Pediatric Stroke Care: Kids are not just little adults!

KU Stroke Symposium
November 6, 2020
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Pediatric Critical Care
Disclosures

- Nothing to disclose
Objectives

▪ Discuss epidemiology and risk factors for pediatric stroke, and how it differs from adults
▪ Discuss barriers to pediatric stroke care
▪ Review common stroke mimickers in children
▪ Discuss diagnosis and treatment options of acute ischemic stroke in children
▪ Discuss acute management of a child with suspected or confirmed acute ischemic stroke
▪ Case-based learning
Pediatric Stroke

- Adult incidence of stroke 200/100,000
- Children 1-2/100,000
  - Excluding neonates
  - Likely underestimated
- Mortality for childhood stroke approx. 3%
  - Long-term neurological impairment 68-74%

Barriers to Pediatric Stroke Care

- **Practical Issues**
  - Diagnosis is often delayed
    - Delayed consideration by frontline providers
    - Majority present within 6hrs of symptom onset, median time to diagnosis 15-24hrs
  - Access to acute MRI and pediatric anesthesia is often limited
  - Pediatric acute ischemic stroke (AIS) differs in etiology, physiology, and natural history
  - Imaging features of AIS (hyperdense vessels, early infarct signs) may be missed
  - Lack of “stroke centers” and standardization of care
    - tPA dosing, endovascular mechanical thrombolytic devices, criteria for intervention

The most common risk factor for acute ischemic stroke in children is

a. Diabetes
b. Congenital heart disease
c. Arteriopathy
d. Acute systemic infection such as a viral illness
Pediatric Stroke Risk Factors…
They are different!

- **Arteriopathy** (highest recurrence rate)
  - Focal cerebral arteriopathy, moyamoya, dissection, vasculitis, post-varicella, etc
- **Cardiac Disease/Congenital Heart Disease**
- **Chronic Systemic Disorders**
  - genetic, malignancy, OCP use, connective tissue disorders, etc
- **Prothrombotic states**
- **Acute systemic disorders**
  - *Fever*, sepsis, shock, *dehydration*, acidosis, hypoxia, *viral gastroenteritis*
- **Chronic head/neck disorders**
  - *Migraine*, brain tumor, VP shunt, aneurysm, AV malformation
- **Acute head/neck disorders**
  - Head/neck trauma, *pharyngitis*, meningitis, recent surgery, *otitis, sinusitis, mastoiditis*
- **Adult associated risk factors**
  - HTN, hyperlipidemia, DM
- **24% considered “idiopathic”**
- **Unvaccinated children are higher risk!**

Figure 4: Arterial ischaemic stroke risk factor categories identified
VIPS study population
355 AIS patients, 354 stroke-free controls
Determine prior exposure to infections and vaccines
Median age: Cases 7.6yrs, Controls 9.3 (p=0.44)

Age-adjusted multi-variate logistic regression
Risk Factors:  
*infection week prior (OR 6.3, p <0.0001) (URI most common)
*undervaccination (OR 8.2, p=0.0004)
*black race (OR 1.9, p=0.009)
*rural residence (OR 3.0, p=0.0003)
Case-controlled, multi-centered prospective study (VIPS)
Aim to determine rates and predictors of recurrent stroke
355 children with AIS 2009-2014
37 international centers

Results:
* 354/355 survived their acute index stroke
* 308/355 (87%) treated with antithrombotic medication, none had hemorrhagic conversion
* sole predictor of recurrence was presence of arteriopathy (5 fold increase)
* 85% were on ASA, anticoagulation, or both at time of recurrence
* 1-year recurrence rate: moyamoya 32% (95% CI 18-51%),
  transient cerebral arteriopathy 25% (95% CI 12-48%), arterial dissection 19% (8.5-40%)
B

Proportion recurrent stroke free

Time from index AIS to first recurrent stroke, months

- Idiopathic
- Cardioembolic
- Possible arteriopathy
- Definite arteriopathy
True or False

- Older children are more likely to present with headache whereas younger children are more likely to present with seizure during an acute ischemic stroke

a. True

b. False
Clinical Presentation

- Often differs from adult stroke, especially younger age groups
- First time seizure with post-ictal neurological deficit (15-20% in ages <6yrs)^2
- Irritability/altered mental status (17-38%)^2
- Symptoms subtle in younger ages
  - Use of non-dominant hand
  - Refusal to walk
  - Language acquisition to describe symptoms challenging
- “Classic Story”

