Assessing and Treating Pediatric Stroke

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Where discovery brings hope

Disclosures

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

The American Heart Association 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 causes of stroke in children

Know the differential diagnosis for acute and subacute hemiparesis in children and how to assess children

Know the acute and chronic treatments for stroke in children

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.

Big Picture: 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.

Causes 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 (1% with good primary prevention)

37% more will have a ***silent infarct***

Hypercoaguable state

More unusual causes… vasculitis, pregnancy, metabolic disorders

Idiopathic (5–15%)

Causes 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%)

Tough because 1:100 children will have a seizure and 1:20 children will have a febrile seizure; less that 1:100,000 will have seizure + stroke

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.

Rapid Assessment of Children with Possible Stroke

Confirm history – sudden onset of symptoms? (Vs weeks/months of symptoms)

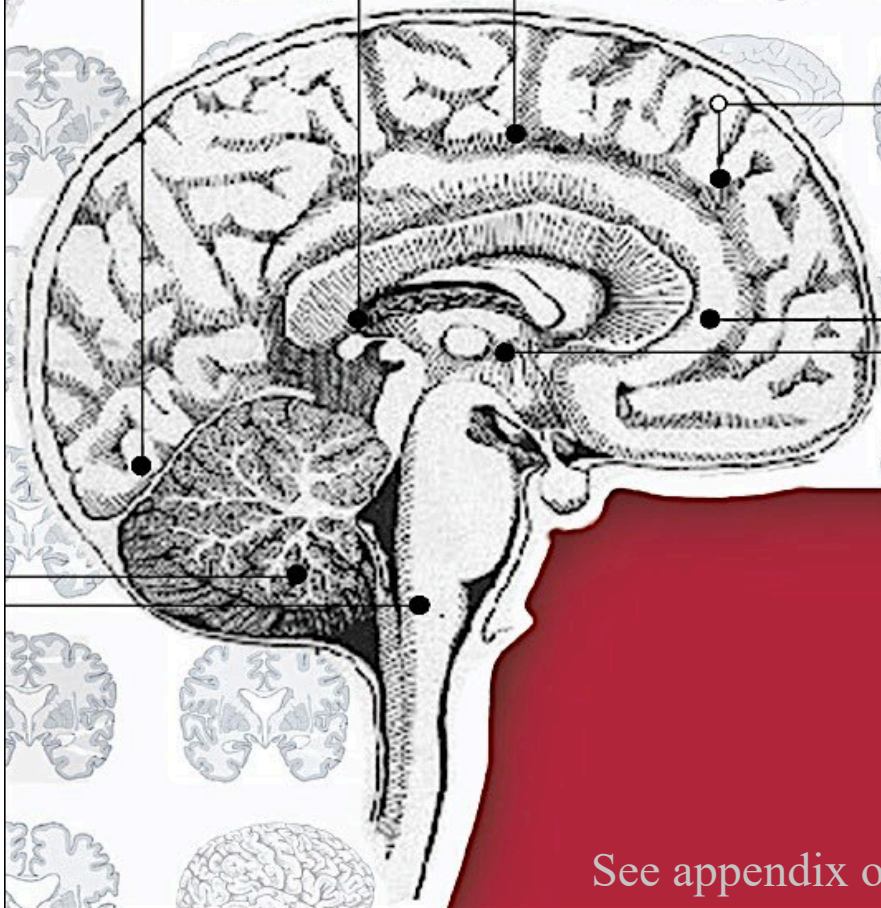
- Does this sound like a stroke?
- Careful in young children sometimes adults are slow to notice

Neuro exam (Pediatric NIH Stroke Scale)

Imaging

Other testing

Pediatric NIH Stroke Scale



www.pednihss.com

Pocket Guide

See appendix of Ichord RN et al, Stroke 2011;43(3) 613.

Full Diagnostic Evaluation if Confirmed Ischemic Stroke

Head, Neck, Heart, Blood

CT/CTA– all adults and unstable children.

MRI Brain – "Stroke protocol with diffusion" – all, often first in kids

Image of brain + NECK vessels - CT Angiography, MR Angiography

Echocardiogram – for cardiac function and undiagnosed

EKG/cardiac monitoring -for cardiac arrhythmia

Labs for risk factors: fasting lipid profile, Hemoglobin A1c, etc

Coag Evaluation – most children (other than newborns) need this – especially if cryptogenic or family history of thrombosis.

