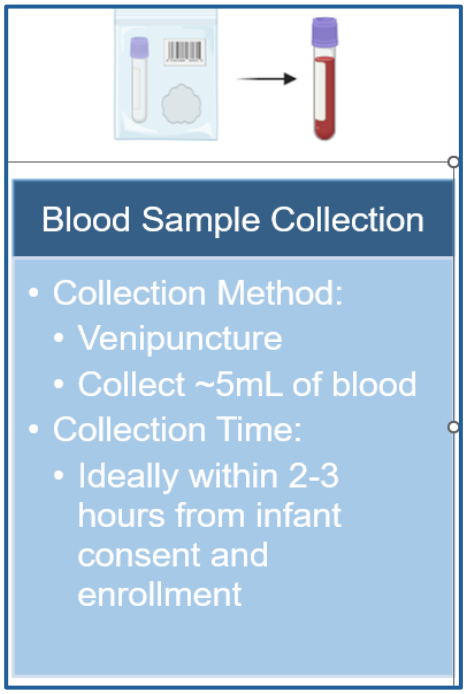
Benefits: There will be no direct benefit to infants participating in this study. However, we hope that we will know more about biomarkers for AIS in the newborn. This may help other newborn babies with AIS in the future.

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The initial specimen collection for the exosome study is time sensitive with a goal to obtain ASAP following consent. After MRI confirmation of Arterial Ischemic Stroke, Drs. Rivkin and Elitt will aim to enroll families and 1st specimen collection would be within 24 hrs. but ideally within 2-3 hrs.







MRI is clinically indicated for diagnosis and is shared with BCH team and will be used for study purposes after enrollment

Urine and Blood sample collection will occur at 3 timepoints:

- ASAP after enrollment (ideally 2-3 hrs)
- At 1 week of life (either still inpt. or with a Neurology appt.)
- At 1 month of life during a Neurology f/u appt.

Tubes will be provided by study team

Due to time sensitive nature of 1st collection it may not be possible to align with a clinical draw.

- Member of BCH team will collect specimen and transport it to BCH for freezing once collected.