Pediatric Stroke Care: Kids are not just little adults!

KU Stroke Symposium

November 6, 2020

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Pediatric Critical Care

Children's Mercy KANSAS CITY

UMKC School of Medicine

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT RANKED IN 10 SPECIALTIES 2018-19

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

Disclosures

- Nothing to disclose

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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

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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%

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Mallick et al. Lancet Neuro 2014;13:35-43

Bernard et al. Ann Neuro 2008;63:679-696

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

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Ferriero et al. AHA/ASA Scientific Statement. Management of stroke in neonates and children. Stroke 2019;50:e00-e46.

Question

- 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!***

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Mallick et al. Lancet Neuro 2014;13:35-43
Lyle et al. Semin Thromb Hemost. 2011;37(7):786-793.
Fullerton et al. Neuro 2015;85-1459-1466.

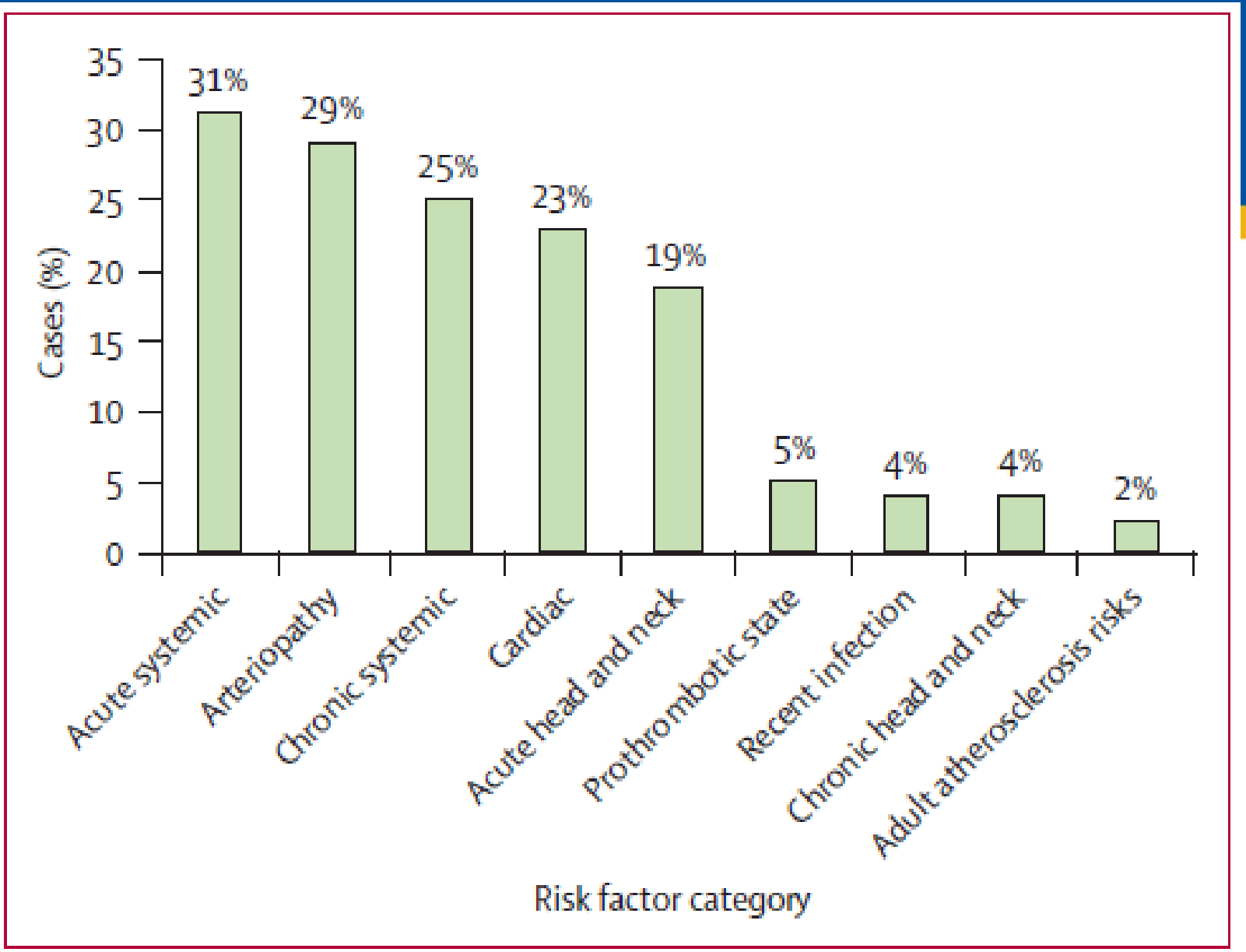

Figure 4: Arterial ischaemic stroke risk factor categories identified

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Mallick et al. Lancet Neuro 2014;13:35-43

Infection, vaccination, and childhood arterial ischemic stroke

Results of the VIPS study

Neurology® 2015;85:1459-1466

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)

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Risk of Recurrent Arterial Ischemic Stroke in Childhood

A Prospective International Study

Heather J. Fullerton, MD, MAS; Max Wintermark, MD; Nancy K. Hills, PhD; Michael M. Dowling, MD, PhD; Marilyn Tan, MD; Mubeen F. Rafay, MD; Mitchell S.V. Elkind, MD, MS; A. James Barkovich, MD; Gabrielle A. deVeber, MD, MSc; and the VIPS Investigators*

(*Stroke*. 2016;47:53-59. DOI: 10.1161/STROKEAHA.115.011173.)

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, non 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%).

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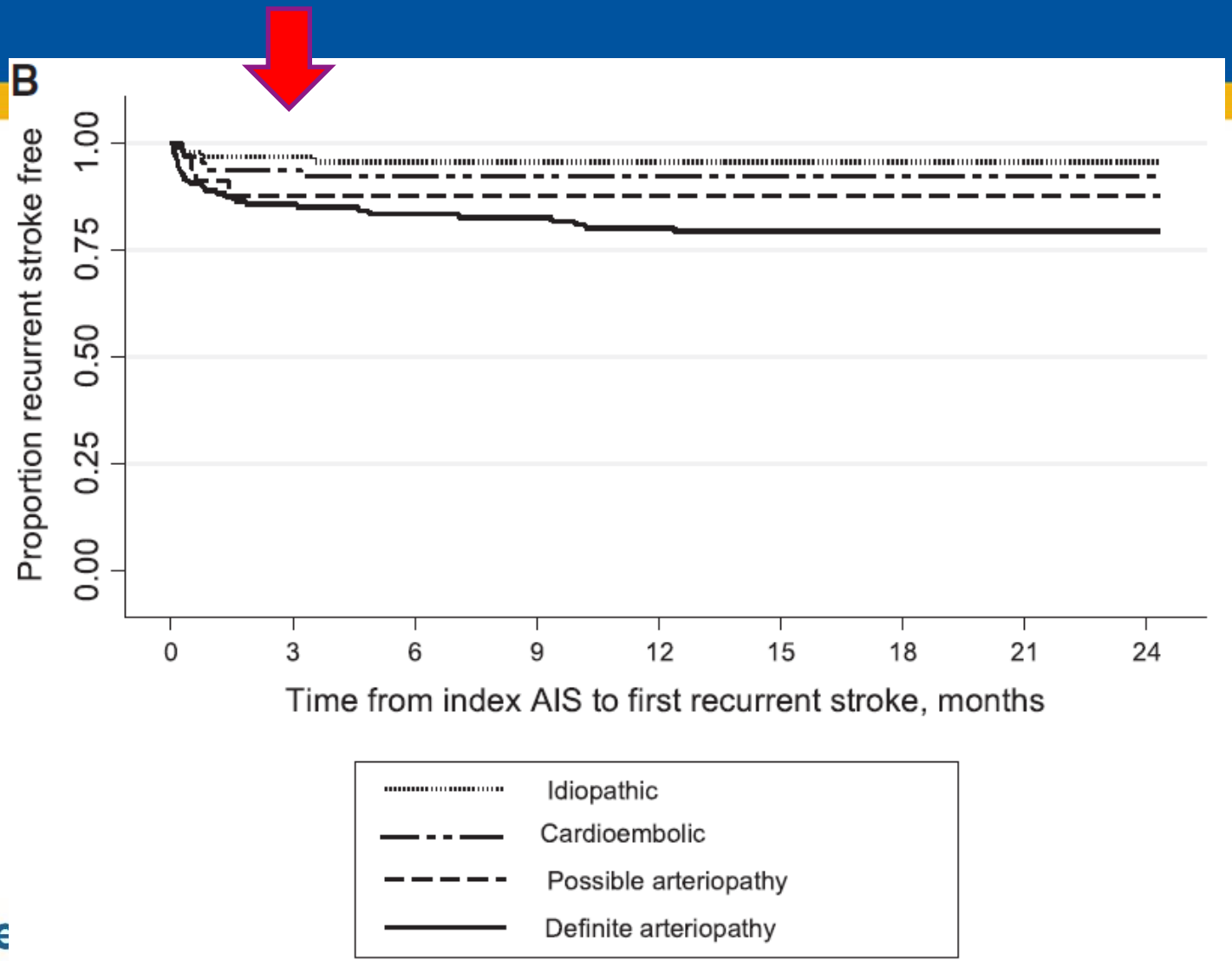

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True or False

- 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

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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-dominate hand
  - Refusal to walk
  - Language acquisition to describe symptoms challenging
- "Classic Story"

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1. Mallick et al. Lancet Neuro 2014;13:35-43
2. Ferriero et al. AHA/ASA Scientific Statement. Management of stroke in neonates and children. Stroke 2019;50:e00-e46.