Acute Treatment: 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)

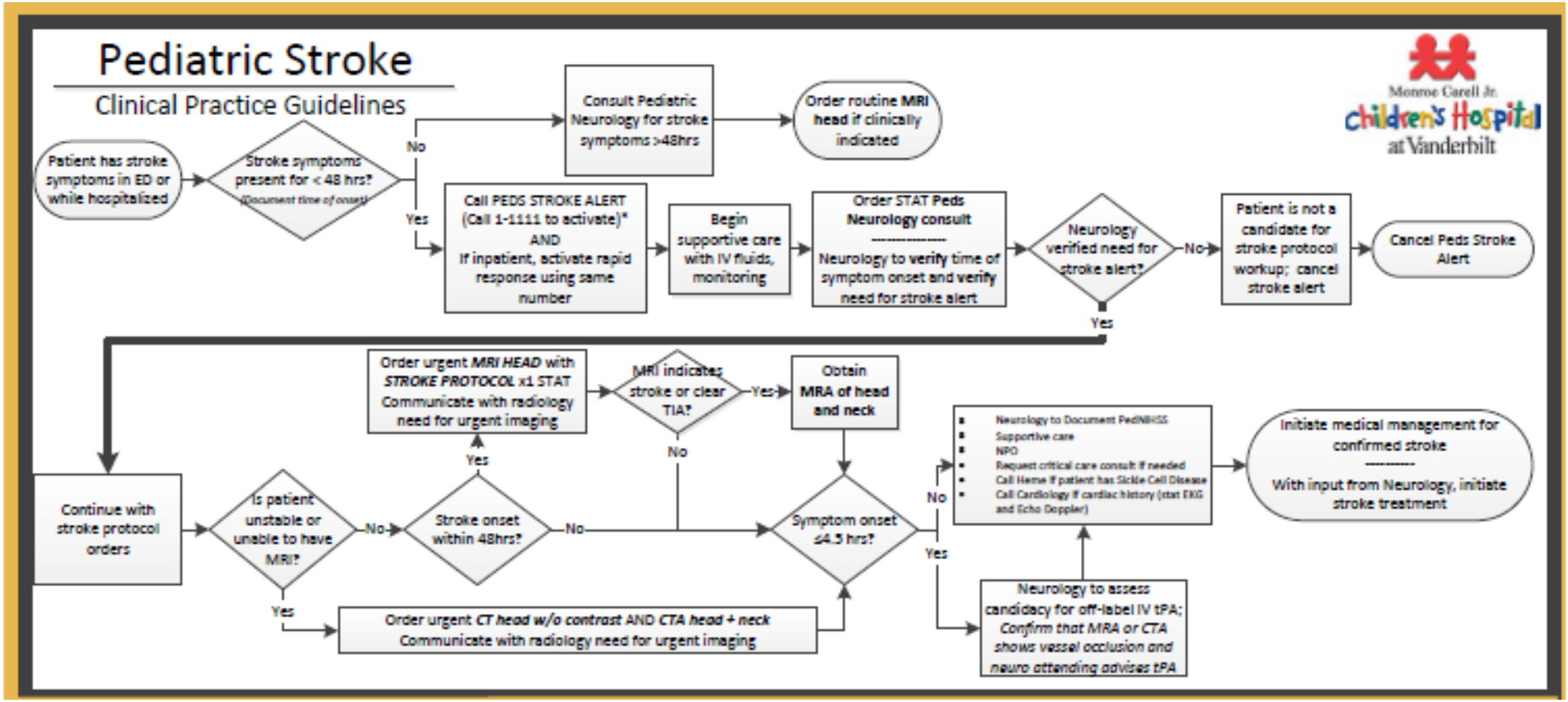
Stroke Centers

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



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

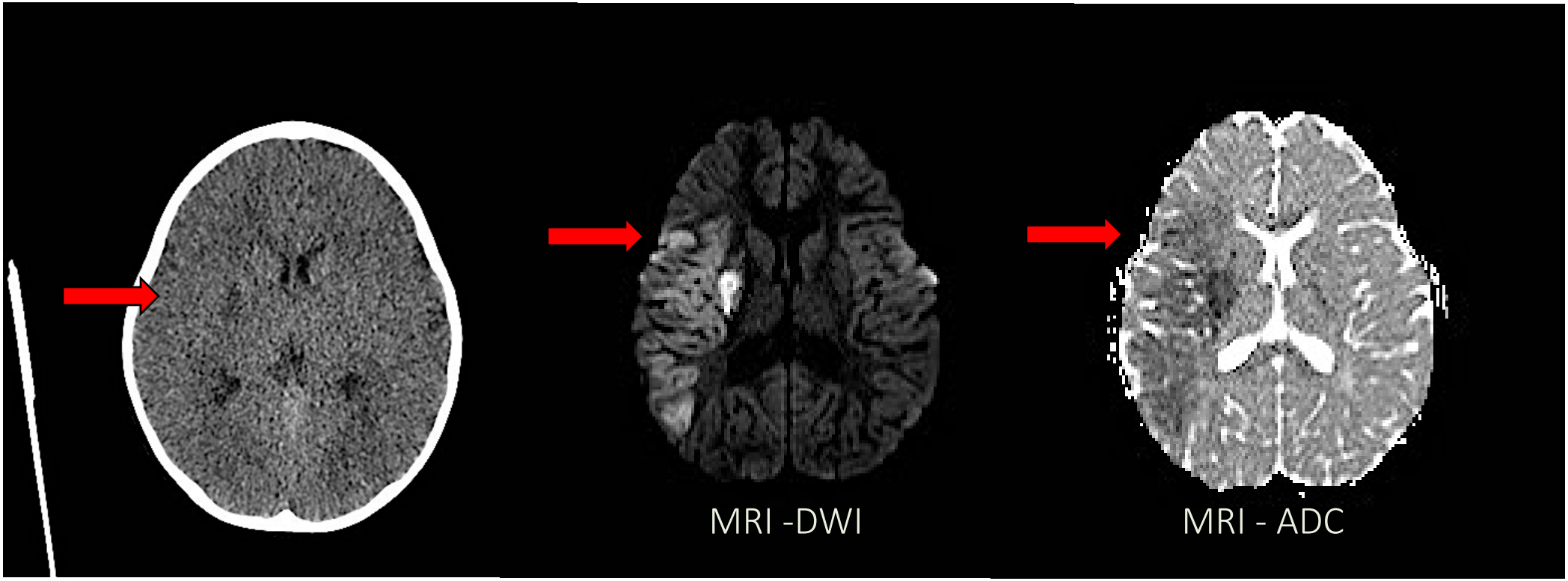
CT misses a lot of smaller or acute strokes….

