Ischemic Stroke in the Young

Melissa Svoboda, M.D.

Assistant Professor of Pediatrics
Child Neurology & Neurodevelopment
The Children’s Hospital of San Antonio
STRAC Conference
June 27, 2018
Conflict of Interest Disclosure

I have no relevant commercial or financial relationships to report.
Objectives

• Discuss risk factors for pediatric stroke and how they differ from adults
• Understand reasons for delayed diagnosis in children
• Be familiar with key concepts of the 3 Pediatric Stroke Guidelines
• Know key components of recommended stroke work-up & management algorithm for peds
• Discuss Future Directions for San Antonio/South Texas
## Pediatric Stroke - Epidemiology

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number per 100,000 per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult</td>
<td>175-200</td>
</tr>
<tr>
<td>Adolescent/Young Adult (&lt;45yo)</td>
<td>3-23</td>
</tr>
<tr>
<td>Child (&gt;1mo to Adolescent)</td>
<td>2-13</td>
</tr>
<tr>
<td>Neonate (&lt;1mo)</td>
<td>25-40</td>
</tr>
<tr>
<td>Premature Infant</td>
<td>Up to 100</td>
</tr>
</tbody>
</table>

Rivkin, 2016
Pediatric Stroke - Numbers

- Mortality rate 2-11%
- Persistent neurological deficit 68-73% of children with stroke
- Only ≈2% of children with acute ischemic stroke receive tPA treatment in the US
- TIME IS BRAIN
  - Rapid identification, diagnosis, and treatment is crucial!

Bernard, 2008
### Ischemic Stroke Risk Factors

<table>
<thead>
<tr>
<th>Adults</th>
<th>Young Adults/Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Drug Ingestion</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Arteriopathies (numerous)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Hemoglobinopathies (Sickle Cell)</td>
</tr>
<tr>
<td>Heart Disease (Usually Acquired)</td>
<td>Heart Disease (Often Congenital)</td>
</tr>
<tr>
<td>Smoking</td>
<td>Recent Head/Neck Infections OR Recent Viral Illness (Varicella)</td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
</tr>
<tr>
<td></td>
<td>Thrombophilias/Hypercoagulable States</td>
</tr>
<tr>
<td></td>
<td>Metabolic Disorders (MELAS)</td>
</tr>
</tbody>
</table>

24% peds stroke considered “idiopathic”
Ischemic versus Hemorrhagic Stroke

**Childhood Stroke Type**
- Ischemic (~45%)
- Hemorrhagic

**Adult Stroke Type**
- Hemorrhagic (8 - 18%)
- Ischemic

Images Courtesy of Dr. Nassif Wright
Delays in Diagnosing Stroke in Children

• Average time from symptom onset to presentation at hospital: 1.7 to 24 hours!!!
• In-hospital delays (presentation to diagnosis): 8.8-16 hours
• Remember – in adults (and some kids) need 4.5 hours from last known normal/onset to get tPA!!!!

• Why the delay??
  • Harder to recognize symptoms in kids
  • Less common so lower on differential for ED doc (or not included in differential)
  • Access to MRI and Peds Anesthesia

Stroke Symptoms

Weakness
Numbness
Loss of language
Loss of vision

Seizures (Focal)
Acute onset severe headache
Irritability

FAST
FACE DROOPING
ARM WEAKNESS
SPEECH DIFFICULTY
TIME TO CALL 911
Emergency Assessment of Stroke
Test Question

A 5 year old woke up at 7 am, and was slurring. At 7:30 am, she was unable to put on her clothes without assistance and walked with a limp.

She went to bed without any noted problems last night at 9pm.

Yesterday, she played on the trampoline at 2 pm.

What is the time of onset of stroke symptoms?
Time of Stroke Onset

Time of Onset = Time last seen normal (LSN)

2pm trampoline, appeared normal
9pm bed, appeared normal
7am woke up slurred
7:30 am focal weakness noted

LSN at 9 pm last night
Interrater Reliability of the Pediatric National Institutes of Health Stroke Scale (PedNIHSS) in a Multicenter Study

Rebecca N. Ichord, MD; Rachel Bastian, BA; Lisa Abraham, MD; Rand Askalan, MD, PhD; Susan Benedict, MD; Timothy J. Bernard, MD; Lauren Beslow, MD; Gabrielle deVeber, MD; Michael Dowling, MD, PhD, MSCS; Neil Friedman, MBChB; Heather Fullerton, MD, MAS; Lori Jordan, MD, PhD; Li Kan, MD; Adam Kirton, MD; Catherine Amlie-Lefond, MD; Daniel Licht, MD; Warren Lo, MD; Chalmer McClure, MD, PhD; Steve Pavlakis, MD; Sabrina E. Smith, MD, PhD; Marilyn Tan, MD; Scott Kasner, MD, MSCE; Abbas F. Jawad, PhD