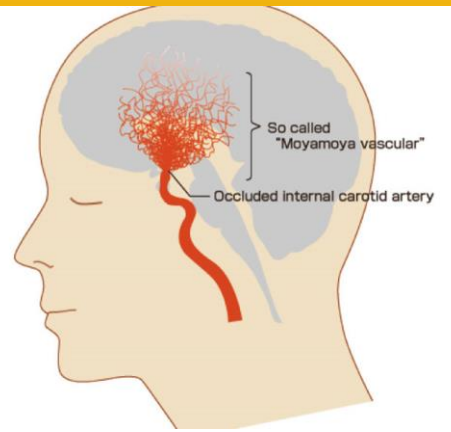
Clinical Presentation

	<1 year (n=16)	1–5 years (n=47)	6–10 years (n=10)	11–15 years (n=23)	p value
Focal features	12 (75%)	42 (89%)	7 (70%)	21 (91%)	0·18
Hemiparesis	11 (69%)	40 (85%)	6 (60%)	12 (52%)	0·02
Facial weakness	4 (25%)	22 (47%)	4 (40%)	9 (39%)	0·50
Speech disturbance	2 (13%)	15 (32%)	4 (40%)	11 (48%)	0·12
Diffuse features	10 (63%)	22 (47%)	10 (100%)	17 (74%)	0·004
Decreased conscious level	9 (60%)	17 (36%)	5 (50%)	9 (39%)	0·39
Headache	0 (0%)	6 (13%)	5 (50%)	12 (52%)	<0·0001
Seizures	12 (75%)	12 (26%)	2 (20%)	2 (9%)	<0·0001

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

Variations of Ischemic Stroke

- Moyamoya-type arteriopathies- high prevalence of TIA and silent infarcts
  - Mean age at diagnosis 7.5years
- 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 7-8years, 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%)



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1. Ferriero et al. AHA/ASA Scientific Statement. Management of stroke in neonates and children. Stroke 2019;50:e00-e46.
2. Amlie-Lefond et al. Predictors of cerebral arteriopathy in children with arterial ischemic stroke: results of the IPSS. *Circulation*. 2009;119(10):1417-1423.

Pediatric Stroke Mimickers

- 60-90% of children presenting with acute neurological deficit have something other than stroke!
  - Todd's paralysis- transient hemi paralysis 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

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Ferriero et al. AHA/ASA Scientific Statement. Management of stroke in neonates and children. Stroke 2019;50:e00-e46.

Pediatric Stroke Mimickers

- Children's Mercy data n=61

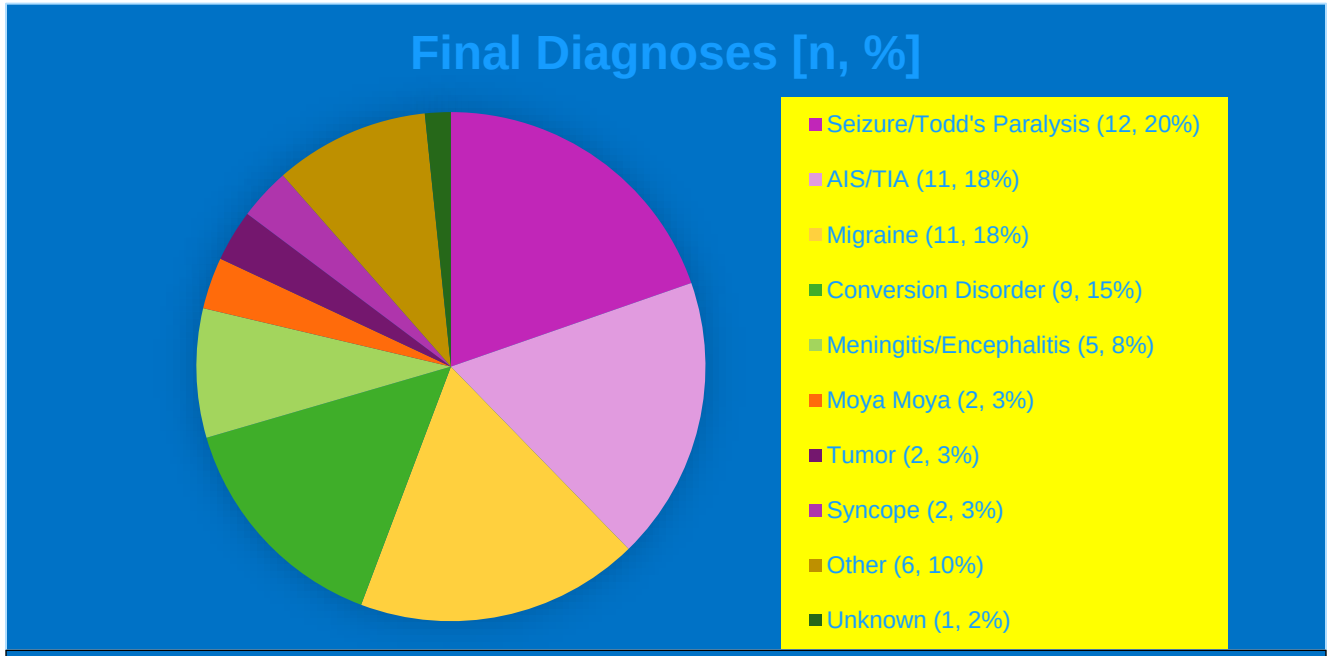

Figure 1. Final Diagnoses of Activations

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

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Diagnosis and Management

- Remember… children are not little adults!

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Adult Stroke Stuff (new and old)

- 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

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Slide courtesy of Roha Khalid, MD

Adult Clinical Trials

- 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**

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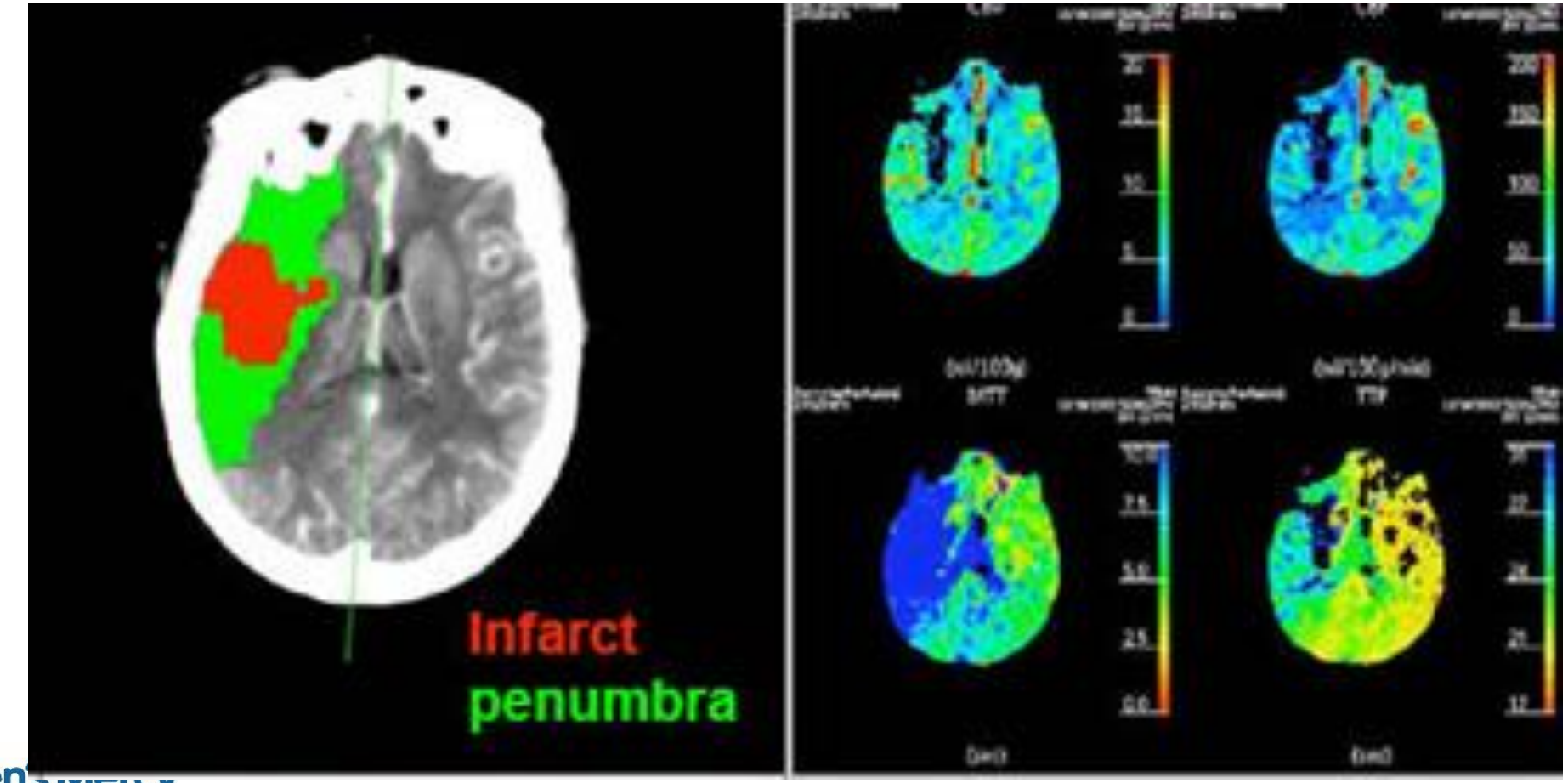
Slide courtesy of Roha Khalid,

