Impact of Creating a Pediatric Stroke Alert Team

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Where discovery brings hope

Disclosures

Off Label use of tPA and mechanical thrombectomy in children will be discussed.

AHA Peds Stroke Scientific Statement will be discussed

- I am a co-author of these guidelines

NIH grants to study:

- Hemorrhagic stroke in children (K23) - complete
- Stroke prevention in Nigerian children with sickle cell anemia (R21 and R01)
- Novel MRI methods in children with sickle cell anemia (R01)

Objectives

- Know the epidemiology of stroke in children
- Know the differential diagnosis for acute and subacute hemiparesis in children
- Understand the improvements that occur with a pediatric stroke alert protocol and team

AHA 2019 Scientific Statement on Stroke in Infants in Children

- All hospitals should have **educational programs for healthcare providers at all levels to develop knowledge and skills in diagnosis and management of pediatric stroke**
- All hospitals should have a plan for a children with suspected stroke (even if it is stabilize and transfer!)

Ferriero DM. Stroke 2019 epub Jan 25.

Challenges in Pediatric Acute Stroke

- **Recognition:** stroke is often not considered in children, especially in referring/non-children's hospitals.
- **Workforce:** pediatric neurologists are often not in-house.
  - So give phone advice, time to drive in, many not comfortable with acute stroke.
- **Imaging:**
  - CT often won't be definitive and differential is broad
  - CTA requires dye and radiation, try to avoid in children
  - MRI not available 24/7 at children's hospitals
  - Staffing costs and time for on-call MRI tech to drive in
  - Sedation may needed for both: MRI takes time; CTA contrast injection often prompts motion.

See: Lehman L. What will improve pediatric stroke care? Stroke 2019;50:249-256.

Results of these Issues

- Adult Stroke Neurologists are often asked to get involved in pediatric stroke triage, protocols, etc.

Epidemiology of Childhood Stroke

- **Incidence:** 3/100,000 children per year and 25/100,000 newborns per year (this is 1:4000 newborns)
  - **60% are ischemic** and 40% are hemorrhagic
  - So about 1.75/100,000 children per year with ischemic stroke.
  - Most hemorrhagic strokes are related to vascular malformations.
- **In the USA:** At least 3200 children per year have a stroke
- Stroke is at least as common as brain tumor in children

The Big Picture: Impact of Pediatric Stroke

- 60% of children with stroke will have persistent disability.
- Children have years to live with deficits.
- Many will need ongoing rehabilitation, educational supports
- Stroke teams aim to provide acute care that prevents disability.

Etiology of Ischemic Stroke in US Children

- **Arteriopathy "blood vessel pathology" 50+%**
  - **Arterial Dissection 25%**, also Focal Cerebral arteriopathy, Moyamoya, Post-Infectious, HIV, Varicella, etc
- **Cardioembolism – clot from heart to brain 25-35%**
- **Sickle Cell Anemia**
  - **11%** will have a ***clinical stroke*** by age 20 if no primary prevention
  - **37%** more will have a ***silent infarct***
- Hypercoaguable state
- More unusual causes… vasculitis, pregnancy, metabolic disorders
- Idiopathic (5–15%)

Etiology of Hemorrhagic Stroke in Kids

- Arteriovenous Malformations (#1 = Vascular)
- Cerebral Cavernous Malformation (CCM)
- Aneurysm
- Coagulation or platelet dysfunction
- Moyamoya
- Cerebral sinus venous thrombosis w/ hemorrhagic infarction
- Idiopathic

Signs and Symptoms of Stroke in Children

- **Hemiparesis 60%+**
  - Facial droop may be subtle, usually arm>> leg weakness.
- Aphasia 20%
- Slurred speech – frequency unclear
- **Focal seizure 25% of kids (adults <5%)**
- Headache 20%
- Loss of consciousness – with hemorrhagic stroke

Differential Diagnosis of Acute Hemiparesis in Children

- Complex migraine = hemiplegic migraine
- Focal seizure with focal weakness after seizure (Todd's Paralysis)
- **Stroke** – Ischemic/Hemorrhagic
- Other focal brain pathology