## Table 4: Presenting features of arterial ischaemic stroke by age group

<table>
<thead>
<tr>
<th>Feature</th>
<th>&lt;1 year (n=16)</th>
<th>1-5 years (n=47)</th>
<th>6-10 years (n=10)</th>
<th>11-15 years (n=23)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Focal features</strong></td>
<td></td>
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<tr>
<td></td>
<td>12 (75%)</td>
<td>42 (89%)</td>
<td>7 (70%)</td>
<td>21 (91%)</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Hemiparesis</strong></td>
<td>11 (69%)</td>
<td>40 (85%)</td>
<td>6 (60%)</td>
<td>12 (52%)</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Facial weakness</strong></td>
<td>4 (25%)</td>
<td>22 (47%)</td>
<td>4 (40%)</td>
<td>9 (39%)</td>
<td>0.50</td>
</tr>
<tr>
<td><strong>Speech disturbance</strong></td>
<td>2 (13%)</td>
<td>15 (32%)</td>
<td>4 (40%)</td>
<td>11 (48%)</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Diffuse features</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 (63%)</td>
<td>22 (47%)</td>
<td>10 (100%)</td>
<td>17 (74%)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Decreased conscious level</strong></td>
<td>9 (60%)</td>
<td>17 (36%)</td>
<td>5 (50%)</td>
<td>9 (39%)</td>
<td>0.39</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td>0 (0%)</td>
<td>6 (13%)</td>
<td>5 (50%)</td>
<td>12 (52%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Seizures</strong></td>
<td>12 (75%)</td>
<td>12 (26%)</td>
<td>2 (20%)</td>
<td>2 (9%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Variations of Ischemic Stroke

- Moyamoya-type arteriopathies- high prevalence of TIA and silent infarcts
  - Mean age at diagnosis 7.5 years
- Focal Cerebral Arteriopathy (FCA)
  - “stenosis” on vascular imaging not otherwise classified
  - Transient Cerebral Arteriopathy (TCA)- form of FCA that resolves over time
- Posterior circulation stroke
  - Median age 7-8 years, predominately previously healthy males
  - Non-localizing symptoms occur 60-70%
  - Vertebral artery dissection most common underlying cause, preceded by minor head or neck trauma
- Cardioembolic in cardiac disease
  - Occurs more in inpatient setting
  - Younger children (6mo-3yrs)
  - Abrupt onset of seizure (40%) and hemiparesis (35-75%)

60-90% of children presenting with acute neurological deficit have something other than stroke!
- Todd’s paralysis - transient hemiparesis following seizure
- Hypoglycemia
- Hemorrhagic stroke/subdural
- Traumatic injury, child abuse
- Electrolyte abnormalities/metabolic disorders
- Complex migraines
- Brain tumor
- Intracranial infection or abscesses
- Carotid dissection
- Moyamoya
- Conversion/psychogenic disorders
Pediatric Stroke Mimickers

- Children’s Mercy data n=61
  
  **Final Diagnoses [n, %]**
  
  - Seizure/Todd’s Paralysis (12, 20%)
  - AIS/TIA (11, 18%)
  - Migraine (11, 18%)
  - Conversion Disorder (9, 15%)
  - Meningitis/Encephalitis (5, 8%)
  - Moya Moya (2, 3%)
  - Tumor (2, 3%)
  - Syncope (2, 3%)
  - Other (6, 10%)
  - Unknown (1, 2%)

  Figure 1. Final Diagnoses of Activations

  Other: Alternating hemiplegia (1), bell’s palsy (1), non-CNS related infection (1), pain (1), recrudescence of previous neurological symptoms (1), vertigo (1)

- 20% Seizure
- 18% AIS/TIA
- 18% migraine
- 15% conversion
- 8% meningitis/encephalitis
- 3% brain tumor
- 3% syncope
- 10% other
Diagnosis and Management

- Remember… children are not little adults!
In clinical trials of adults with AIS, the optimal time window for recanalization therapy after documented stroke onset is within:

- ≈4.5 hours for intravenous tPA treatment and
- 6 hours for intra-arterial tPA
- 6 hours for endovascular thrombectomy
- but up to 24 hours for thrombectomy in a **subgroup** of patients
Multiple clinical trials demonstrate that among **highly selected** adults with AIS and large vessel occlusion, thrombectomy improves 90-day survival without disability over standard medical therapy.

In early 2018 TWO clinical trials extended the treatment window further for select patients with *smaller completed infarcts yet large penumbra territories at risk for infarction.*

- Requires CT perfusion imaging!
- **CT Perfusion has radiation equal to 540 Chest X-Rays** or 27 CT head
- Lack of standardized pediatric data for CT perfusion studies
CT Perfusion
Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

206 adult patients with intracranial ICA or proximal MCA occlusion
Randomized to thrombectomy + standard care vs standard care alone
Conclusion: thrombectomy from 6 to 24 hours after onset can be beneficial in adults with mismatch between clinical deficit and infarct (small infarct with large penumbra)
Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging

180 adults with ICA or proximal MCA occlusion infarct size <70ml, ischemic : infarct ratio ≥ 1.8
Randomized to thrombectomy + standard therapy vs standard therapy alone
Conclusion: similar benefit when the thrombectomy was performed in an extended time window (6-16 hours after onset) in patients selected by perfusion imaging
Treatment of AIS in Pediatrics
A pediatric NIH stroke scale is not available for clinical use and neurologists must rely on the adult NIH stroke scale for children.

a. True

b. False
Pediatric NIH Stroke Scale

Instructions: Administer stroke scale items in the order listed. Follow directions provided for each exam item. Scale scores reflect what the patient does, not what the examiner thinks the patient can do. MODIFICATIONS FOR CHILDREN: Modifications to testing instructions from the adult version for use in children are shown in bold italic with each item where appropriate. Items with no modifications should be administered and scored with children in the same manner as for adults.