CT Perfusion



https://www.google.com/search?q=ct+perfusion+imaging+in+acute+stroke&rlz=1C5CHFA_enUS781US781&source=lnms&tbm=isch&sa=X&ved=2ahUKEwihl5-15sLqAhXVaM0KHRHVDMIQ_AUoAXoECA4QAw&biw=1412&bih=727#imgrc=u3WqMGNLmpDpnM&imgdii=jTMYo0zXZP-8uM

DAWN Trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 4, 2018 VOL. 378 NO. 1

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)

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DEFUSE 3 Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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*

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Treatment of AIS in Pediatrics

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True or False

- 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

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PedNIHSS INSTRUCTIONS: Administer stroke scale items in the order listed. Follow directions provided for each exam item. Scores should reflect what the patient does, not what the clinician 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.*

Item# and Instructions	Scale Definition and Scoring Guide
1a. Level of Consciousness: the investigator must choose a response, even if a full evaluation is prevented by such obstacles as an endotracheal tube, language barrier, orotracheal trauma/bandages. A 3 is scored only if the patient makes no movement (other than reflexive posturing) in response to noxious stimulation.	0 = Alert; keenly responsive. 1 = Not alert, but arousable by minor stimulation to obey, answer, or respond.
1b. LOC Questions: The patie must be correct - there is no pa patients who do not comprehenc because of endotracheal intubat cause, language barrier or any 1. It is important that only the "help" the patient with verbal or ***and up. A familiar Family Me "how old are you?" Or "How one. Give credit if the chil number of fingers for his/he "where is XX?", XX referring member present. Use the na e.g. "mommy". Give credit if in the direction of the family m***	
1c. LOC Commands: The pat grip and release the non-pare ***command to grip the hand wi your nose".*** Substitute another one step command if the hands cannot be used. Credit is given if an unequivocal attempt is made but not completed due to weakness. If the patient does not respond them (pantomime) and score th Patients with trauma, amputatio suitable one-step commands. O	2 = Performs neither task correctly
2. Best Gaze: Only horizontal (oculocephalic) eye movements patient has a conjugate deviatio reflexive activity, the score will be 1. If a patient has an isolated peripheral nerve paresis (CN III, IV or VI) score a 1. Gaze is testable in all aphasic patients. Patients with ocular trauma, bandages, pre-existing blindness or other disorder of visual acuity or fields should be tested with reflexive movements and a choice made by the investigator. Establishing eye contact and then moving about the patient from side to side will occasionally clarify the presence of a partial gaze palsy.	abnormal in one or both eyes, but where forced deviation or total gaze paresis are not present. 2 = Forced deviation, or total gaze paresis not overcome by the oculocephalic maneuver.
3. Visual: Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting ***(for children > 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 the moving fingers appropriately, this can be scored as normal. If there is unilateral blindness or enucleation, visual fields in the remaining eye are scored. Score 1 only if a clear-cut asymmetry, including quadrantanopia is found. If patient is blind from any cause score 3. Double simultaneous stimulation is performed at this point. If there is extinction patient receives a 1 and the results are used to answer question 11.	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia (blind including cortical blindness)
4. Facial Palsy: Ask, or use pantomime to encourage the patient to show teeth or raise eyebrows and close eyes. Score symmetry of grimace in response to noxious stimuli in the poorly responsive or non-comprehending patient. If facial trauma/bandages, orotracheal tube, tape or other physical barrier obscures the face, these should be removed to the extent possible.	0 = Normal symmetrical movement 1 = Minor paralysis (flattened nasolabial fold, asymmetry on smiling) 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)
5 & 6. Motor Arm and Leg: The limb is placed in the appropriate position: extend the arms (palms down) 90 degrees (if sitting) or 45 degrees (if supine) and the leg 30	**5a. Left Arm** **5b. Right Arm** drift, limb holds 90 (or 45) degrees for full 10 onds. ft, Limb holds 90 (or 45) degrees, but drifts down ore full 10 seconds; does not hit bed or other support. me effort against gravity, limb cannot get to or intain (if cued) 90 (or 45) degrees, drifts down to bed, has some effort against gravity. effort against gravity, limb falls. movement nputation, joint fusion explain:
	t Leg **ht Leg** drift, leg holds 30 degrees position for full 5 seconds. ft, leg falls by the end of the 5 second period but does hit bed. me effort against gravity; leg falls to bed by 5 seconds, has some effort against gravity. effort against gravity, leg falls to bed immediately. 4 = No movement putation, joint fusion explain:
	sent sent in one limb sent in two limbs
a toy or the examiner's hand, in children too young (< 5 years) or otherwise uncooperative for the standard exam item. Ataxia is absent in the patient who cannot understand or is paralyzed. Only in the case of amputation or joint fusion may the item be scored "9", and the examiner must clearly write the explanation for not scoring. In case of blindness test by touching nose from extended arm position.	
8. Sensory: Sensation or grimace to pin prick when tested, or withdrawal from noxious stimulus in the obtunded or aphasic patient. ***For children too young or otherwise uncooperative for reporting gradations of sensory loss, observe for any behavioral response to pin prick, and score it according to the same scoring scheme as a "normal" response, "mildly diminished" or "severely diminished" response.*** Only sensory loss attributed to stroke is scored as abnormal and the examiner should test as many body areas [arms (not hands), legs, trunk, face] as needed to accurately check for hemisensory loss. A score of 2, "severe or total," should only be given when a severe or total loss of sensation can be clearly demonstrated. Stuporous and aphasic patients will therefore probably score 1 or 0	0 = Normal; no sensory loss. 1 = Mild to moderate sensory loss; patient feels pinprick is less sharp or is dull on the affected side; or there is a loss of superficial pain with pinprick but patient is aware he/she is being touched. 2 = Severe to total sensory loss; patient is not aware of being touched in the face, arm, and leg.

1. It is important that only the initial answer be graded and that the examiner not "help" the patient with verbal or non-verbal cues. ***Modified for children, age 2 years and up. A familiar Family Member must be present for this item: Ask the child "how old are you?" Or "How many years old are you?" for question number one. 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 "where is XX?", XX referring to the name of the parent or other familiar family member present. Use the name for that person which the child typically uses, e.g. "mommy". Give credit if the child correctly points to or gazes purposefully in the direction of the family member.***

3. **Visual:** Visual fields (upper and lower quadrants) are tested by confrontation, using finger counting ***(for children > 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

PNIHSS

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***	0 = No aphasia, normal

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

g items for PedNIHSS:

f 4 word-repetition tasks is presented: top top and go it rains we play inside he President lives in Washington
f 3 items is presented for the child to read in Fig 1. Adjust ations according to child's age/school level
s are presented and of a clock, pencil, skateboard, shirt, baseball, (Fig 2).
cture (Fig 3) is presented and the child is asked to describe what sees.

provided from patient response.

