# The Many Faces of Pediatric Stroke


- Jo Ellen M. Lee MSN APRN
- Division of Neurology
- Nationwide Children's Hospital
- joellen.lee@nationwidechildrens.org


# Disclosures

Nothing to disclose

I am involved in recruiting for various research studies but do not have any direct financial relationship

# Objectives –

At the end of this program the participant will be able to

- Differentiate between the different types of pediatric stroke.
- Discuss treatment options including advances in pediatric stroke care.

Arterial Ischemic Stroke

Cerebral Sinus Venous Thrombosis

# Pediatric Stroke

Perinatal Arterial Ischemic Stroke

Presumed Perinatal

# Types of Pediatric Stroke

Perinatal -Occurring after 20 weeks of gestation up to 28 days of age

Perinatal arterial ischemic stroke (PAIS)

Perinatal venous infarctions

Presumed Perinatal ischemic stroke (PPIS) – Delayed diagnosis

Childhood Arterial ischemic stroke (AIS) – after 28 days of age through adolescence. Occurs when blood flow in an artery to part of the brain is blocked – embolism, narrowed or damaged artery

Hemorrhagic stroke – can occur in either age group. May be secondary to venous congestion.

Cerebral sinovenous thrombosis (CSVT) - can occur in either age group. Occurs when a blood clot develops in a venous sinus or larger deep veins of the brain. Smaller cortical veins can be involved.

Strokes can happen at any age. Strokes in children are sometimes hard to diagnose because other neurologic (brain) problems have the same symptoms.

# Why a Delay in Diagnosis?

- Lack of awareness of neonatal and pediatric stroke
- Median time from symptom onset to parent seeking care 1.7-21 hrs ( average 6 hrs)
- Median time to radiological confirmation of diagnosis is 15-24 hrs
- Neuro deficits may be overlooked in children
  TIA symptoms may be attributed to behavior or cooperation.
- Transient nature of some symptoms – some one sided deficits may be subtle
- Need for MRI due to CT scan not always reliable

# Stroke Mimics

- Migraine with aura
- Alternating Hemiplegia
- Seizures followed by Todd's paralysis
- Bell's Palsy
- Severe encephalitis
- Syncope
- Conversion disorder
- CNS Tumors
- Demyelinating disease
- Metabolic Disease
- Intoxication
- Cerebellitis
- Epidural abscess
- Traumatic Brain Injury

# Stroke Mimics – How to differentiate

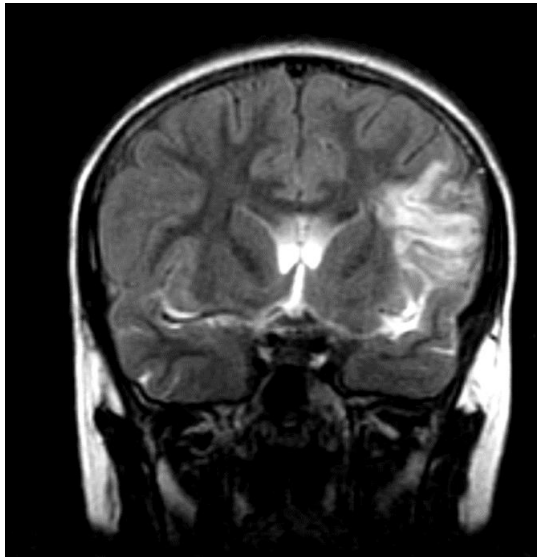
| | | | |
|---|---|---|---|
| Symptoms Associated with Stroke Diagnosis | Well the week prior (HS) | Inability to walk | Focal face or arm weakness (AIS) |
| Associated with migraine diagnosis – visual disturbances | Nondiscrimatory - Seizure | Nondiscrimatory – Altered mental status | Nondiscrimatory – Sudden symptom onset |

Mackay MT, Chua ZK, Lee M, Yock-Corrales A, Churilov L, Monagle P, Donnan GA, Babl, FE Stroke and non stroke brain attacks in children. Neurology 2014: 82 1434-1440.