<table>
<thead>
<tr>
<th>Item and Instructions</th>
<th>Scale Definition and Scoring Guide</th>
</tr>
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<tbody>
<tr>
<td>1a. Level of Consciousness: the investigator must choose a response, even if a full evaluation is not possible by such obstacles as encephalitis, language barrier, coma, or amnestic syndromes. A is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.</td>
<td>0 = Alert, easily responsive. 1 = Alert, but unresponsive to minor stimulation to obey, answer, or respond. 2 = Poorly responsive (flaccid, asymmetry on testing). 3 = Comatose (or death)</td>
</tr>
<tr>
<td>1b. LOC Questions: The patient must be awake - there is no point in asking patients who do not comprehend because of encephalitis, language barrier, or any of the above. It is important that only the &quot;real&quot; the patient with verbal and up. A familiar Family Member must be present. Give credit if the child is holding or playing with the examiner if the &quot;real&quot; is seen. Ask &quot;how old are you?&quot; or &quot;how are you?&quot; Give credit if the child can name things (e.g. &quot;Grandma&quot;, &quot;Dad&quot;). Give credit if the child states the correct age or shows the correct number of fingers for his/her age. For the second question, ask the child &quot;where's X&quot;, where X refers to the name of the parent or other familiar family member present. Use the name for which the child typically uses e.g. &quot;mommy&quot;. Give credit if the child correctly points to or gazes purposefully in the direction of the family member.</td>
<td>2 = Performs task correctly. 3 = Performs task correctly but partial. 0 = No movement.</td>
</tr>
<tr>
<td>2. Best Eye: Horizontally (cosoptically) eye movements patient has a conjugate deviation reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve (CN III, IV, or VI) score a 1. If there is no movement in both eyes, patient is required to make a vertical gaze. Establish eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.</td>
<td>0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia</td>
</tr>
<tr>
<td>3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting (for children &gt; 6 years) or visual threat (for children age 2 to 6 years) as appropriate. Patient must be encouraged, but if they look at the side of a finger or examiner's hand, in children too young (&lt; 6 years) or otherwise incooperative for the standard exam item. Arrows are absent in the patient who cannot understand or cooperate. Only in the case of amblyopia or pontine lesions, the item must be scored a 0, and the examiner must clearly explain the scoring for the patient. In case of blindness test by touching nose from extended arm position.</td>
<td>0 = Normal sensory loss 1 = Mild to moderate sensory loss; patient feels pinprick is less painful or dim or dull on the affected side, or there is a loss of superficial pain with pinprick but patient aware headache is being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the arm, leg, and trunk.</td>
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</tbody>
</table>

5.5. Motor Arm and Leg. The limb is placed in the appropriate position: extend the arm (45 degrees) in the sagittal plane and in the frontal plane, and the leg (50 degrees). 0 = Normal symmetrical movement 1 = Mild paralysis (flaccid, vestibular asymmetry on testing) 2 = Partial paralysis (total or near total paralysis of lower face) 3 = Complete paralysis of one or both sides (absence of facial movement in the upper and lower face)
9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For children age 6 years and up with normal language development before onset of stroke: The patient is asked to describe what is happening in the attached picture, to name the items on the attached naming sheet, to repeat words from the attached list, and to read from the attached list of sentences (Table S1; Fig S1, S2, S3). Comprehension is provided from patient response.

2 = No aphasia, normal
0 = No aphasia, normal
3 = Mute, global aphasia; no usable speech or auditory

9. Best Language: A great deal of information about comprehension will be obtained during the preceding sections of the examination. For children age 6 years and up with normal language development before onset of stroke: For children age 2 yrs to 6 yrs (or older children with premorbid language skills < 6 yr level), score this item based on observations of language comprehension and speech during the examination.