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***	0 = No aphasia, normal

one step commands. ***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.***

item. The examiner must choose a score in the patient with stupor or limited cooperation but a score of 3 should be used only if the patient is mute and follows no one step commands. ***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.***	2 = Severe aphasia; all communication is through fragmentary expression; great need for inference, questioning, and guessing by the listener. Range of information that can be exchanged is limited; listener carries burden of communication. Examiner cannot identify materials provided from patient response. 3 = Mute, global aphasia; no usable speech or auditory

Stop

e dog run

Little children like to play outdoors

Fig S1. Reading items for PedNIHSS

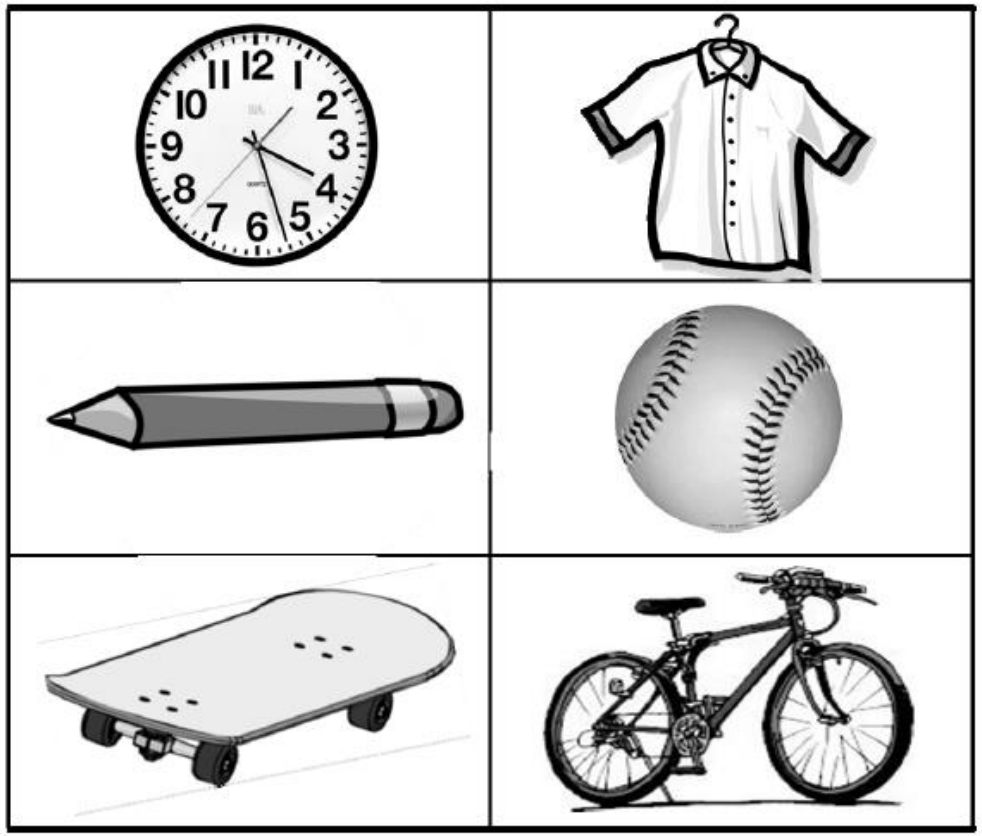

Fig. S2 Pictures to test naming for Item 9 Best Language of PedNIHSS

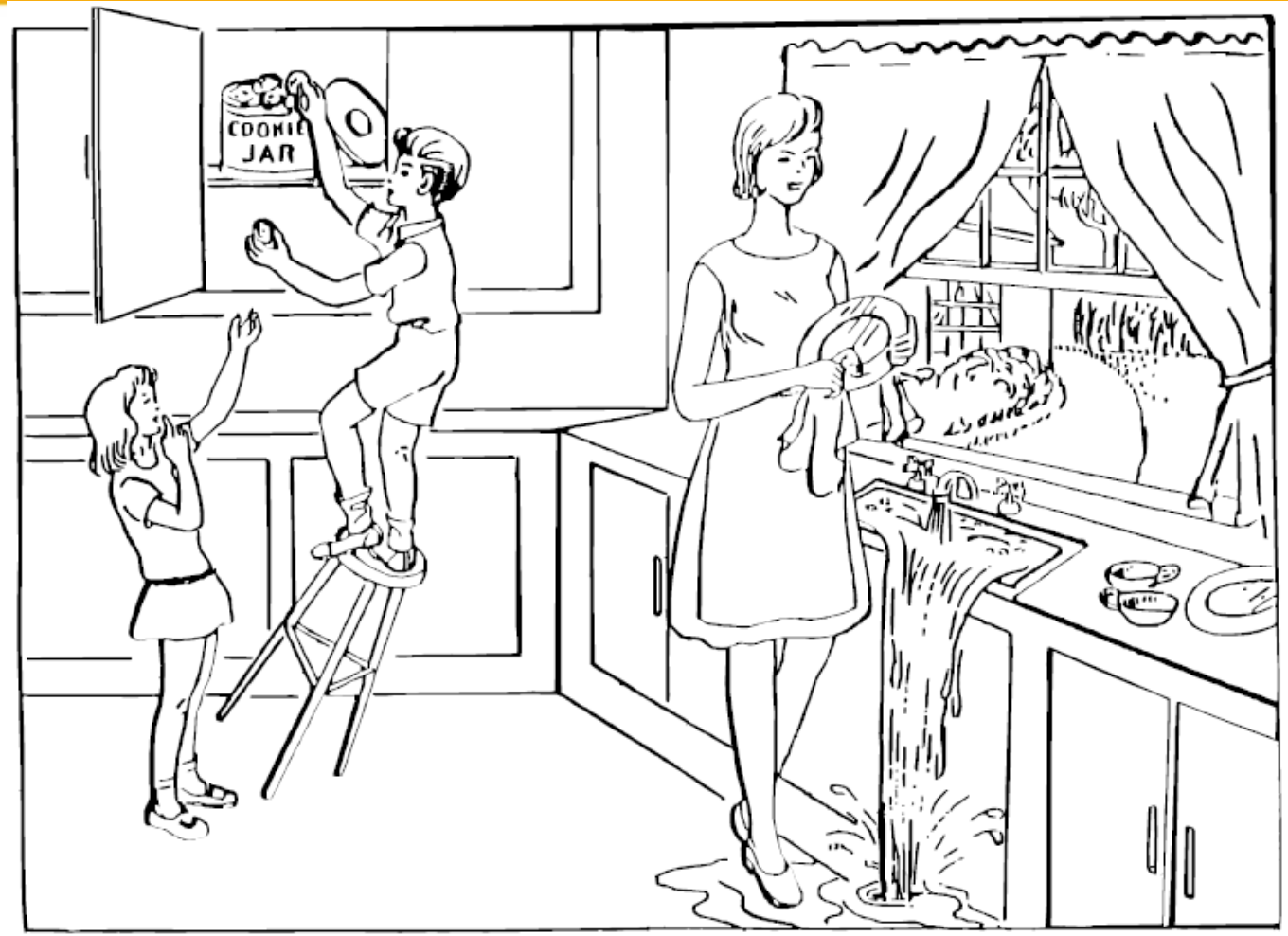

Fig. S3 Picture to test story-telling for Item 9 Best Language of PedNIHSS

Pediatric NIH Stroke Scale

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***"

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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

(*Stroke*. 2015;46:880-885.)

- 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 peds 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

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Bernard et al. Stroke.2014;45:2018-23.

Question

- 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

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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:
    - ≤ 100kg: total dose 0.9mg/kg, 10% IV bolus over 5min, remainder given over 55min
    - ≥ 100kg: total dose 90mg, 9mg IV bolus over 5 min, remainder over 55 min
    - ***may actually have higher requirement!

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Rivkin et al. Thrombolysis in Pediatrics Study. Stroke. 2015;46:880-885.

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)

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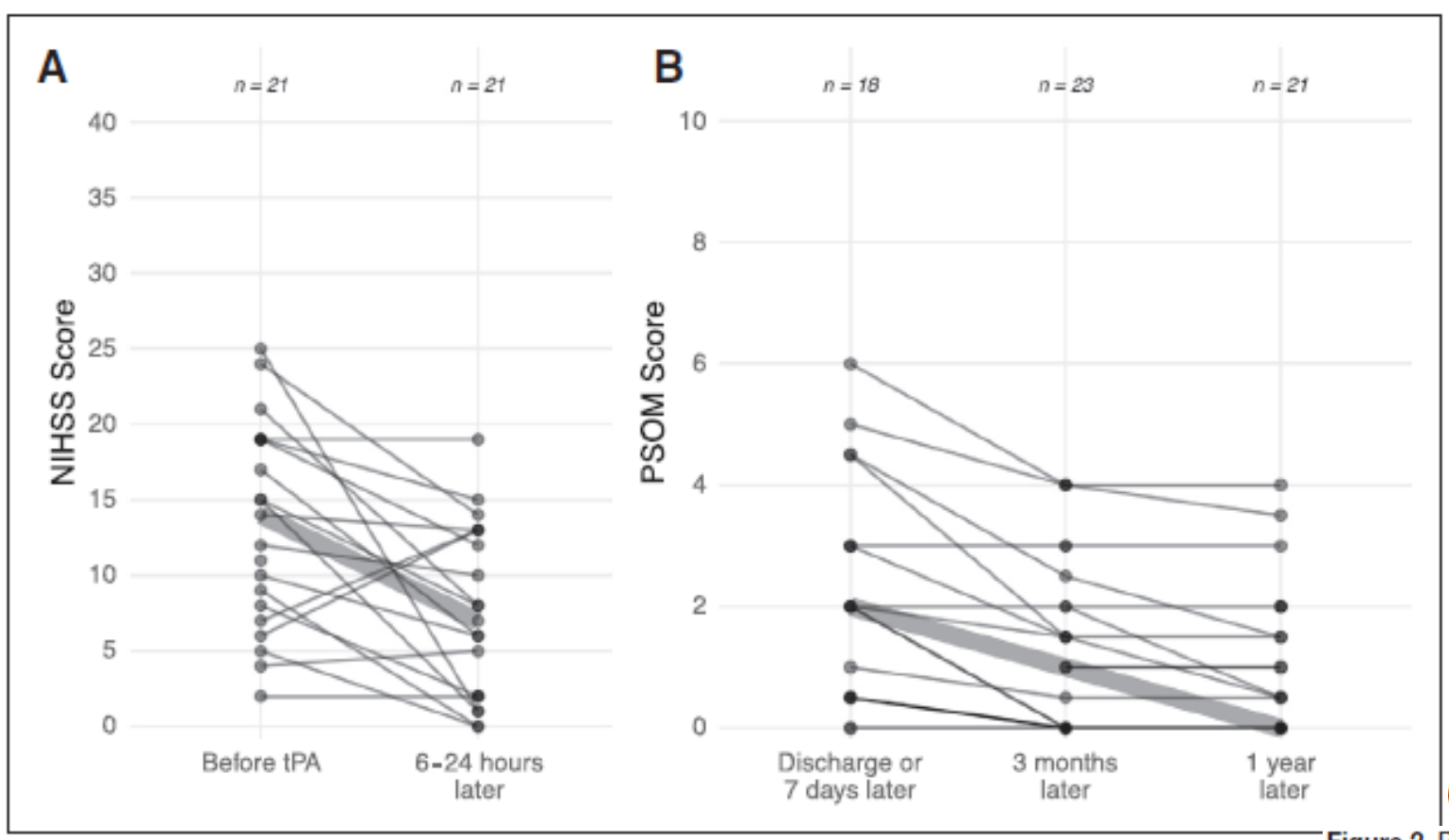
PNIHSS after tPA