# Arterial Ischemic Stroke

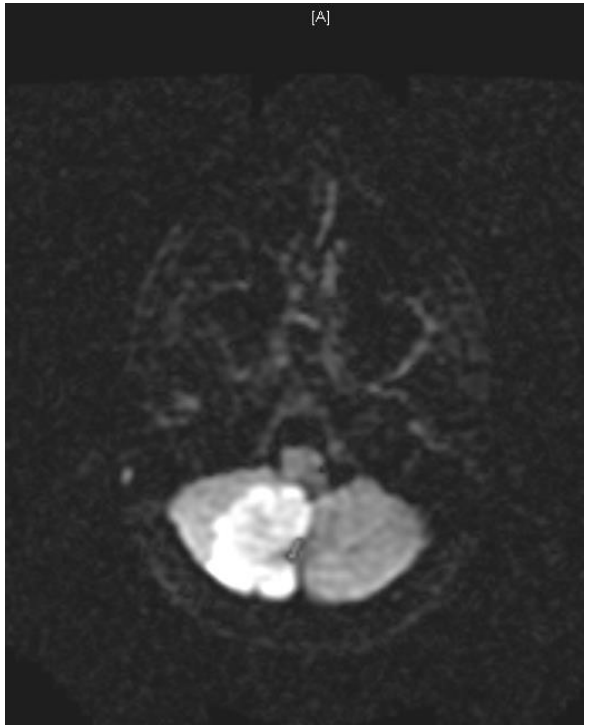
## 16 yo female with sudden onset

- right sided facial paralysis and paresthesia
- Diplopia
- Dysarthria
- Nausea and vomiting
- Vertigo
- Swallowing difficulties



Old left frontal infarction

New right cerebellar infarction on DWI
PICA
Vertebral artery occlusion – possible dissection
Positive for Factor V Leiden mutation



# Incidence and Epidemiology Arterial Ischemic Stroke

- One of the top 10 causes of childhood mortality in the United States
- 1.3-5.4/100,000 /yr in United States
- 4 -5 % children die after stroke (50% related to underlying condition)
- In children Ischemic and hemorrhagic stroke occur equally.
- Ethnicity:  African American > white  (not explained by Sickle Cell Disease)
- Boys > Girls (trauma)
- Age at first stroke –
  - greatest risk in < 1 yr. old
  - Increases again in 15-19 age group
  - Elderly group

# Causes of Arterial Ischemic Stroke

Cardiac

Arteriopathies

Acute Systemic Conditions

Hemato oncological

Chronic Head and Neck Disorders

Hypercoagulable States

- Acquired
- Inheritable

Metabolic/ Genetic

- Mitochondrial disorder

Other

Trauma

# Arterial Ischemic Stroke

## Presenting Symptoms – dependent on location of stroke

- Abrupt onset 51%
- Progressive onset 36%
- Wax and Waning onset 13%
- Hemiparesis- hemifacial weakness 67-90 %
- Seizures 15-25% esp < 6 yrs of age – Focal, Generalized, Both
- Ataxia 8-10 %
- Headache 20-50% versus 25% in Adults
- Altered Mental Status 17-38 %
- Visual loss or changes – occipital 10-15 % Papilledema 1%
- Changes in speech- dominant frontal (Broca) – posterior temporal (Wernicke) 20-50%
- Vomiting 10%
- Other 19% - focal signs Other 8 % - Non-localizing features

## Red flags: vomiting w/o fever, diplopia, ataxia - Cerebellar

# Outcomes AIS - predictors

- Larger infarct volume and younger age associated with poorer outcome
  - Poorer psychosocial and cognitive function
- Functional outcome predictors
  - Specific infarct locations associated with worse outcome – connection regions
  - Use of rehab services – better
- Seizures during the acute stroke phase predict poorer outcome
- Arteriopathy associated with abnormal functional outcome
- Pediatric Stroke Outcome Measure score of 2 – less functional recovery
- Less functional recovery occurs > 1 year after stroke
- Functional status at 1 year poststroke predicts long term outcome
- 35% with some type of psychological or psychiatric disorder (anxiety, depression)

# Outcomes

- Normal outcomes in 30%
- 70% with deficits
  - 36% mild
  - 23 % moderate
  - 10% severe
- Cognitive
  - Wechsler scales -- 3 years after stroke (Canadian data)
    - Overall intelligence, verbal ability, working memory, and processing speed were significantly lower in children who had a stroke than normal population
    - Injury to cortical and subcortical areas –performed more poorly than those with damage to either the cortical or subcortical area alone
  - Difficulties with poor attention, impulsivity and executive function

Ferriero DM, Fullerton HJ, Beonard TJ, etal. Management of Stroke in Neonates and Children: A Scientific Statement from the American Heart Association/American Stroke Association. Stroke 2019, 50(3) e51-e96.