1 = Mute, global aphasia; no usable speech or auditory
0 = Mute, global aphasia; no usable speech or auditory

Stop

The dog runs

Little children like to play outdoors

Fig S1. Reading items for PedNIHSS
Pediatric NIH Stroke Scale

- PedNIHSS- same elements as adult NIHSS (11 neurological domains, 15 scored items)
- For children ages 2 to 18- based on age and development
- Total score range 0-42 (most severe)
- Good IRR for “trained pediatric neurologists”
Multi-institutional study from 2010-13 to determine safety, best dose, and feasibility of tPA in children ages 2-17

- 3 dosing tiers of tPA (0.75, 0.9, and 1mg/kg)

93 children screened
- 43/93 (46%) had acute ischemic stroke
- 21 had medical contraindication to tPA
- 10 outside of treatment window at final diagnosis (7+ presented within 5hrs of symptom onset!!)
- 2 lacked evidence of arterial occlusion on imaging
- 9 excluded for low PedsNIHSS score <6
- Only one patient met inclusion criteria for tPA

Study closed by NIH for lack of enrollment
Emergence of Pediatric Stroke Centers

- Lessons from the TIPS study
  - 17 active enrollment sites
    - Prior to TIPS protocol, <25% had 24/7 access to pediatrics stroke team, MRI capability, or stroke order sets
    - After TIPS study, >80% have acute pediatric stroke systems in place
  - Areas of difficulty
    - 24/7 pediatric sedated MRI access, institutional support, QI and CME efforts
  - Created a standardization of care for pediatric stroke

Which statement is true regarding treatment options for pediatric stroke?

a. Children are not candidates for endovascular therapies
b. Alteplase is not FDA approved for use in pediatric stroke
c. Candidacy of intervention does not rely on the PNIHSS
d. Visualization of clot is not required for tPA administration
Alteplase

- Recombinant tissue-type plasminogen activator
  - IV fibrinolytic- converts plasminogen to plasmin, facilitates clot breakdown
  - Children have immature fibrinolytic system
    - low baseline free-tPA
    - plasminogen activator inhibitor-1 (inhibitor of tPA) increased
  - Larger Vd
  - Increased hepatic clearance
  - NOT FDA APPROVED!
  - Recommended dose:
    - $\leq$ 100kg: total dose 0.9mg/kg, 10% IV bolus over 5min, remainder given over 55min
    - $\geq$ 100kg: total dose 90mg, 9mg IV bolus over 5 min, remainder over 55 min
  - ***may actually have higher requirement!

tPA Risks

Risk of Intracranial Hemorrhage Following Intravenous tPA (Tissue-Type Plasminogen Activator) for Acute Stroke Is Low in Children (Stroke. 2020;51:542-548).

16 former TIPS sites
Retrospective study of children receiving tPA for AIS and risk for intracranial hemorrhage
N= 26, median age 14yrs (1.1-17yrs) treated with tPA within 2-4.5hrs
excluded if tPA was followed by endovascular therapy/intervention

*NO children had symptomatic ICH, 2 epistaxis
*2.1% risk of symptomatic ICH
**reported adult risk 6.4% (lower risk 1.7% 18-40yrs)
Figure 2. Pediatric National Institutes of Health Stroke Scale (NIHSS) and Pediatric Stroke Outcome Measure (PSOM) trajectories. (A) NIHSS and (B) PSOM pre/post-tPA (tissue-type plasminogen activator) treatment trajectories for each patient (thin lines, points), with overall median for each time period (thick band).
Mechanical Thrombectomy

- Review of published case reports/case series of pediatric patients who were treated with for ischemic stroke using modern devices from 2008-2015
  - 29 patients included, ages 2-18yrs
  - Average age 10.3yrs, 74.1% male
  - MCA and basilar arterial stroke 89.6%
  - Average time from symptom onset to intervention 8.8hrs, range 3 to >72hrs
  - Only 13.8% received tPA prior to intervention
  - Low number symptomatic adverse events
  - High report of favorable clinical outcome scores (86.7% achieved mRS ≤ 2)
More than 35 cases of recanalization therapy in pediatric AIS have now been reported and pooled in the published literature, most with successful outcomes.

However, the total number of children treated with thrombectomy remains unknown, and those with treatment-related complications and adverse outcomes are likely underreported in the medical literature.

True safety profile of endovascular thrombectomy in children remains unknown.

Special pediatric considerations include:
- smaller arteries (groin and cerebral)
- weight-based limitations for radiological contrast
- radiation exposure in young children

- CT Perfusion has radiation equal to 540 Chest X-Rays or 27 CT head
- Lack of standardized pediatric data for CT perfusion studies

Slide courtesy of Roha Khalid, MD
Mechanical Thrombectomy

- Potential Complications
  - Cerebral artery damage from catheter
    - Focal Cerebral Arteriopathy (FCA)-acutely inflamed artery
    - Moyamoya- chronic stenosis

- Risk-to-Benefit Ratios
  - Presumption that children recover better than adults
  - Numerous studies indicate good outcome (no functional deficits) can be expected in 30-50% of children with AIS without any intervention.