(*Stroke*. 2020;51:542-548.

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).

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Mechanical Thrombectomy

REVIEW

Mechanical thrombectomy for pediatric acute ischemic stroke: review of the literature

Sudhakar Satti,[1] Jennifer Chen,[2] Thinesh Sivapatham,[1] Mahesh Jayaraman,[3] Darren Orbach[4]

Satti S, *et al*. *J NeuroIntervent Surg* 2017;**9**:732–737.

- 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)

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Mechanical Thrombectomy

- **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**

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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.

1. Goyal et al 2016
2. Goeggel Simonetti B et al. Long term outcome after arterial ischemic stroke in children and young adults. *Neurology*. 2015;84:1941–1947.

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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

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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

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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

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Rivkin et al. Thrombolysis in Pediatrics Study. Stroke. 2015;46:880-885.
Rivkin et al. Guidelines for urgent management of stroke in children. Pediatr Neurol 2016;56:8-17.

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***

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Rivkin et al. Guidelines for urgent management of stroke in children. Pediatr Neurol 2016;56:8-17.

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*

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Rivkin et al. Thrombolysis in Pediatrics Study. Stroke. 2015;46:880-885.
Rivkin et al. Guidelines for urgent management of stroke in children. Pediatr Neurol 2016;56:8-17.

True or False

Large Vessel Occlusion Scores are validated for clinical use by first responders in children with concern for acute ischemic stroke.

a. True

b. False

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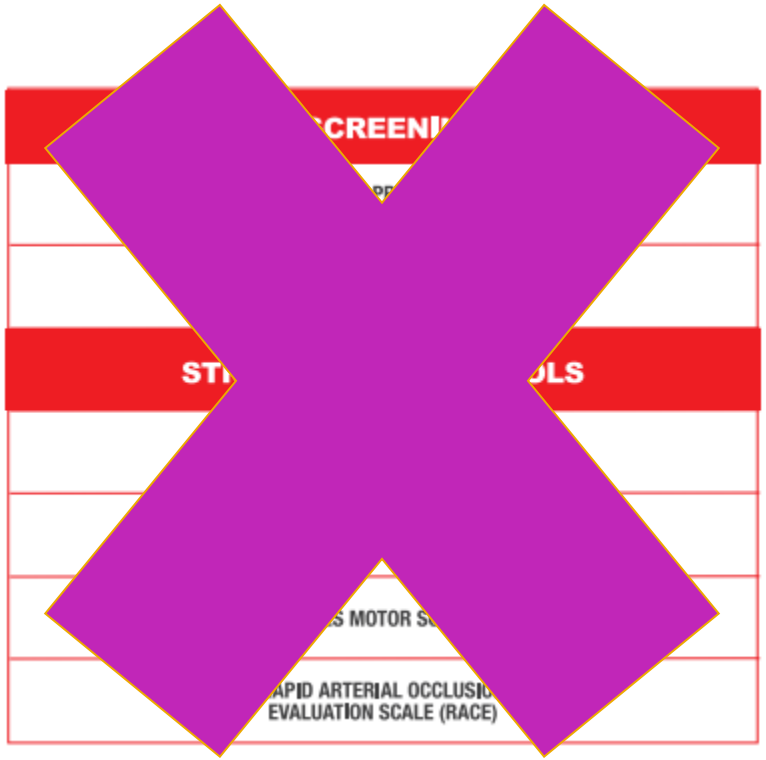
Acute Management of Suspected Stroke



https://www.strokeassociation.org/-/media/stroke-files/ems-resources/about-the-severity-based-stroke-triage-algorithm-ucm_491893.pdf?la=en&hash=EDCA499683C70CB1551FFE9D19750C67D4B3DB6A

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Adult vs Pediatric Center

The Top Stroke Certification Offerings

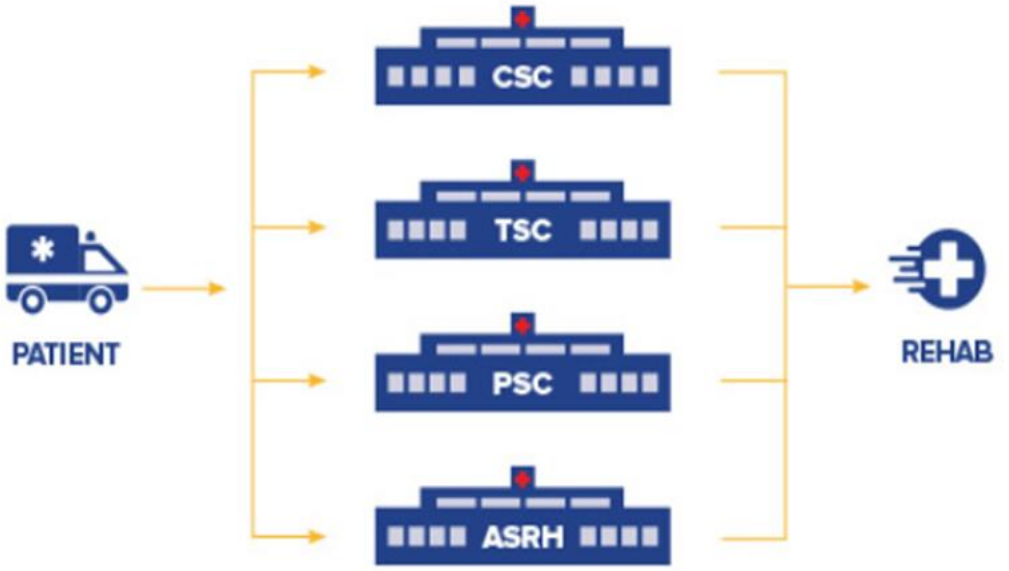
The Joint Commission offers four advanced levels of stroke certification for Joint Commission-accredited hospitals:

- 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

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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

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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

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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 55minutes

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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

AGE	50%ile for SBP	95%ile for SBP	>15% above 95%ile for SBP	>20% above 95%ile for SBP
1-4 years	90	112	129	134
5 years	95	113	130	136
6-10 years	96	121	139	145
11-18 years	105	140	161	168
>18 years	110	140	161	168

  - 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

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tPA Administration and Monitoring Guidelines

- HTN Management
  - Hydralazine 0.1mg/kg/dose IV q20 minutes x 3 doses (max dose 20mg)
  - Nicardipine infusion 0.5mcg/kg/min, titrate by 0.5mcg/kg/min q15-30 minutes
  - AVOID lowering SBP by >25% of highest SBP during the first 24 hours
- Anaphylaxis or angioedema
  - DC tPA immediately and notify MCP
  - Monitor for tongue swelling/airway edema
  - Methylprednisolone 2mg/kg IV (max dose 60mg), diphenhydramine 1mg/kg IV (max dose 50mg), ranitidine 1mg/kg (max dose 150mg)
  - Avoid racemic epi (may increase risk of intracranial bleeding)
  - Fluid bolus and epinephrine gtt for hypotension
- Indications to STOP tPA immediately
  - New, severe headache, acute HTN, nausea/vomiting, or other concern for acute intracranial hemorrhage
  - Acute hypotension
  - Anaphylaxis or angioedema
  - Serious bleeding