# Outcomes

- Quality of life
  - Significantly lower than published normal for children of the same age across all domains (physical, emotional, social, school and cognitive functioning)
  - Cognitive/behavioral deficits and low verbal IQ adversely affected quality of life, especially among older children and girls
  - However neurological outcome and family socioeconomic status did not
- Motor and Speech
  - Hemiparesis 55% (mild)
  - Speech 21% (mild)

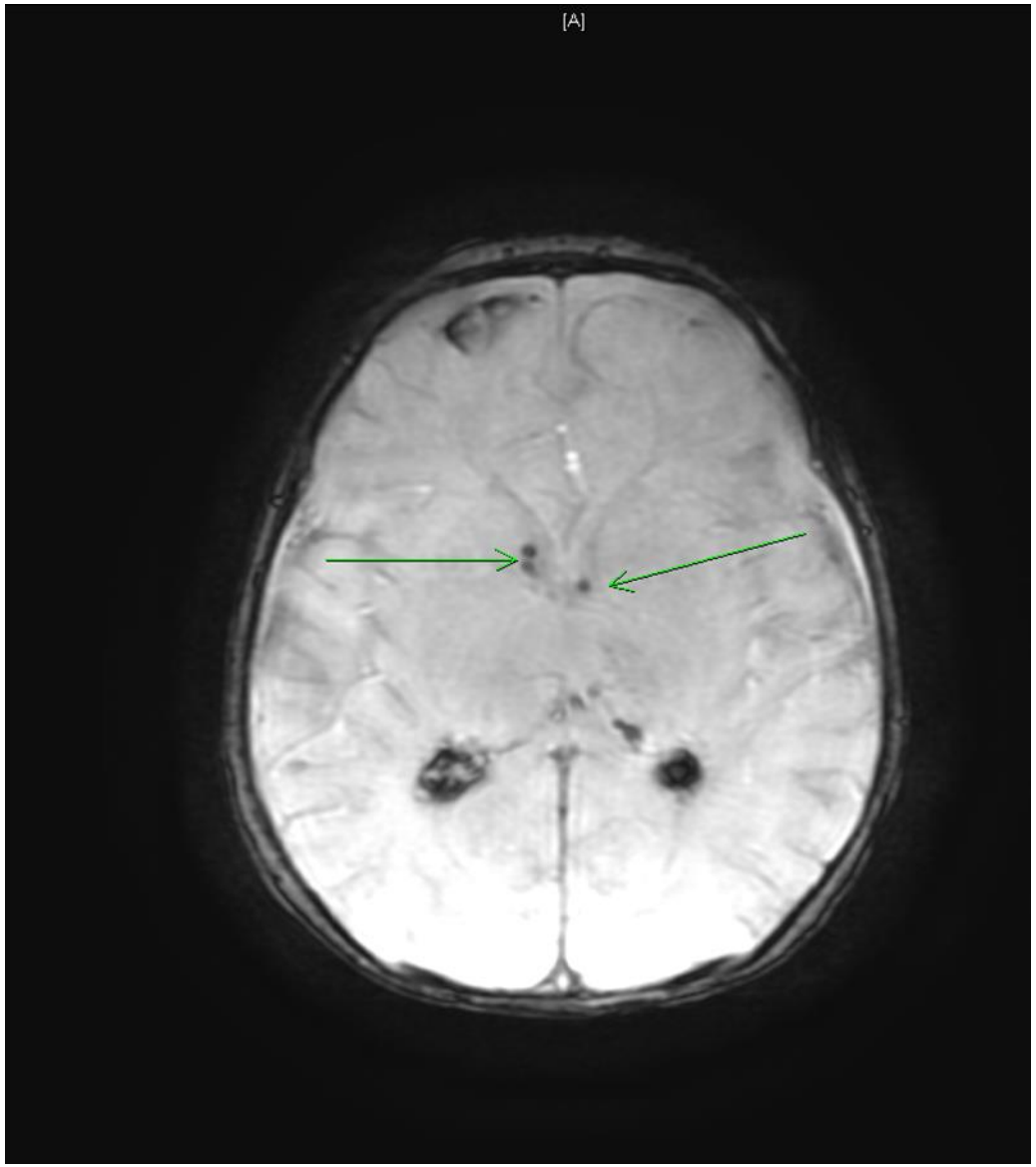
Ferriero DM, Fullerton HJ, Beonard TJ, etal. Management of Stroke in Neonates and Children: A Scientific Statement from the American Heart Association/American Stroke Association. Stroke 2019, 50(3) e51-e96.