AHA/ASA Recommendations

AHA/ASA Scientific Statement

Management of Stroke in Neonates and Children
A Scientific Statement From the American Heart Association/American Stroke Association

The American Academy of Neurology affirms the value of this statement as an educational tool for neurologists.

Donna M. Ferriero, MD, MS, FAHA, Co-Chair; Heather J. Fullerton, MD, MAS, Co-Chair; Timothy J. Bernard, MD, MSCS; Lori Billinghurst, MD, MSc, FRCPC; Stephen R. Daniels, MD, PhD; Michael R. DeBaun, MD, MPH; Gabrielle deVeber, MD; Rebecca N. Ichord, MD; Lori C. Jordan, MD, PhD, FAHA; Patricia Massicotte, MSc, MD, MHSc; Jennifer Meldau, MSN; E. Steve Roach, MD, FAHA; Edward R. Smith, MD; on behalf of the American Heart Association Stroke Council and Council on Cardiovascular and Stroke Nursing
AHA/ASA Recommendations

- Reasonable to consider acute intervention for children meeting specific criteria
  - Persistent neurological deficit (PNIHSS ≥ 6)
  - Confirmation of large cerebral arterial occlusion by radiographic imaging
  - “Larger children” due to size-based limitations of devices and contrast dye
  - Decision made with support from neurologists experienced in treatment of childhood stroke
  - Treatment by endovascular surgeon experienced in both children and adult thrombectomy

- Pre-established pathways and systems for treatment of children with acute ischemic stroke

- Establish pediatric stroke centers at tertiary care pediatric facilities
  - 24/7 access to trained experts, technology in neuroimaging, vascular neurology, and neuro critical care
Candidates for intervention in children at CMH

- **tPA (alteplase) candidates**
  - ≥ 24 months
  - Last seen well <4.5 hrs from presentation
  - Confirmed clot on neuroimaging
  - PedsNIHSS ≥ 6

- **Neurointerventional radiology candidates**
  - ≥ 24 months
  - Last seen well >4.5 hrs but <24hrs, or after tPA administration
  - Confirmed clot on neuroimaging
  - PedsNIHSS ≥ 6

Contraindication for tPA

- Similar to adult contraindications
  - Major stroke, head trauma, intracranial surgery in last 3mo
  - GI or urinary bleeding in last 21 days
  - Major surgery within last 10 days
  - History of prior ICH
  - Known cerebral vascular malformation
  - Coagulopathy (plts <100, INR >1.4, elevated aPTT for age)
  - LWWH within 24hrs
  - Intracranial hemorrhage or dissection
  - HTN >15% above 95%ile for age

Contraindication for tPA in Children

- More conservative contraindications
  - Large territory stroke (>1/3 MCA distribution)
  - PedsNIHSS >24
  - PedsNIHSS <6
    - Except posterior circulation/basilar arterial stroke
  - No clot identified on neuroimaging
Large Vessel Occlusion Scores are validated for clinical use by first responders in children with concern for acute ischemic stroke.

a. True

b. False
The Top Stroke Certification Offerings

The Joint Commission offers four advanced levels of stroke certification for Joint Commission-accredited hospitals:

- Comprehensive Stroke Center Certification (CSC)
- Thrombectomy-Capable Stroke Center (TSC)
- Primary Stroke Center Certification (PSC)
- Acute Stroke Ready Hospital Certification (ASRH)

The Joint Commission also offers a core stroke certification for rehabilitation hospitals.

View Revisions to TSC and CSC Eligibility

Joint Commission Advanced Certifications for CSC, TSC, PSC, and ASRH are offered in collaboration with the American Heart Association/American Stroke Association.

https://www.jointcommission.org/certification/dsc_neuro2.aspx
Adult vs Pediatric Center

- AHA/ASA scientific statement
  - Pre-established *pediatric stroke specific* pathways and systems
  - Experienced pediatric stroke experts
  - Adult and pediatric neuro-endovascular experience
Acute Management of Suspected Stroke

- Same adult principles apply!

**Stroke Specific Clinical Questions**

- Time child was last seen well
- Time of symptom onset
- Current aspirin, lovenox, or other anticoagulation use
- Major stroke, head trauma, or intracranial surgery in last 3 months
- GI or urinary bleeding with last 21 days
- Major surgery within last 10 days
- Past Medical History (congenital heart disease, sickle cell disease, cancer)
- NPO status
Acute Management of Suspected Stroke

Clinical Management

- Obtain hard copy of any neuroimaging
- NPO
- Large bore IV in antecubital vein (at least 22g for small children)
- Isotonic IVF
- Avoid hypotension
- Avoid hyper/hypoglycemia
- Keep HOB flat to promote cerebral perfusion
- Treat seizures per transport protocol, may load with Keppra 20mg/kg IV
- Maintain normothermia, treat with Tylenol if febrile
- Evaluate at CMH Adele Hall ER
tPA Administration and Monitoring Guidelines