CMH Demographics

- 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

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CMH Data

- 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

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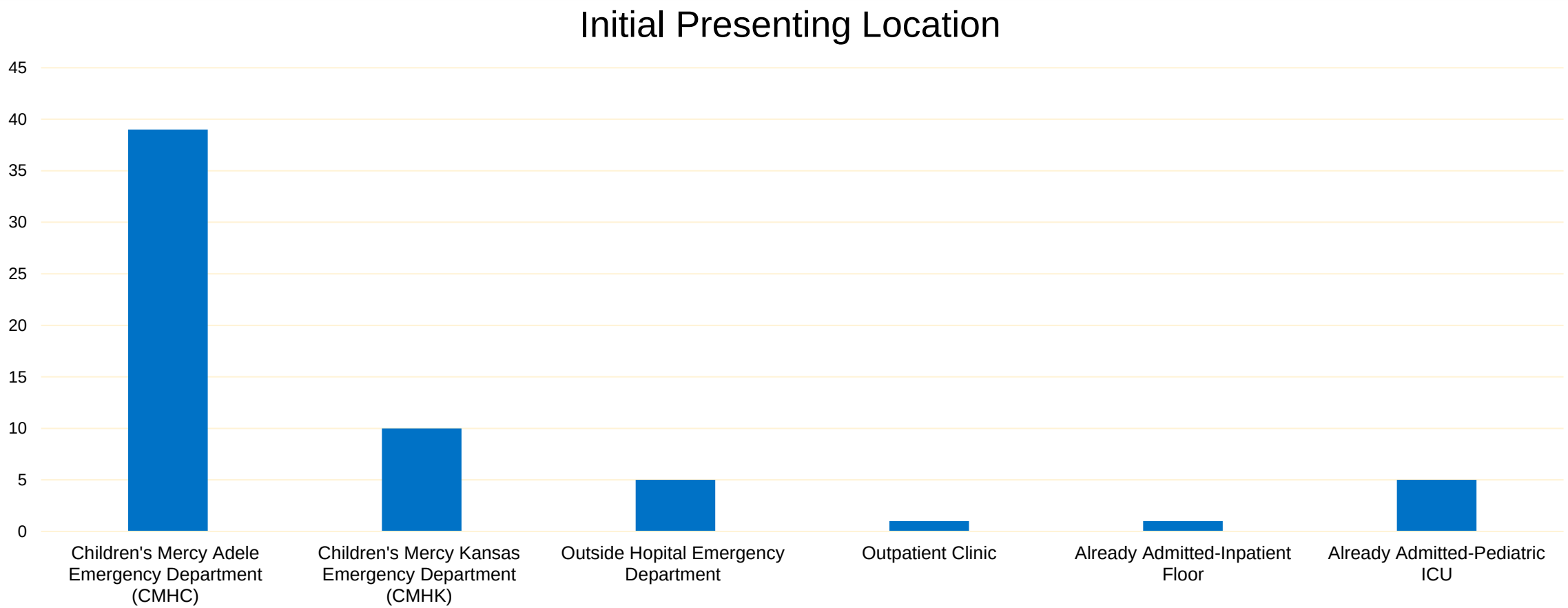
CMH Data



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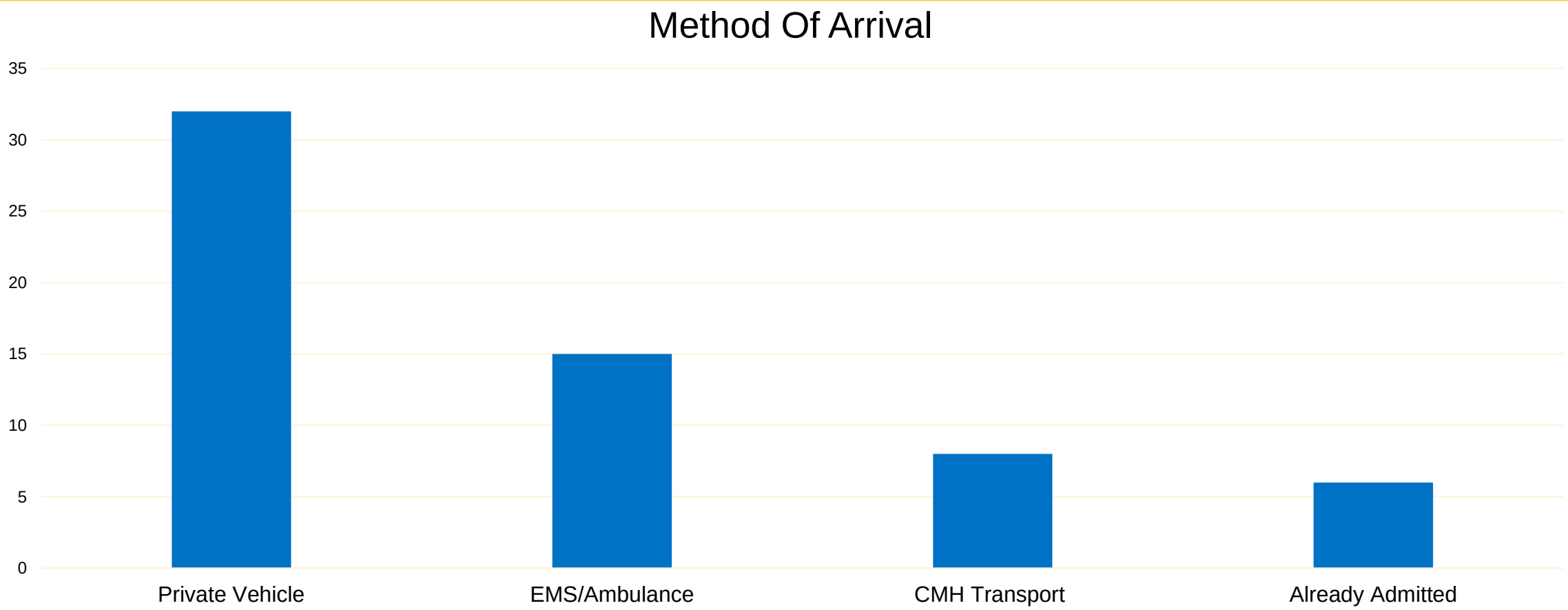
CMH Data



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Summary

- 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

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Case Reviews

- Stroke vs non-stroke

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Case1

- 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

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VOTE

A. Stroke

B. Non-stroke

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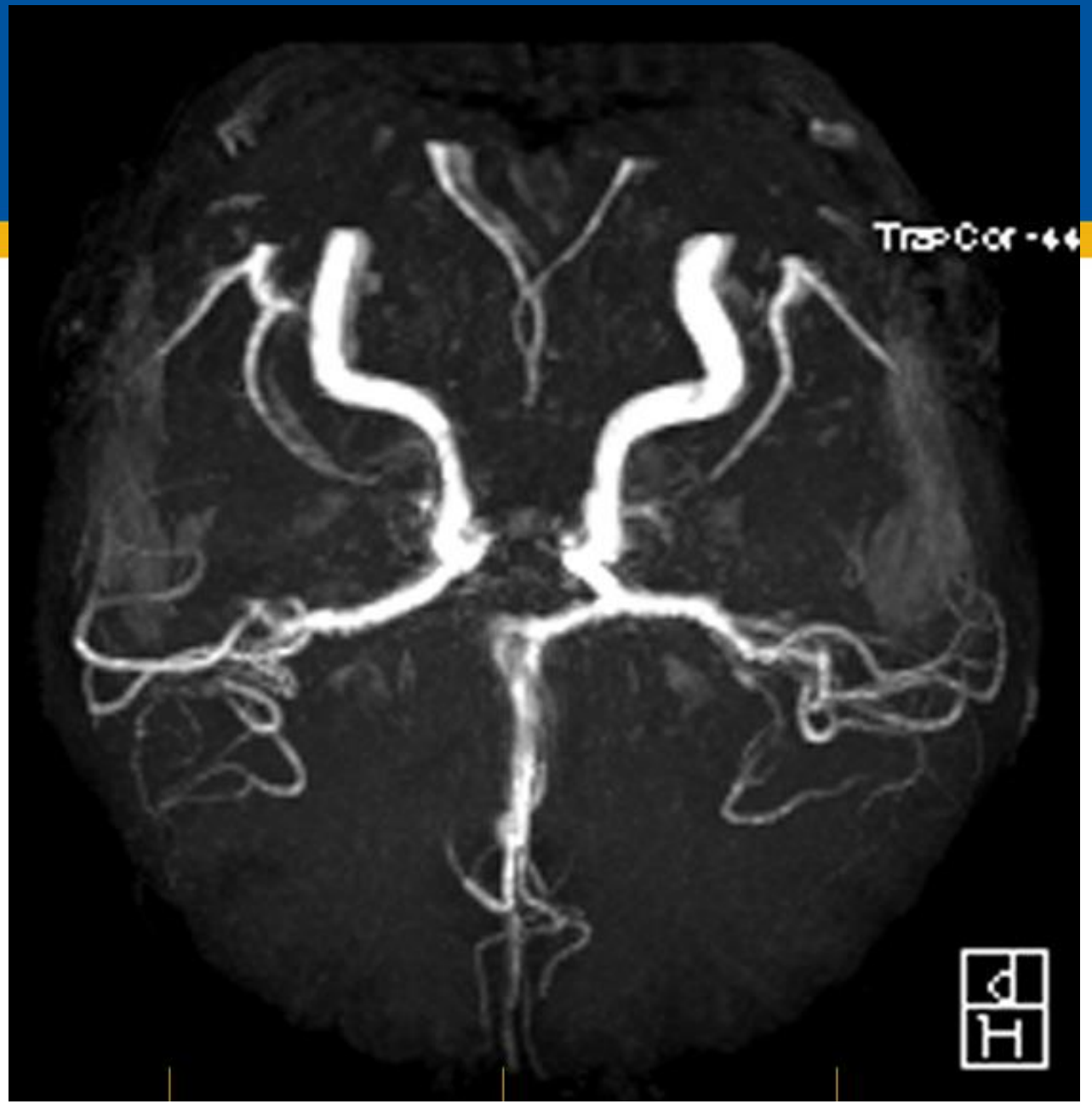