# Long term outcomes – Adults who had stroke as a child

- 80% complete recovery or mild deficit
- > 25% reported mental illness (depression, anxiety)
- If they had rehab in first year – Maximal outcomes
- Presence of Epilepsy lead to poorer scores
- Memory and executive function impairments
- Fatigue
- > initial severity & longer duration of follow-up were significantly  associated with greater risk for unemployment.

# Hemorrhagic Stroke

- Significant hemorrhagic conversion after ischemic stroke appears to be rare in children and associated with large infarct volume
- Hemorrhagic conversion can occur  with Sinus venous thrombosis
- 4% risk of intracranial hemorrhage secondary to anticoagulation treatment
- Structural lesion – 75% (AVM most common)
  @ 10% idiopathic



# Causes of Hemorrhagic Stroke

Tumors

Abnormal blood vessels in brain or neck -75%

Significant Premature birth

Injury to the blood vessel wall

Inflammation or infection

Hypercoagulable States

- Acquired
- Inheritable

Metabolic

- Mitochondrial disorder

Trauma

- Dissection

# Perinatal Arterial Ischemic Stroke (PAIS)

- Incidence is around 1 per 4000 live births (figures range from 1/2300 to 1/5000)
- There is a slight male predominance
- PAIS is usually unilateral (87%) and typically affects the Left Middle Cerebral Artery (58-64%)
    - This is thought to be due to hemodynamic differences from a patent ductus arteriosus and a more direct route from the left common carotid

# Perinatal Arterial Ischemic Stroke (PAIS)

PAIS is a common cause of cerebral palsy and the 2nd most common underlying etiology of neonatal seizures

**PAIS is easy to miss since many newborns do not show focal deficits so early clinical recognition is important to improve neurologic outcomes**

Children with history of perinatal stroke have higher neurologic morbidity than children with strokes occurring later in infancy or childhood.

Children with a history of perinatal stroke are felt to “grow into” their deficits so in infancy we are unable to provide accurate assessment of future ability.

# Risk factors for PAIS

**Maternal**

- Thrombophilia
- Infertility/Miscarriage
- Prolonged rupture of membranes
- Preeclampsia
- Smoking
- IUGR
- Infection with or without maternal fever

**Placenta**

- Chorioamnionitis
- Placental infarcts

**Fetal**

- Thrombophilia > 50%
- Congenital heart disease
- Arteriopathy
- Hypoglycemia
- Low oxygen - perinatal asphyxia
- Infection
- Need of resuscitation
- Apgar <7 at 5 minutes (rated 0-10)

# PAIS Clinical Presentation

Seizures – 70-90%

- Usually within 12 hr of life up to 1st 3 days
- Seizures are typically focal clonic seizure
  - repetitive facial movements, including sucking, chewing, or eye movements
  - unusual bicycling or pedaling movements
  - staring
  - apnea, or pauses in breathing associated with slowing of the heart
  - rhythmic jerking movements involving the muscles of the face, tongue, arms, legs, or other regions
  - stiffening or tightening of muscle groups
  - quick, single jerks involving one arm or leg or the whole body

- Neurologic exam typically normal, abnormal exam 30%
- Encephalopathy (change in level of consciousness) 39%
- Change in muscle tone 38%
- Respiratory issues 26%
- Feeding difficulties 24%