Stroke Mimics[1] can include:

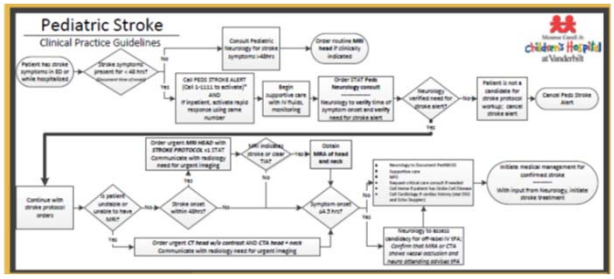
- Encephalopathy related to hypertension, intracranial infection, tumor, drug toxicity, pseudotumor cerebri, inflammatory disease, epilepsy

[1]Shellhaas R et al. Mimics of Childhood Stroke. *Pediatrics* 2006;118:704-709.

What Has Improved Outcomes in Adults with Stroke?

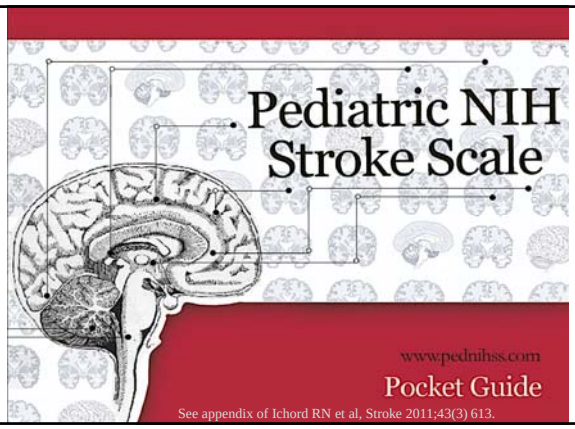
- **Thrombolytic Therapy – IV tPA and endovascular therapy!**
  - Break up the clot, reperfuse the brain (10% qualify and receive this therapy)
- **Stroke Centers**
  - Have brain attack teams
  - Provide supportive care
    - Fluids to maximize cerebral perfusion and care that avoids complications (control of blood glucose, swallowing assessment, DVT prophylaxis, etc)

Have a Process: Pediatric Stroke Alerts at Vanderbilt



When do We Activate a Pediatric Stroke Alert?

- When diagnosing a stroke may cause an urgent change in management.
- Child with symptoms for <48 hours.
- Why 48 hours rather than a shorter time window?
  - Edema/need for hemicraniectomy
  - Change in management that will occur based on the differential diagnosis



URGENT Stroke Imaging in Children - Details

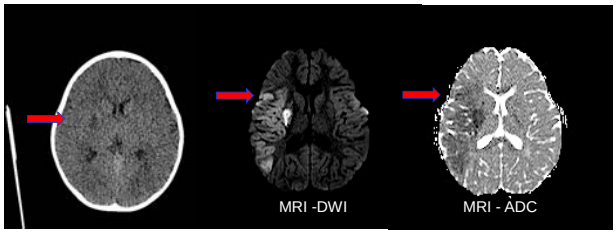
- **Non-contrast stroke protocol brain MRI = 1st choice**
  - Radiology should make a protocol for this study- looking for ischemia, bleeding and major structural issues.
  - For kids with symptom(s) within 48 hours where diagnosis of stroke will cause a large change in management.
- **Short protocol MRI takes <10 minutes**
- **An abbreviated MRI with sequences to confirm acute ischemia and assess for hemorrhage.**
  - DWI, GRE, T1 and T2 axials
- **MRA (8 min) can be added if needed.**
- **Why MRI?**

Sensitivity of CT vs. MRI for Detection of Stroke in Children

- CT misses a lot of smaller or acute strokes….
- UK data - CT missed 47% of peds strokes later confirmed by MRI[1]
- Australia data – CT missed 84% of peds strokes later seen on MRI (62 of 74 kids)[2]