**DOSING:**

- **Patients ≤100 kg:** Total dose 0.9mg/kg (maximum total dose: 90mg)
  - 10% of total dose given as bolus over 5 minutes
  - Remaining 90% of dose as continuous infusion over 55 minutes
- **Patients >100 kg:** Total dose 90mg
  - 9mg (10% of 90mg) as IV bolus over 5 minutes
  - Remaining 81mg (90% of 90mg) as continuous infusion over 55 minutes
tPA Administration and Monitoring Guidelines

**MONITORING:**
- Neuro checks q15 minutes during infusion and first 2 hours post infusion
  - STOP tPA infusion if patient develops severe HA, nausea/vomiting, acute HTN, or other concern for acute intracranial hemorrhage
- VS q15 minutes during infusion and first 2 hours post infusion
  - BP parameters for tPA

<table>
<thead>
<tr>
<th>AGE</th>
<th>50%ile for SBP</th>
<th>95%ile for SBP</th>
<th>&gt;15% above 95%ile for SBP</th>
<th>&gt;20% above 95%ile for SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4 years</td>
<td>90</td>
<td>112</td>
<td>129</td>
<td>134</td>
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<tr>
<td>5 years</td>
<td>95</td>
<td>113</td>
<td>130</td>
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<tr>
<td>6-10 years</td>
<td>96</td>
<td>121</td>
<td>139</td>
<td>145</td>
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<tr>
<td>11-18 years</td>
<td>105</td>
<td>140</td>
<td>161</td>
<td>168</td>
</tr>
<tr>
<td>&gt;18 years</td>
<td>110</td>
<td>140</td>
<td>161</td>
<td>168</td>
</tr>
</tbody>
</table>

- Goal SBP >50%ile for age but no more than >20% above 95%ile for age
- IF SBP >15% above 95%ile for 1+hr, notify MCP, start anti-hypertensive therapy
- IF SBP >20 above 95%ile at ANY TIME, notify MCP, start antihypertensive therapy
tPA Administration and Monitoring Guidelines

☐ HTN Management
  o Hydralazine 0.1mg/kg/dose IV q20 minutes x 3 doses (max dose 20mg)
  o Nicardipine infusion 0.5mcg/kg/min, titrate by 0.5mcg/kg/min q15-30 minutes
  o AVOID lowering SBP by >25% of highest SBP during the first 24 hours

☐ Anaphylaxis or angioedema
  o DC tPA immediately and notify MCP
  o Monitor for tongue swelling/airway edema
  o Methylprednisolone 2mg/kg IV (max dose 60mg), diphenhydramine 1mg/kg IV (max dose 50mg), ranitidine 1mg/kg (max dose 150mg)
  o Avoid racemic epi (may increase risk of intracranial bleeding)
  o Fluid bolus and epinephrine gtt for hypotension

☐ Indications to STOP tPA immediately
  o New, severe headache, acute HTN, nausea/vomiting, or other concern for acute intracranial hemorrhage
  o Acute hypotension
  o Anaphylaxis or angioedema
  o Serious bleeding
Children’s Mercy Hospital

- Free-standing tertiary pediatric hospital in downtown KC metro
  - Main campus: 314 beds, 87 NICU beds, 41+PICU beds
  - Level 1 Pediatric Trauma Center
  - Heart, liver, kidney, bone marrow transplant programs
  - Satellite hospital and multiple satellite clinics
- Busy critical care transport team
  - 5700 transports/year, 24/7 coverage
  - 10 teams/24hr
  - 13 ground ambulances, 1 helicopter, 1 fixed wing, 1 jet
  - Inter-facility transport only
August 2016-August 2018

- 61 stroke alert activations (average 2.5/month)
- Average age 14yrs for all activations
- 14/61 (23%) met final diagnosis of ischemic stroke or TIA
  - Average age 4yrs
  - No patients received tPA, 2 referred for neuro endovascular intervention, 1 patient underwent successful mechanical thrombectomy
- Common non-stroke diagnosis included Seizure (20%), migraine (18%), conversion disorder (15%), meningitis/encephalitis (8%) and tumor (3.0%)
- 90% of activations occurred in ER setting
  - 49% arrived by private vehicle
  - 21.3% by our CMH Transport Team
  - 19.7% by local EMS
CMH Data

Initial Presenting Location

- Children's Mercy Adele Emergency Department (CMHC)
- Children's Mercy Kansas Emergency Department (CMHK)
- Outside Hospital Emergency Department
- Outpatient Clinic
- Already Admitted-Inpatient Floor
- Already Admitted-Pediatric ICU
While mortality is low for pediatric stroke, children have high percentage of morbidity.

Risk factors and clinical presentation differ compared to adults with AIS.

Stroke mimickers are more common in children.

Time sensitive treatment options are available for a subgroup of children who meet strict criteria.