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

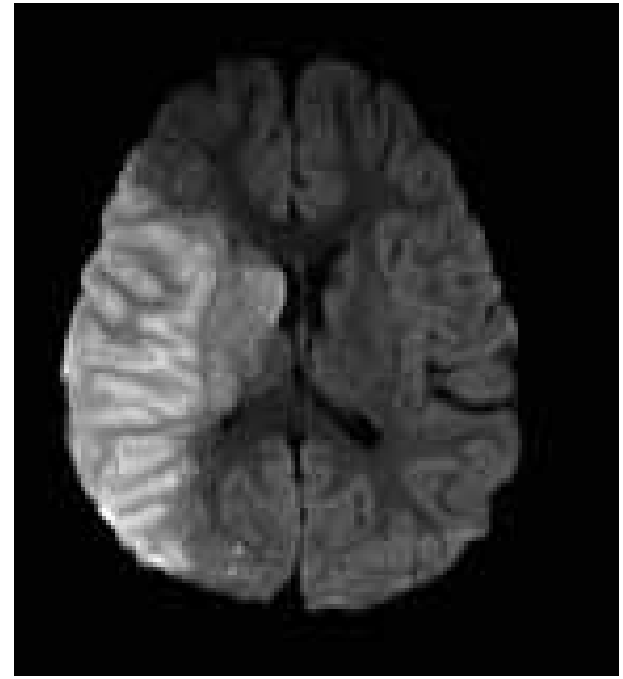


CT – low sensitivity for ischemic stroke… especially within 12 hours

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