1. McGlennan C, Ganesan V. *Dev Med Child Neurol* 2008;50:537–540
2. Srinivasan J, Mackay M. *Pediatrics* 2009;2:e227-34

Example: 2-year-old with left arm "dystonia" after high dose of "Dayquil" CT vs. MRI of the brain

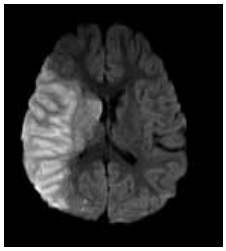


CT – low sensitivity for ischemic stroke… especially within 12 hours

Healthy 4-year-old. Focal left-sided seizure, transferred intubated

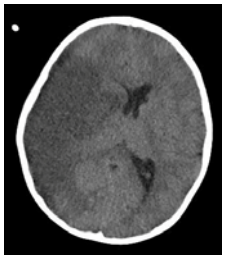
Presented with seizure, transferred with CT Head

Persistent left-sided weakness:MRI !

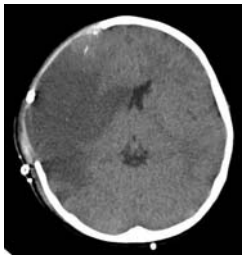


MRI helped a lot. Monitored for and prepared for cerebral edema. Neurosurgery consulted.

26 hours later, less alert.



27 hours later. Hemicrani.



Healthy kids don't have cerebral atrophy, so big strokes are dangerous.

Brief Report

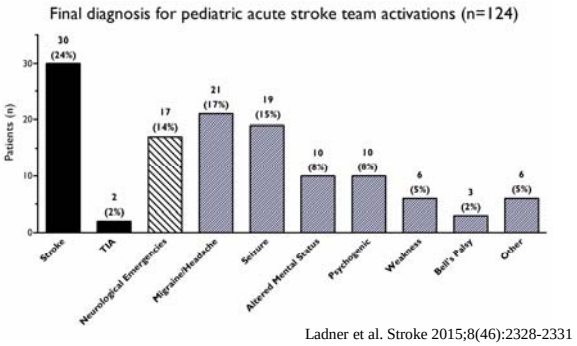
Pediatric Acute Stroke Protocol Activation in a Children's Hospital Emergency Department

Travis R. Ladner, BA; Jasia Mahdi, MD; Melissa C. Gindville, MS; Angela Gordon, RN; Zena Leah Harris, MD; Kristen Crossman, MD; Sumit Pruthi, MBBS; Thomas J. Abramo, MD; Lori C. Jordan, MD, PhD

Ladner et al. *Stroke* 2015;8(46):2328-2331

What is the data?

Peds Stroke Alerts in the ED at Vanderbilt



Ladner et al. Stroke 2015;8(46):2328-2331

Pediatric Non-Stroke Stroke Alerts: Neurological Emergencies N=17

- Intracranial neoplasm 4 (24%)
- Meningitis/encephalitis 5 (29%)
- Traumatic brain injury 2 (12%)
- Methotrexate toxicity 2 (12%)
- Epidural abscess 1 (6%)
- Hydrocephalus 1 (6%)
- Ketotic hypoglycemia 1 (6%)
- Demyelinating disorder 1 (6%)

Summary: Pediatric Acute Stroke Alerts, N=124

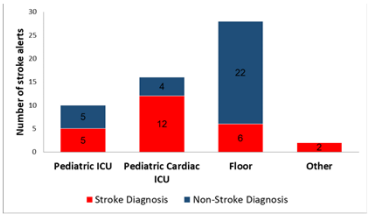
- 24% had a final diagnosis of stroke
- 2% had a final diagnosis of TIA
- 14% had very serious non-stroke diagnoses

So… 40% had neurological emergencies.

- **Two things have improved outcome in adult stroke:** Stroke Centers (protocolized and supportive care) and stroke interventions.