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Case 1

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

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Posterior Strokes

- Median age 7-8years, 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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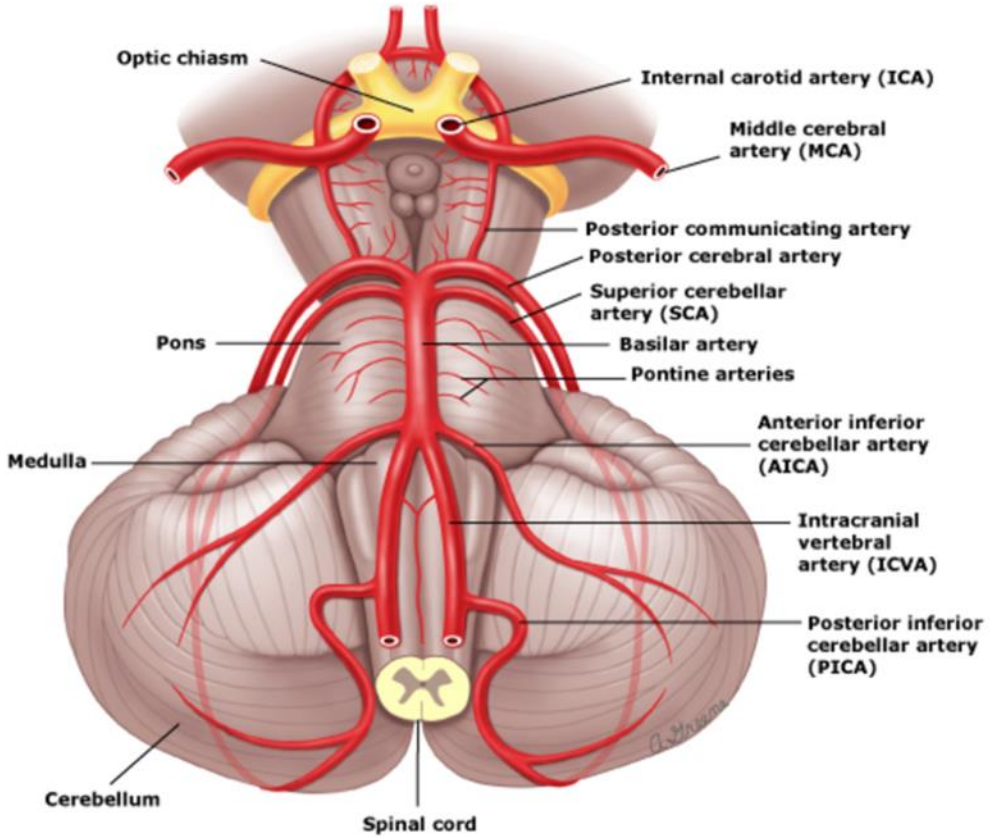

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https://www.google.com/url?sa=i&url=https%3A%2F%2Fcoreem.net%2Fcore%2Fposterior-circulation-stroke%2F&psig=AOvVaw0tP_Gafe_Je8zYNJgbwIr-&ust=1594315029754000&source=images&cd=vfe&ved=0CAIQjRxqFwoTCKC-4rqUvuoCFQAAAAAdAAAAABAD

IPSS experience

Dev Med Child Neurol. 2013 May;55(5):434-9. doi: 10.1111/dmcn.12092. Epub 2013 Feb 11.

Basilar artery strokes in children: good outcomes with conservative medical treatment.

Lagman-Bartolome AM[1], Pontigon AM, Moharir M, MacGregor DL, Askalan R, Yau I, Deveber G.

⊕ Author information

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.

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Case 2

- 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.

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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

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VOTE

A. Stroke

B. Non-Stroke

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Case 2

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

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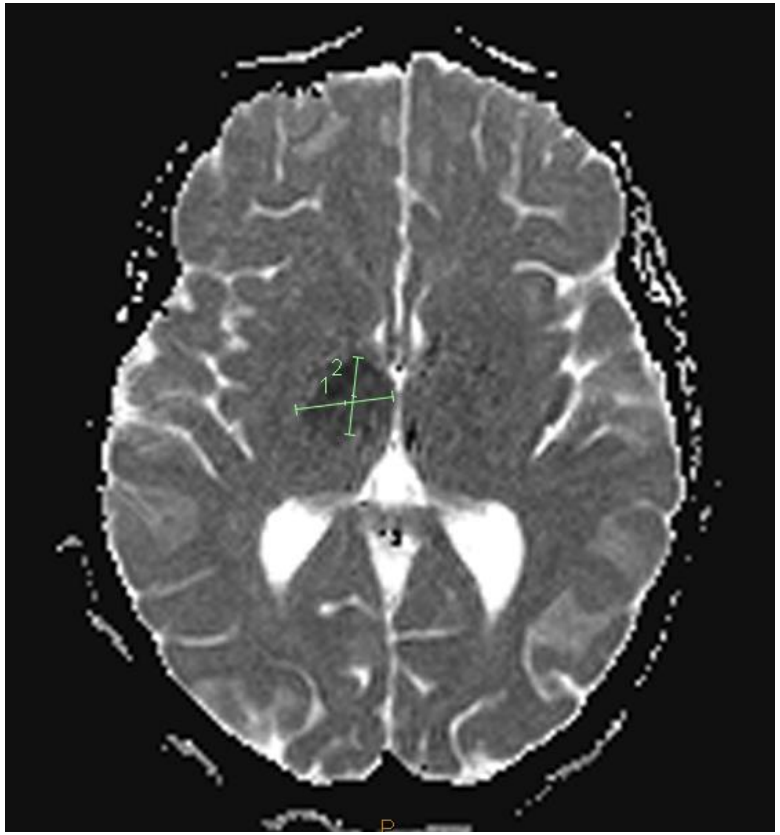
Case 2



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

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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.

Case 3

- 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.

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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

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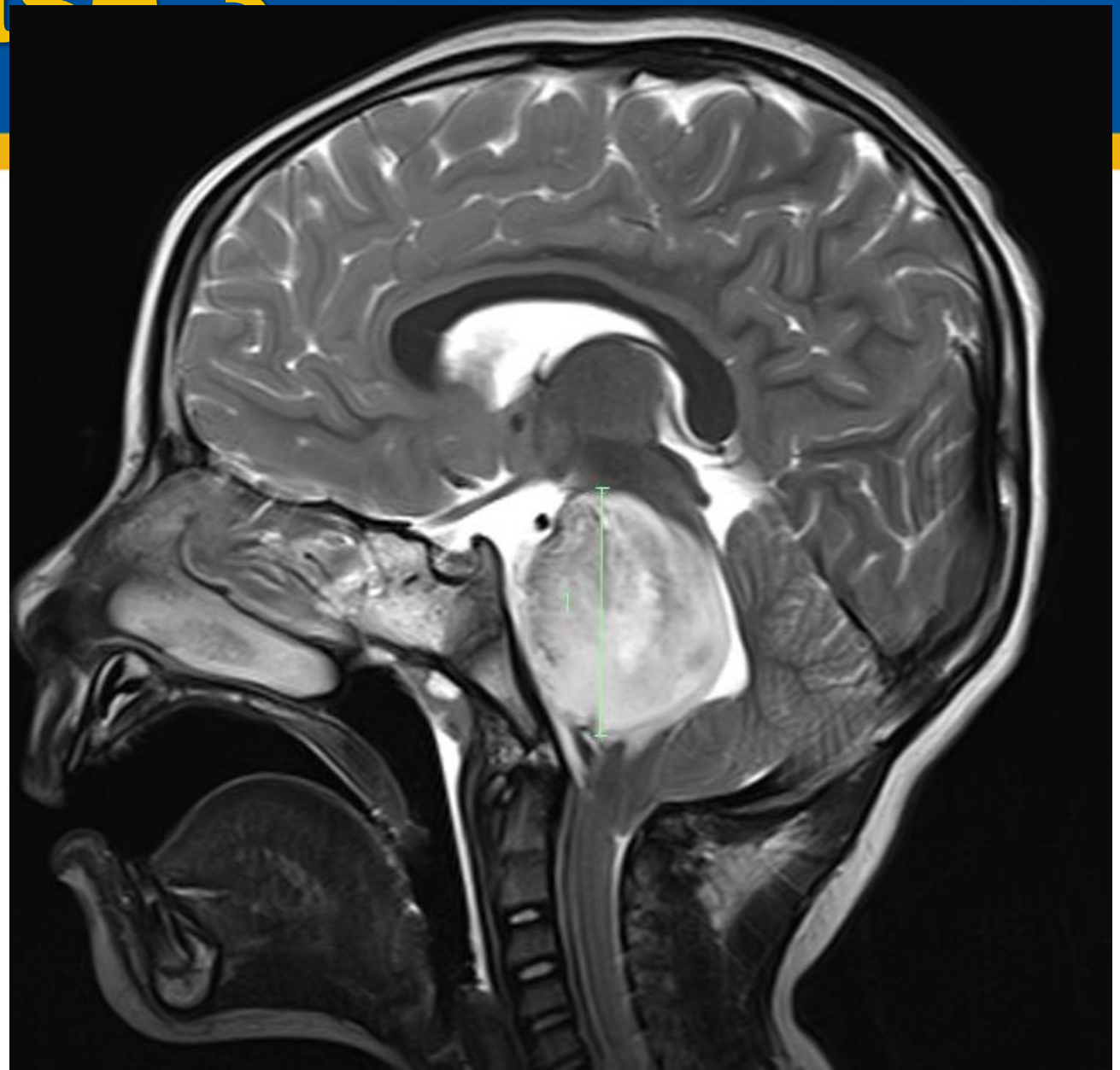
Case 3



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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.