- 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”
- Evaluates: Level of consciousness, language, neglect, visual field loss, extraocular movements, motor strength, ataxia, dysarthria, sensory loss
- Takes less than 10 minutes
- Some items require intact language – underestimates right hemispheric stroke severity

Stroke 2011
## NIHSS scoring (PedNIHSS also)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No stroke symptoms</td>
</tr>
<tr>
<td>1-4</td>
<td>Minor stroke</td>
</tr>
<tr>
<td>5-15</td>
<td>Moderate stroke</td>
</tr>
<tr>
<td>15-20</td>
<td>Moderate/severe stroke</td>
</tr>
<tr>
<td>21-42</td>
<td>Severe stroke</td>
</tr>
</tbody>
</table>
App Store Preview

This app is only available on the App Store for iOS devices.

NIH Stroke Scale from StatCoder
Austin Physician Productivity, LLC

4.8, 8 Ratings
Free

iPhone Screenshots
Childhood Ischemic Stroke Management
Pediatric Ischemic Stroke Guidelines

3 published treatment guidelines

• 2004 Royal College of Physicians
  • decision to not update -- paucity of new evidence

• 2012 American College of Chest Physicians

• 2008 American Heart Association Stroke Council

• (2015 AHA/ASA Update, Endovascular Treatment)
Paucity of Evidence for Peds Stroke

- No randomized controlled treatment trials
- Few prospective studies, small cohorts
- Treatment approaches adapted from:
  - adult studies/guidelines
  - case reports, small cohorts
  - expert opinion
Acute Stroke Guideline: INITIAL APPROACH

1. Any child with potential stroke
   Including all BCH ED and children from outside BCH via Critical Care Transport Team (BCH or other)

2. Stroke Screening Questions
   I. Is there a focal neurological deficit?
      a. Unilateral weakness or sensory change
      b. Vision loss or double vision
      c. Speech difficulty
      d. Dizziness or trouble walking
   II. Did the problem begin or get worse suddenly?
   III. Has the problem been present for less than 5 hours?
        (When was the child last seen well?)

3. Child meets all acute stroke criteria (I-III)
   Yes/Not sure
   Consider urgent consult to Neurology and urgent MR while considering other diagnoses and initiating neuroprotective care

4. Call Stroke Stat IMMEDIATELY
   Via Comm Center (x5-2170) ALL HOURS

5. Possible stroke confirmed by ED neurology resident in consultation with stroke attending
   Pediatric NIHSS performed
   Yes

Initial Supportive Rx:
- NPO, head of bed flat

Stroke Stat team:
- Stroke Fellow/Attending
- ED Neurology resident
- Neuroradiologist
- ED Pharmacist
- [MSICU Fellow, Intensive Care Neurology resident, Anesthesia (FYI Only)]

See Acute Stroke Team Activation Plan
**Supportive Rx** (ER and admission EPIC order sets)

- Normothermia: tylenol as need to keep temp <37.5
- Normoglycemia: CBG q4 hours for minimum 24 hours
  - Start insulin sliding scale (ISS) if ≥200 mg/dL on initial run
  - Start ISS if repeated levels are 140-199
  - Goal serum glucose level 60-140 mg/dL
- Normotension to permissive hypertension; avoid hypotension
  - NS bolus if BP < 1 s.d.
  - Pressors if BP < 2 s.d. (IV phenylephrine [neosynephrin optimize cerebral perfusion pressure in animal studies])
  - IV labetalol if BP > 2 s.d. (to be used prn)
- Bedrest with HOB flat **(first 24 hours)**
- O2, if needed to keep sats > 95%
- Isotonic maintenance fluids (consider fluid bolus with clinical signs of dehydration or >8 hours since last oral intake)
  - Neurochecks q1 hr x 4 hrs, then q2 hrs x 8 hrs, then q4 hrs, if seizure risk
  - Antiepileptic drug for ongoing seizures.
  - Formal swallow evaluation prior to PO intake for significant alteration of consciousness, bulbar deficits, or large territory strokes.

**Make Child NPO if:**
- Need sedated study
- Significant altered mental status
- Bulbar symptoms
- Large stroke territory

---

Peds Stroke Initial Care

OK to do this if stroke is just suspected while waiting for confirmation!!