Diagnostic evaluation and therapeutic interventions should be performed at centers meeting recommended AHA guidelines for pediatric stroke care.
References

Case Reviews

- Stroke vs non-stroke
Case 1

- 7 yo previous healthy male presents to CMH Kansas ER at 11:46am with headache and slurred speech upon wakening at 9am. He spent the entire previous day at the pool and family initially attributed headache to fatigue. He seemed “out of it” (inappropriately laughing/crying) when the family was out to eat for breakfast earlier that morning but was able to eat “ok”. He became incontinent on the way home. While mom was cleaning him up, she noticed he was unsteady on his feet and unable to communicate his words.

- In the ER, VSS, uncooperative with exam. He has inappropriate and slow responses to verbal commands/stimuli. Smiles and cries on and off inappropriately. Tries to speak but cannot. No facial droop but drooling intermittently.

- PNIHSS= 1
A. Stroke
B. Non-stroke
Case 1

- MRI/MRA- basilar artery filling defect with ventral pontine stroke
- Transferred for neurointerventional consult
  - Successful clot retrieval
- Discharged home 5 days later neurologically intact
  - Remains on Lovenox
Posterior Strokes

- Median age 7-8 years, predominately previously healthy males
- Non-localizing symptoms occur 60-70%
- Vertebral artery dissection most common underlying cause, preceded by minor head or neck trauma

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Abstract

AIM: To describe outcomes and outcome predictors in childhood basilar artery stroke (BAS).

METHOD: We prospectively enrolled children with BAS with or without basilar artery occlusion (BAO) in the Toronto Children’s Stroke Registry from 1992 to 2009. We assessed presenting features and outcomes including Pediatric Stroke Outcome Measure scores.

RESULTS: Among 578 children with acute arterial ischemic stroke, 27 had BAS (4.6% including neonates, 6% excluding neonates). Twenty-four (14 males, 10 females) children met study criteria (mean age at stroke was 8 y 10 mo; range 0-17 y). Eleven children had BAO. Aspirin or anticoagulation was given to 15 children. None received tissue plasminogen activator or endovascular treatments. At mean follow-up (3 y 2 mo, range 1 mo-11 y 8 mo), 12 had a 'good outcome' (seven normal, five insignificant deficit) and 12 had 'poor outcome' (10 moderate or severe deficit, two acute deaths). Larger infarct size (≥50% of axial brainstem diameter) independently predicted poor outcome (p=0.02; odds ratio 21.2, 95% confidence interval 1.6-274.9) but not BAO, altered level of consciousness, or age.

INTERPRETATION: Compared with adults, in childhood BAS death is rare and survivors frequently have good outcomes. Aggressive endovascular interventions may not be justifiable in this population.
10yo female presents with left sided weakness when she woke. Last known normal was the night before when she went to bed. She developed a headache and fatigue the day prior and is on amoxicillin for sinusitis. She woke this morning with slurred speech, asymmetric smile, with left arm and leg weakness. She continues to complain of headache but denies fevers or other symptoms.

She was seen in the ER a month prior for photophobia and headache with normal CT head, treated for migraine with resolution of symptoms at that time.
Case 2

- PE: VS Temp 36.9 HR 96 RR 18 BP 103/63 98% RA
- 4/5 strength in LUE/LLE improves with encouraged effort, asymmetric smile with left sided drooping, able to puff out cheeks, raise eyebrows, close/open eyes, EOMI, sensation intact, coordination intact, no pronator drift. Remainder of physical exam normal
- PNIHSS not documented
Case 2

- Labs: BMP normal, glucose 121
- WBC 9.88 Hgb 11.7 Hct 34.6 plt 246
- ESR 87
- Coags normal
- UCG negative
VOTE

A. Stroke

B. Non-Stroke
Case 2

- Hypoattenuation within R internal capsule concerning for subacute infarct. Near complete opacification of sphenoid sinuses. Recommend MRI
Case 2

- Acute infarct of R internal capsule and anterior thalamus. Right ICA short segment narrowing near the ophthalmic segment. MRV normal with right dominant system.
Case 2

- MRI also showed extensive sinusitis involving posterior left ethmoid air cells and sphenoid sinuses with clivus osteomyelitis and suprasellar abscess.
- Went OR with ENT for sphenoid sinus debridement, treated with IV antibiotics x4 weeks, started on ASA for stroke thought to be related to acute inflammation and mass effect from abscess.
- Continues to struggle with LUE/LLE dystonia with abnormal gait, requires PT/OT, and IEP for school.
5yo previous healthy female presents to ER with sudden onset left sided weakness and refusal to walk. Last known normal 10pm night before. Around 6am next morning, mom found her crying on the floor after she had rolled out of bed. She c/o nausea and had small episode of emesis, ?unable to stand. Mom put her back to bed. At 10:30am she was in her room and mom noted she was not walking well and unable to move L arm. She also c/o headache.