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Case 4

- 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

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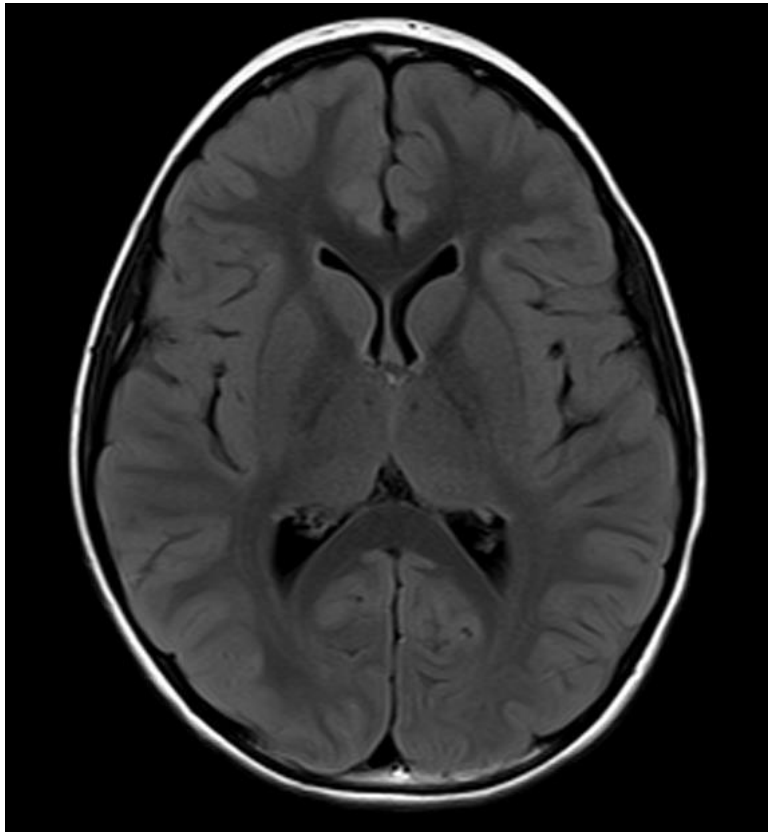
Case 4



- 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.

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Case 4

- 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.

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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

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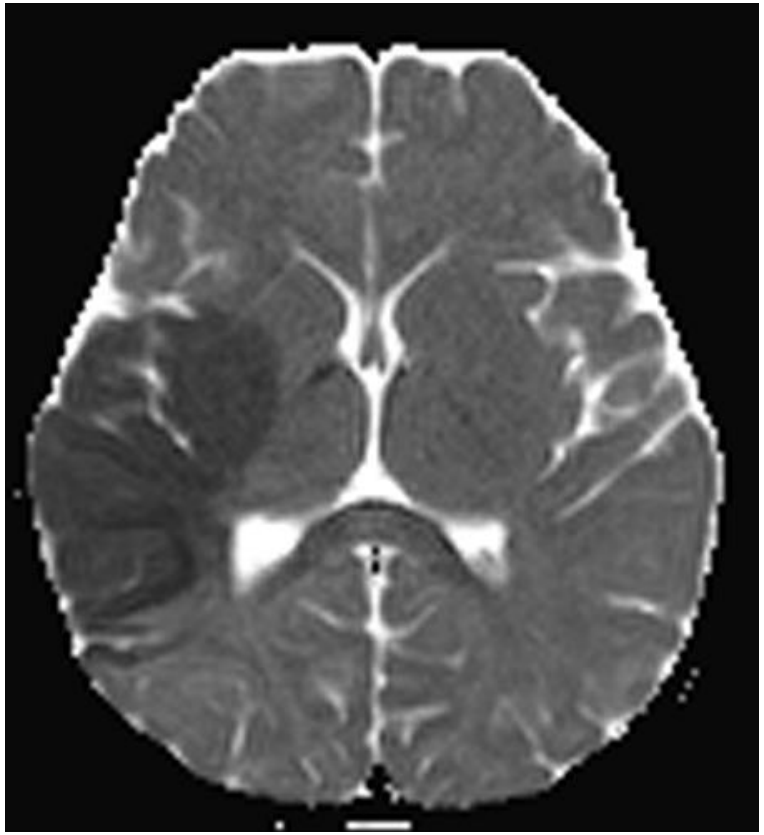
Case 5



- 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

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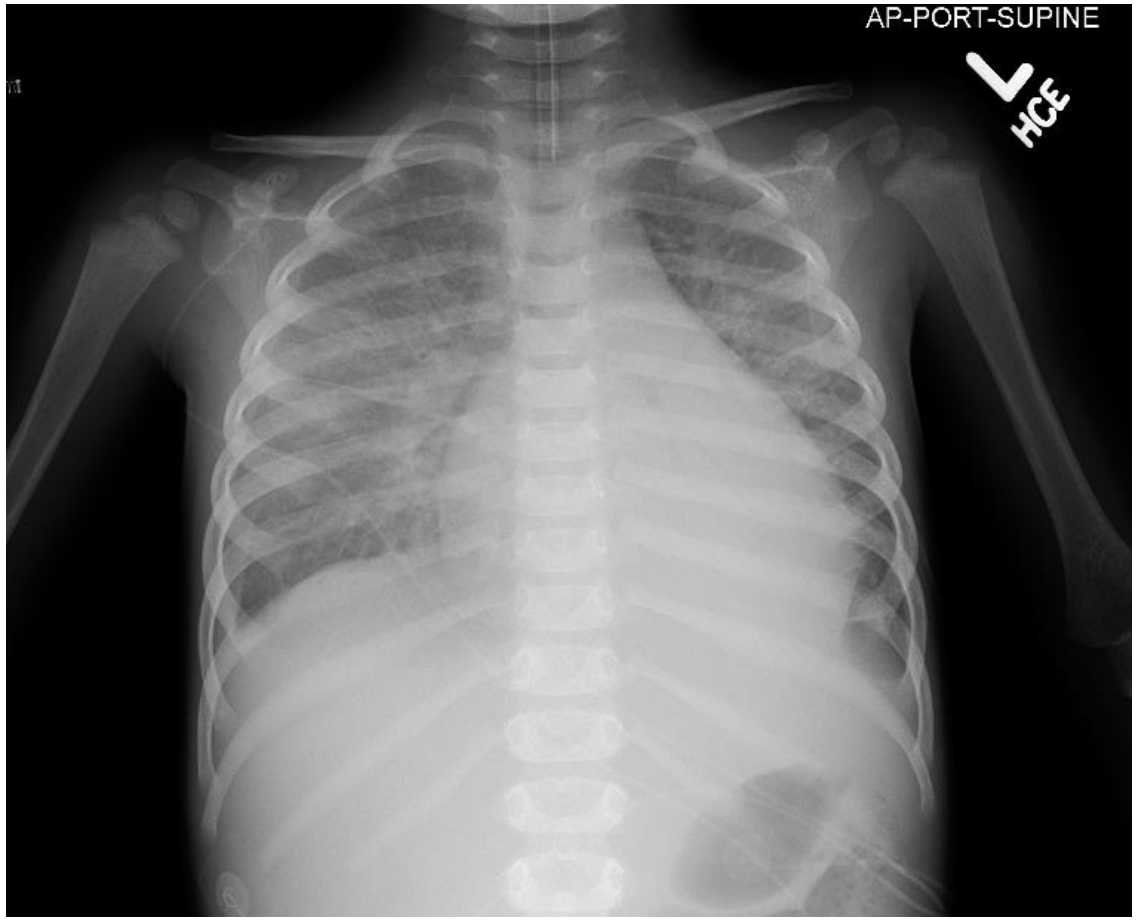
Case 5



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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.

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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 (2yrs post stroke)
- Etiology of dilated cardiomyopathy remains unclear, genetic testing inconclusive, continues on oral medications with improving cardiac function

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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

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Ferriero et al. Management of stroke in neonates and children. Stroke. 2019;50:e00

Thank You!

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