# Outcomes

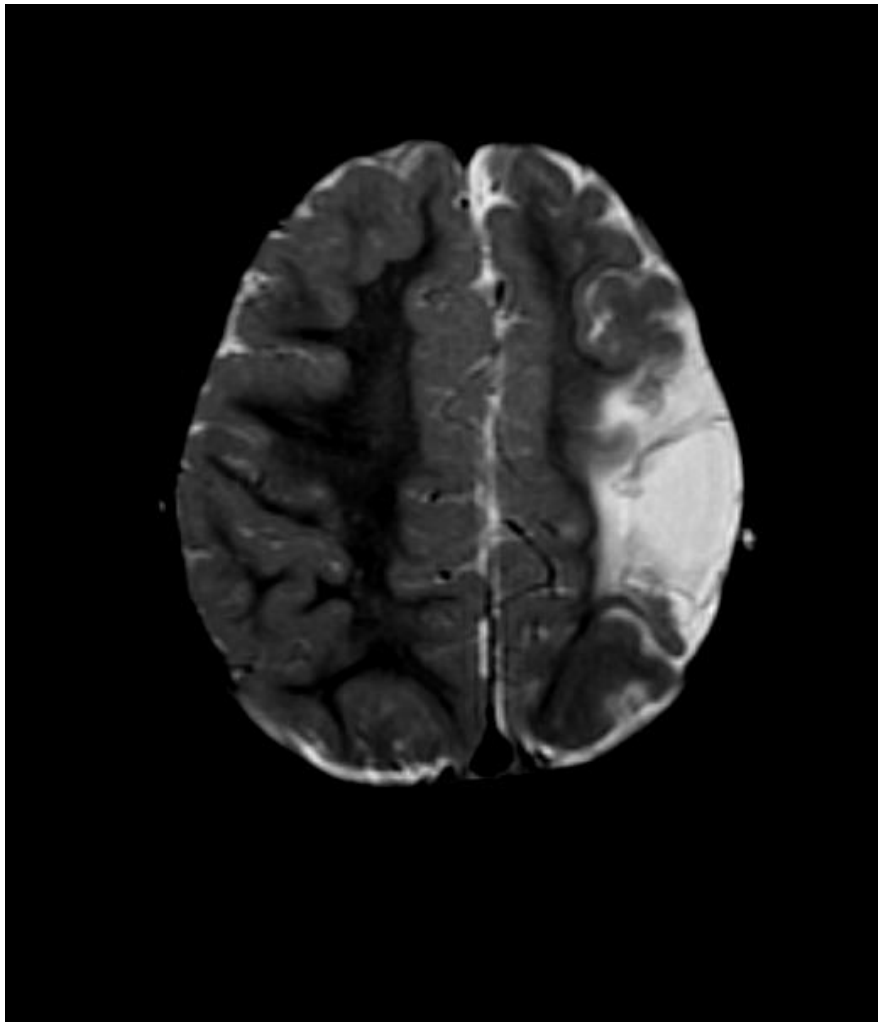
- Motor deficits-48-59%
  - Speech delay- 21%
  - Neuropsychological morbidity in 60% of children

    This includes language, cognition, behavior

    Attention problems and hyperactivity are also common
  - Cognitive ability—some studies show IQ scores within normal range for age while other studies show that follow up IQ scores are below normal range for age
  - Epilepsy-38-46%