She had been seen 2mo prior in the ER after a minor fall and required stitches to her forehead. Since that time mom noticed she drools occasionally and seems more clumsy. She has otherwise been acting normal and able to run/play without difficulty.
Case 3

- PE: VS afebrile, HR 92 RR 16 BP 130/63 100% RA
- Normal LOC for age, left facial droop, 5/5 strength on right side, 0/5 strength of LUE, 3/5 strength LLE, sensation intact throughout, good coordination of right side, dysarthric speech
- PNIHSS 8
A. Stroke
B. Non-Stroke
Case 3

- MRI: large tumor within the pons, consistent with diffuse intrinsic pontine glioma.

- Admitted to PICU and started on steroids. Tumor deemed inoperable by neurosurgery with poor prognosis. She received palliative radiation, was followed by palliative care/hospice, and died 15 months later.
8yo male with autism presents to ER by EMS after collapsing at school. He was found to be confused with right sided weakness and slurred speech. Glucose 94. EMS reports he was starting to converse and move his right arm just prior to arrival to CMH. Teacher who witnessed the event denies seizure like activity or loss of bowel/bladder function.

- VS: afebrile HR 95 RR 23 BP 124/71 100% room air
- Mild to moderate right facial droop, 2-3/5 RUE and RLE strength, right pronator drift, moderate confusion, inability to follow instructions (worse than baseline per teacher), slurred speech noted (has lisp at baseline)
- Started complaining of headache prior to MRI
- PNIHSS 7
A. Stroke
B. Non-stroke
Case 4

- MRI: normal
- Time of flight MRV: slow/sluggish flow within medullary veins of L cerebral hemisphere with decreased flow-related enhancement, consistent with vascular changes related to migraine headache.
Diagnosed with hemiplegic migraine. Admitted to neurology service for observation. Treated with IVF, diphenhydramine and prochlorperazine for migraine with resolution of symptoms.

Neurology recommended avoiding Triptan family for migraine treatment due to risk of vasoconstriction and stroke given his MRI findings.
Case 5

- 21mo health female presented to ER after waking with left facial droop and left sided weakness. She was unable to stand or bear weight on the left leg. She was last seen normal 930pm night before.

- She was evaluated 10days prior for irritability, decreased po intake, and increased work of breathing. Dx with acute otitis and completed course of amoxicillin. She continue to be irritable and intermittently refusing to walk. She could sit/stand without difficulty but wanted to be carried. During this time she continue to have poor oral intake, decreased activity, and not talking as much. She was evaluated again, noted to have a normal exam, and sent home with supportive care for possible viral illness. She did not have any URI symptoms or fever during this time period but was noted to be breathing faster than normal.
Case 5

- PE: VS afebrile HR 143 RR 45 BP 102/64 98% room air
- Sinus tachycardia without murmur, increased work of breathing but clear breath sounds, abdomen soft, moves right side without difficulty, no movement noted of LUE, 2/5 strength, minimal movement of LLE 3/5 strength, normal speech, crying and upset with exam
- Went to MRI with anesthesia, initially tolerated induction and intubation. Became hypotensive with propofol and dexmedetomidine, requiring fluid boluses and 3 doses of ephedrine for blood pressure support
VOTE

A. Stroke

B. Non-Stroke
MRI: acute infarct right posterior MCA distribution involving basal ganglia. Occlusive thrombus in R ICA termus/proximal M1 segment. High-grade narrowing vs complete occlusion of common carotid artery.
Case 5

- Remained intubated after MRI and admitted to PICU. CXR concerning for cardiomegaly and pulmonary edema with history concerning for heart failure.

- Echo revealed mod-severely dilated thin-walled LV with mod-severe global hypokinesis, EF 14% and moderate mitral valve regurgitation. No intra-cardiac thrombus.

- Not a candidate for tPA due to age and late presentation. Not a candidate for neuro IR due to age/size.
Case 5

- Started on bivalirudin for anticoagulation and eventually transitioned to low-molecular weight heparin injections.
- Medically managed for new-onset dilated cardiomyopathy
- Required surgical Gtube for feeds, has persistent left hemiparesis but is learning to ambulate with assistance and crawls, non-verbal but learning sign language, learning to take some foods po (2 yrs post stroke)
- Etiology of dilated cardiomyopathy remains unclear, genetic testing inconclusive, continues on oral medications with improving cardiac function
Cardioembolic Stroke

- 30% of all childhood strokes
  - Congenital heart disease, procedure-related, acquired heart disease
    - Unclear if PFO is pathogenic in pediatric stroke
  - First line transthoracic echo with bubble study
    - TEE for recurring stroke or inconclusive TTE
- VIPS study- preceding infection seen in 22% of cardioembolic strokes
  - Suggests infection is a trigger to children predisposed