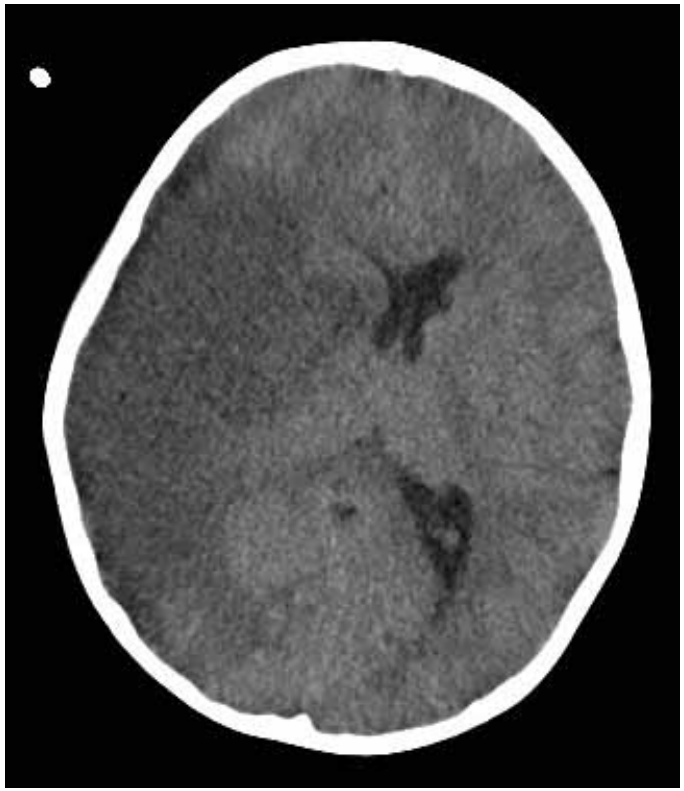
PRESENTED WITH SEIZURE, TRANSFERRED WITH CT HEAD

PERSISTENT LEFT-SIDED WEAKNESS:MRI !



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

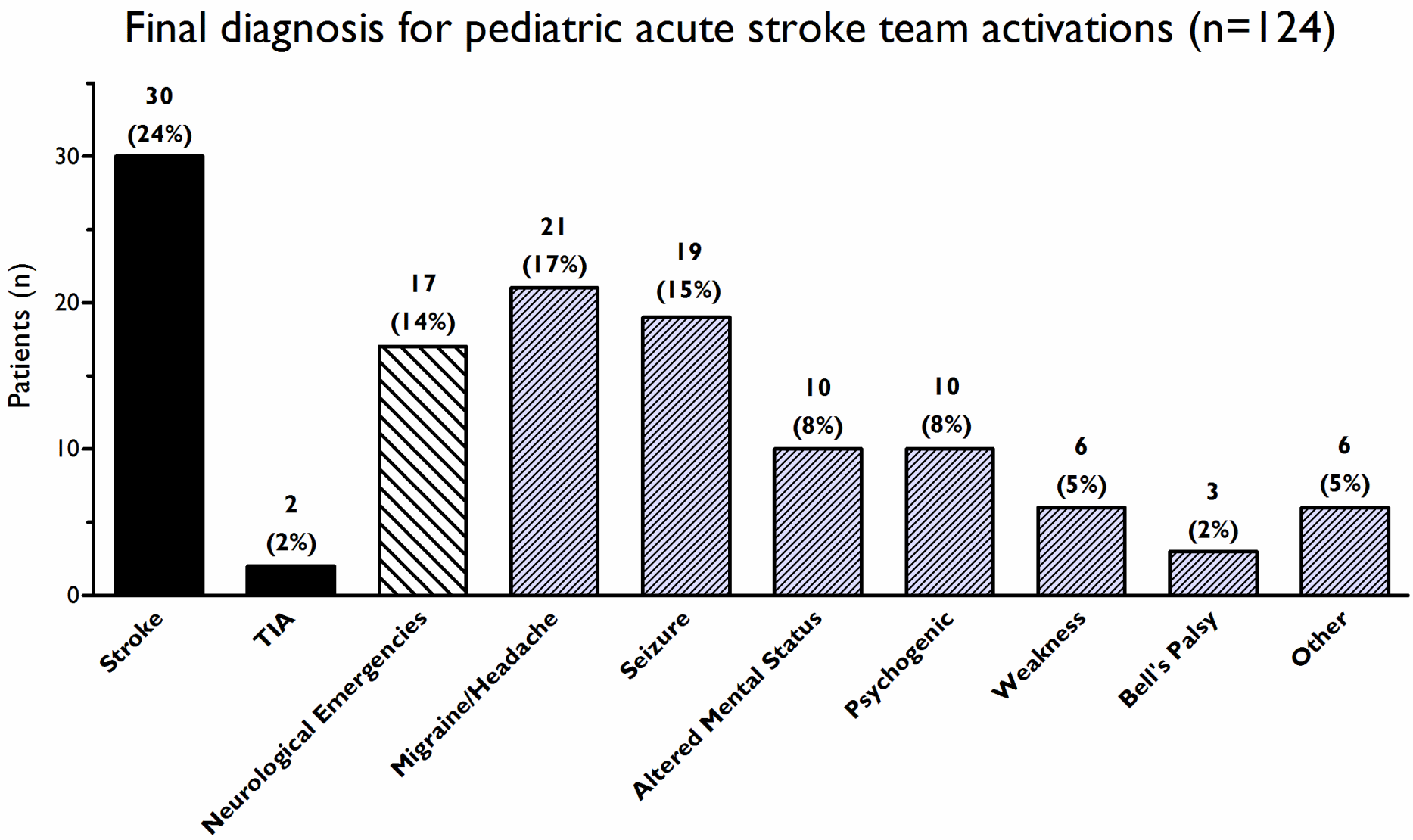
26 HOURS LATER, LESS ALERT.