**AHA/ASA Guideline**

Adult data, expert consensus

(Class I, Level C)
### Blood Pressure Considerations

| Table 4. 120<sup>th</sup> Percentile for Systolic/Diastolic BP by age group |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age             | 1-3y            | 4-6y            | 7-9y            | 10-12y          | 13-15y          | > 16y           |
| Girls           | 135/84          | 140/95          | 146/100         | 154/104         | 160/108         | 163/109         |
| Boys            | 136/82          | 144/96          | 148/103         | 155/106         | 163/108         | 170/112         |

| Table 5. 50<sup>th</sup> Percentile for Systolic/Diastolic BP by age group |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Age             | 1-3y            | 4-6y            | 7-9y            | 10-12y          | 13-15y          | > 16y           |
| Girls           | 88/45           | 93/54           | 98/58           | 103/61          | 109/64          | 111/66          |
| Boys            | 88/42           | 95/53           | 99/59           | 104/61          | 111/63          | 117/66          |
Initial Labs/Studies

Initial Evaluation
- CBC, BMP, PT, PTT, pregnancy test in girls of childbearing age, HbS% if known sickle cell disease
- Urgent neuroimaging
- NIHSS by pediatric neurologist on initial evaluation
- EKG and telemetry for first 24 hours

 Neuroimaging results
- Arterial ischemic stroke (AIS)
- Cerebral venous sinus thrombosis (CVST)
- Hemorrhage
- Normal
Neuroimaging of Stroke

- CT head is generally considered POOR for assessing acute ischemic stroke!!!!!
- Need MRI brain with DWI (diffusion weighted imaging)
- If cannot get MRI right away:
  - OK to get head CT first to evaluate for hemorrhage (very unlikely to see acute ischemia) within first hour of arrival
  - Then, get brain MRI and MRA (head and neck) within 24 hours if initial CT is negative and stroke is still suspected
- Some centers using QB-MRI (includes T1) with quick DWI sequence as “stroke protocol” initial scan to avoid sedation need
- Others, using CT with a single DWI MRI sequence added
- Eventually, need full MRI brain (including axial T1 with fat saturation for dissection) AND MRA of head AND neck. (can use CTA instead, but more radiation)
- Add MRV for neonates unless prior imaging strongly establishes arterial cause
Ischemic Stroke

Imaging: MRI with DWI

Ischemic Stroke?

Aspirin Therapy Unless:
- High risk disease (cardiac thrombus, LVAD, catastrophic APA).
- Follow-up imaging if anticoagulated early.

Sickle cell-related?
- yes
- no

Aspirin**
- 3-5 mg/kg/day (max 81 mg)
- ICU monitoring
- Neuroprotective Strategies

Off algorithm

Off algorithm
Second Tier Work-Up (Usually After Patient Stabilized)

- Vascular Imaging (if not already done)
- TTE with bubble study
- AIS prothrombotic work-up
- Other work-up per individual patient

- Antithrombin III deficiency
- Protein C or protein S deficiencies
- Activated protein C resistance
- Factor V Leiden mutation
- Prothrombin gene mutation (G20210A)
- MTHFR mutation
- Antiphospholipid antibody syndrome
- Homocysteine
- Lipoprotein(a)
- Anemia

Prothrombotic Disorders

AHA/ASA Pedi Guideline

Evaluate for prothrombotic states even when another stroke risk factor identified.

Discontinue oral contraceptives in adolescents.

Anticoagulation in “selected hypercoagulable states.”

Stroke Management

Acute Ischemic Stroke

Acute Treatment (Recanalization)
- IV thrombolitics
- IA

Secondary Prevention
- Antiplatelets (Aspirin)
- Anticoagulants (Heparin)
Acute Treatment (Recanalization)

- tPA (Alteplase) – Not FDA approved
- Very limited peds data – TIPS closed in 2013 due to lack of recruitment

Special Report

Thrombolysis in Pediatric Stroke Study

Michael J. Rivkin, MD; Gabrielle deVeber, MD, MHSc; Rebecca N. Ichord, MD; Adam Kirton, MD, MSc; Anthony K. Chan, MBBS; Collin A. Hovinga, PharmD, MS; Joan Cox Gill, MD; Aniko Szabo, PhD; Michael D. Hill, MD; Kelley Scholz, MSW; Catherine Amlie-Lefond, MD
Acute Treatment (Recanalization)
- Thrombolytics

“tPA generally is not recommended ... outside a clinical trial”  (Class III, Level of Evidence C) -- AHA/ASA Pediatric Guidelines 2008

• Adolescents? – Many say reasonable >13yo
• Life-threatening basilar occlusions, large artery occlusions?