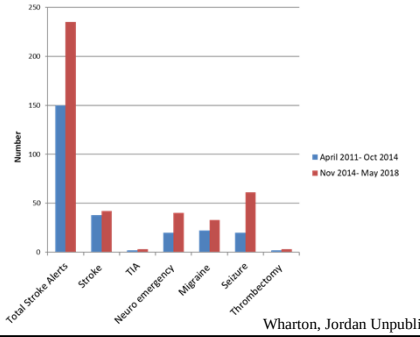
In-Hospital Peds Stroke Alerts at Vanderbilt, N=56

- Of the children with final diagnosis of stroke (N=25)
- **76% were in the pcicu, picu or pacu (post cath).**



Barry M, In hospital pediatric stroke alerts. *Pediatric Neurology* 2019.

Updated: 2011-2018 Pediatric Stroke Alerts, Final Diagnoses and Interventions over time (n=385)



Wharton, Jordan Unpublished data

Summary

- At our 271 bed children's hospital, moderate size, we have about 55 stroke alerts per year, 4.5 stroke alerts per month.
- Confirmed acute strokes are ~ 11.4 per year.
- 70% ischemic and 30% hemorrhagic.
- Improvements in care over time.
- There are additional kids with stroke after procedures and acute hemorrhage where neurosurgery is called (no stroke alert).
- **Uncommon events require attention and training.**

Importance of Supportive Care

- Chart review of 98 children with confirmed ischemic stroke at Vanderbilt.
- **Prevalence of hypertension 65%, hypotension 68%, hyperglycemia 18%, and fever 38%**
- Hyperglycemia was independently associated with poor outcome (Odds Ratio 3.9, CI 1.2-12.4, p=0.02).
- Hypertension and fever were not significantly associated with stroke size, poor outcome, or death. Only 28% had hypertension at follow-up (cardiac).
- Support the brain – minimize cerebral metabolic demands (avoid fever, hypoglycemia, hypotension)

Grelli et al. JAMA Neurology 2016

tPA and Thrombectomy and Kids

- tPA is not approved for use in children.
- Thrombolysis in Pediatric Stroke (TIPS) NIH closed this 20 site phase I safety and dose finding study for tPA for pediatric stroke for poor enrollment in December, 2013.
  - Kids didn't arrive in the 4.5 hour window.
  - Lack of established pediatric stroke systems.
  - However, TIPS resulted in significant systems improvement.
- Off label tPA in teens is not unreasonable. Use in younger kids is dicey.
- Off label mechanical thrombectomy may be considered. Risk of vessel injury, vasospasm seems more common in kids, etc.

AHA Guidelines 2019

- Criteria for off label use of Mechanical thrombectomy:
  - Persistent disabling neuro deficit - NIHSS >6
  - Radiographically confirmed large artery occlusion
  - "Larger" child due to contrast dye limitations with small size
  - Treatment decision made in conjunction with neurologists with pediatric stroke expertise
  - Experienced endovascular surgeon with expertise in thrombectomy in adult stroke patients and pediatric endovascular procedures
- **Recommendation:** Establish systems and pathways for hyperacute pediatric stroke care.

Ferriero DM. Stroke 2019 epub Jan 25.

Impact of a Peds Stroke Protocol

Our group has found:

- Improved use of PedNIHSS
- Shorter door-to-imaging time
- Identify candidates for intervention
- Identify serious stroke mimics more quickly

Canada and US teams have reported improvements in:

- Proportion of children receiving antiplatelet therapy within 24 hours (36% to 84%). Shack et al. 2016
- More rapid identification of children with mild stroke (Shack)
- Greater use of MRI and shorter time to MRI – from 17 hours to 4 hours. Delaroche et al. 2017

Take Home Points

- Hemiparesis in children can be migraine, focal seizure, stroke or a host of other things.
- 20-25% of children will have a stroke when stroke is suspected.
- Lots of unusual causes of pediatric stroke.
- Acute stroke care in children takes a team and a plan.
- Implementation of pediatric acute stroke protocols can be challenging but may prevent long-term disability

Thanks!

QUESTIONS?

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