27 HOURS LATER. HEMICRANI.

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

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.

ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

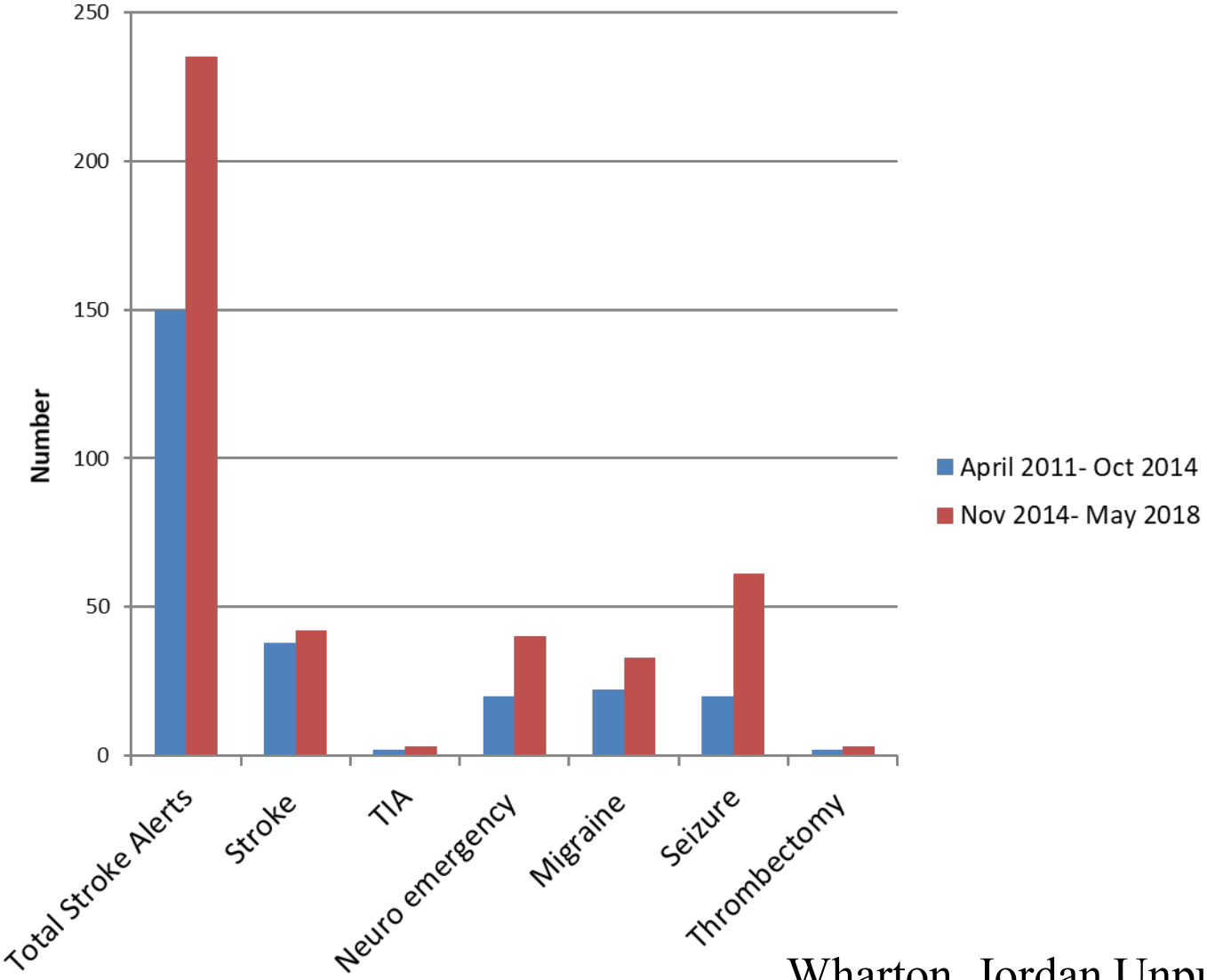
Pediatric Acute Stroke Protocol Implementation and Utilization Over 7 Years