Not enough evidence to recommend or reject use of tPA
Used in trials >2yo

“Endovascular therapy with stent retrievers may be reasonable for some patients <18 years of age with acute ischemic stroke who have demonstrated large vessel occlusion in whom treatment can be initiated (groin puncture) within 6 hours of symptom onset, but the benefits are not established in this age group (Class IIb; Level of Evidence C).”

2015 AHA/ASA Focused Update of the 2013 Guidelines for the Early Management of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment
Adult AHA/ASA Guideline: Initial management for Secondary Stroke Prophylaxis

Early Anticoagulation

- Increased risk of ICH
- Does not lower risk of early recurrence (even with cardioembolic stroke)
- Does not reduce early worsening

Class III, level A—risk>benefit, strong evidence

Published Guidelines: Initial management for Secondary Stroke Prophylaxis

**AHA/ASA Pedi Guideline**

UFH/LMWH until etiology determined, up to 1 week (IIb, level c)

Or Aspirin (if not SCD, high embolic risk, or hypercoagulable state) (IIa, level c)

**Chest Pedi Guideline**

Aspirin or UFH/LMWH until etiology determined (level Ib)

**UK Guideline**

Aspirin 5 mg/kg (consensus)
Our Approach (Generally)

• Aspirin 3-5 mg/kg/day (unless contraindication) for all AIS UNLESS:
  - Cervical arterial dissection
  - Cardiac thrombus or vegetation (except infectious endocarditis)
  - Critical major vessel stenosis (may need to corroborate with conventional angiography)
  - Recurrent stroke or TIA while on full-dose aspirin
  - Major prothrombotic state: - Anti-Phospholipid Syndrome - Congenital deficiency of protein C, protein S, or antithrombin

• If any of above, start full anticoagulation (UFH/LMWH)
Case

• 16yo boy with acute onset of right sided weakness and halting speech who Mom found in living room at 12:45pm.
• LKN: 12:30pm – totally at baseline prior
• In ED at 1:45pm: R hemiparesis, expressive aphasia
• NIHSS: 7
• MRI showed Diff Restr in L postcentral gyrus
<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No stroke symptoms</td>
</tr>
<tr>
<td>1-4</td>
<td>Minor stroke</td>
</tr>
<tr>
<td>5-15</td>
<td>Moderate stroke</td>
</tr>
<tr>
<td>15-20</td>
<td>Moderate/severe stroke</td>
</tr>
<tr>
<td>21-42</td>
<td>Severe stroke</td>
</tr>
</tbody>
</table>
MRA

Abrupt, focal change in caliber of M2 branch of L MCA within Sylvian fissure
Treatment/Outcome

• Got IV tPA (within 4.5 hours) at 0.9mg/kg (10% of dose given in 5 mins, rest given over the hour)
• Clinically improved – NIHSS next day was 3
• Follow-up Imaging showed improved flow through the vessel
• Aspirin at 81mg started after 24 hours
• Discharged home on hospital day 3 and NIHSS was 1
Future Directions for South Texas/San Antonio

- Collaboration with centers on best practices
  - Maybe city-wide pediatric protocol?? Involve EMS??
- Education on when to suspect stroke in kids
  - EDs (especially non-pediatric EDs)
  - PCPs
  - Schools?
- Setting up quick-brain (QB) MRI protocols to quickly diagnose stroke without need for peds sedation
- Work on peds-specific interventionalist/site for thrombectomy
Clinical Resources

American Heart Association/American Stroke Association Statements and Guidelines online:

http://myamericanheart.org/statements

Thank you to Dr. Lisa Nassif Wright, Medical Director of Pediatric Stroke Clinic at Texas Children’s Hospital who shared some of her slides with me for this presentation.
Summary for Peds Stroke

- Pediatric stroke etiology/risk factors are very different from adults
- Diagnosis of Pediatric Stroke is commonly quite delayed
- Despite 3 Pediatric Stroke Guidelines, there is a paucity of pediatric evidence (so extrapolate from adults along with case series and expert opinion)
- Algorithm for components of recommended stroke work-up & management algorithm for peds is important!
- tPA can be considered in those over 2 years old, but really not used outside of research settings for those <13yo
- Discuss Future Directions for San Antonio/South Texas
Questions?

Melissa Svoboda, MD
(clinic) 210-704-4715
Melissa.svoboda@bcm.edu
References