Jessica D. Wharton, MD[1], Megan M. Barry, DO[2,3], Chelsea A. Lee, BS[1], Kayla Massey, BS[4], Travis R. Ladner, MD[5], and Lori C. Jordan, MD, PhD[1,6,7]

Wharton et al. *J Peds* 2020

What is the updated data?

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



Wharton, Jordan Unpublished data

Comparing the first 3.5 years to second 3.5 years of the protocol

Table 1. Comparison of Demographics, Patient Location and Time-to-Imaging for 385 pediatric stroke protocol activations over 7 years			
	Period 1, n=150	**Period 2, n=235**	**P-value**
Age, median, interquartile range (IQR)	11 years (IQR 7-15)	9 years (IQR 3-14)	p=.006
Male, n (%)	75 (50%)	122 (52%)	p=.714
PedNIHSS documented, n (%)	63 (42%)	192 (82%)	p<.001
PedNIHSS, median, IQR	3 (1-7)	4 (1-12)	p=.067
Door-to-imaging time (ED only) for those in thrombolysis window, median, IQR	101 min (IQR 80-132) *n=43	79 min (IQR 58-121) *n=58	p=0.058
Confirmed stroke as final diagnosis, n (%)	38 (25%)	42 (18%)	p=.078
Non-stroke neurological emergency, n (%)	20 (13%)	40 (17%)	p=.331

Wharton, Jordan 2020

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.

Treatment: Sickle Cell Disease (HbSS) and Acute Stroke

For Stroke In SCD (different than other individuals with stroke):

Rapid blood transfusion in ED to bring up hemoglobin in 9-10 g/dL with 2 hours

- Then, PICU for exchange transfusion (add blood and remove blood) to rapidly reduce hemoglobin S% levels to less than 30%.

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.

Steroids for Acute Stroke?

For focal cerebral arteriopathy (narrow blood vessel that we think is due to inflammation)

Two clinical trials just starting:

Europe: High Dose Steroids in Children With Stroke (PASTA)

USA: Focal Cerebral Arteriopathy Steroids Trial (FOCAS)

High dose intravenous steroids x 3 days followed by steroid taper.

Long Term Treatments after Stroke in Children

-Aspirin

Typical treatment

-Anticoagulation (stronger blood thinners)

Less common

-Chronic blood transfusions for children and adults with sickle cell disease

Rehabilitation therapies!

Treatment with Aspirin

For all older children with ischemic stroke except kids with sickle cell disease

Typical ASA dose is 3-5 mg/kg/day

Risk of Reye's syndrome is very low

-Still, we strongly recommend annual flu vaccine. Some will hold aspirin with high fever or flu-like symptoms (I don't).

Appropriate duration of therapy on a case-by-case basis.

-If otherwise healthy and no risk factors found with a careful evaluation, we often treat for 2 years and then stop aspirin. No data (yet).

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.
- Detailed evaluations are need.
- 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

Interested in Pediatric Stroke? Get involved!

International Pediatric Stroke Organization

Website: https://internationalpediatricstroke.org/
Twitter: @curekidstroke
membership@internationalpediatricstroke.org