# Presumed Perinatal Ischemic Stroke (PPIS)

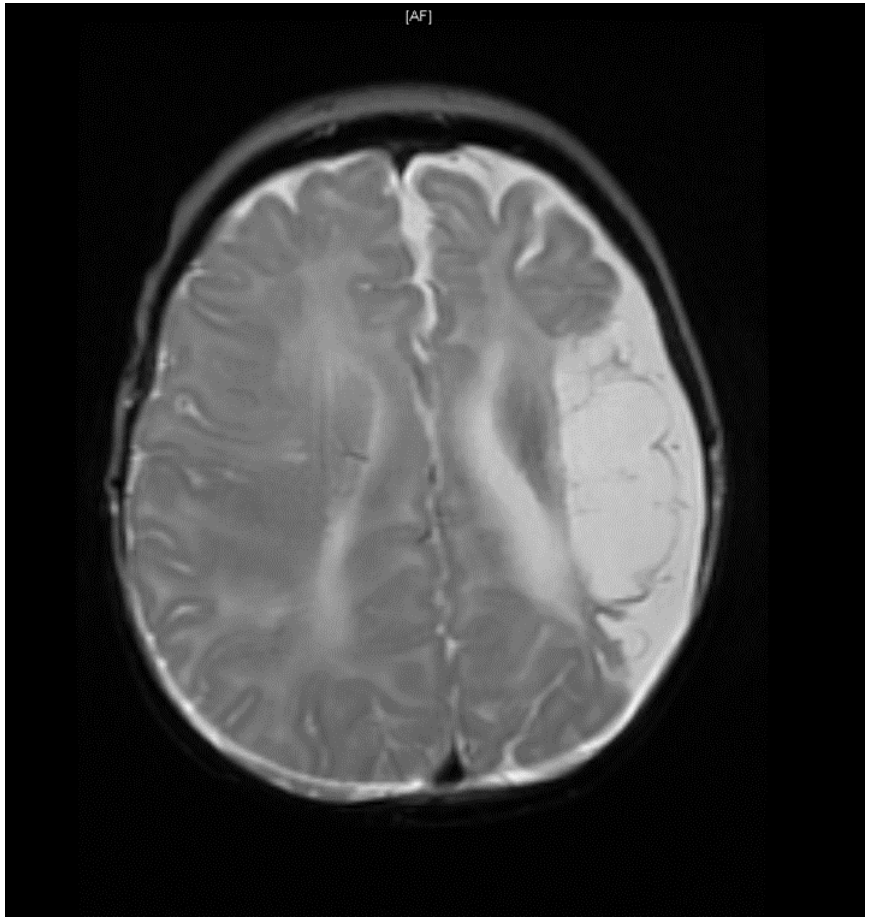
- Definition: normal newborn course with presentation within first 18 months of life of focal signs of hemiplegia. Neuroimaging shows vascular event in either the middle cerebral artery or periventricular territories. No history suggestive of stroke in infancy then stroke is “presumed” to have occurred in the perinatal period



Axial T2

# PPIS – 7 months of age

- Female
- Birth – 40 wk, G2P2
- Emergent Cesarean – placenta previa – fetal distress, meconium aspiration, pneumothorax
- First noticed right hand fisted at 4-5 months of age
- Heterozygous FVL
- Heterozygous MTHFR
- hypofibrinogenemia



# Presumed Perinatal Ischemic Stroke (PPIS)

Normal newborn who present before 18 months of age with signs of deficits. No history suggestive of stroke in infancy then stroke is “presumed” to have occurred in the perinatal period

Injury is same as in PAIS; suggesting that PPIS is an acute perinatal event

In PPIS the diagnosis is often challenging. A high clinical suspicion and early clinical recognition is important to initiate early interventions.

Studies have shown median age of parental concern 5 months of age, provider concern 7 months of age and median age of diagnosis 12 months of age.

Risk Factors - Many PPIS patients have maternal histories of preeclampsia, maternal infections, bleeding during pregnancy or gestational diabetes

Inherited thrombophilia may be common in PPIS

Cardiac abnormalities are rare

# PPIS clinical presentation

- **Early hand preference or hand fisting noted 81-86%**
- Seizures 14-15%
- Gaze preference 5%
- Differential: consider various diagnostic possibilities of what can lead to unilateral weakness:
  - Cerebral injury
  - Spinal cord
  - Anterior horn cell
  - Peripheral nerve –brachial plexus injury/Erb's palsy
  - Neuromuscular junction
  - Muscle
  - **Only Cerebral injury (or rarely spinal cord) will cause spasticity with unilateral weakness**

# PPIS outcomes

- 95% of children with PPIS have hemiparesis
- 50% with cognitive or behavioral difficulty
- 38% with epilepsy
- Children with PPIS have higher morbidity and rehab needs than children with PAIS – delay in therapy????

# Periventricular Venous Infarct (PVI)

- Occurs earlier in gestation than Arterial Ischemic Stroke
- PVI is common in premature infants but new studies have also shown this is a common cause of PPIS.
- Felt to be a germinal matrix hemorrhage prior to 34 weeks gestation that may compress medullary veins causing focal venous infarction of the periventricular white matter (Kirton 2010)
- There may be more potential of leg involvement than with arterial ischemic stroke
- Sensory deficits may be less common since sensory tracts can reroute around the early lesions
- Risk factors seen with PAIS and PPIS are less commonly found with PVI
- Seizures less common since more of a white matter injury

# PAIS and PPIS summary

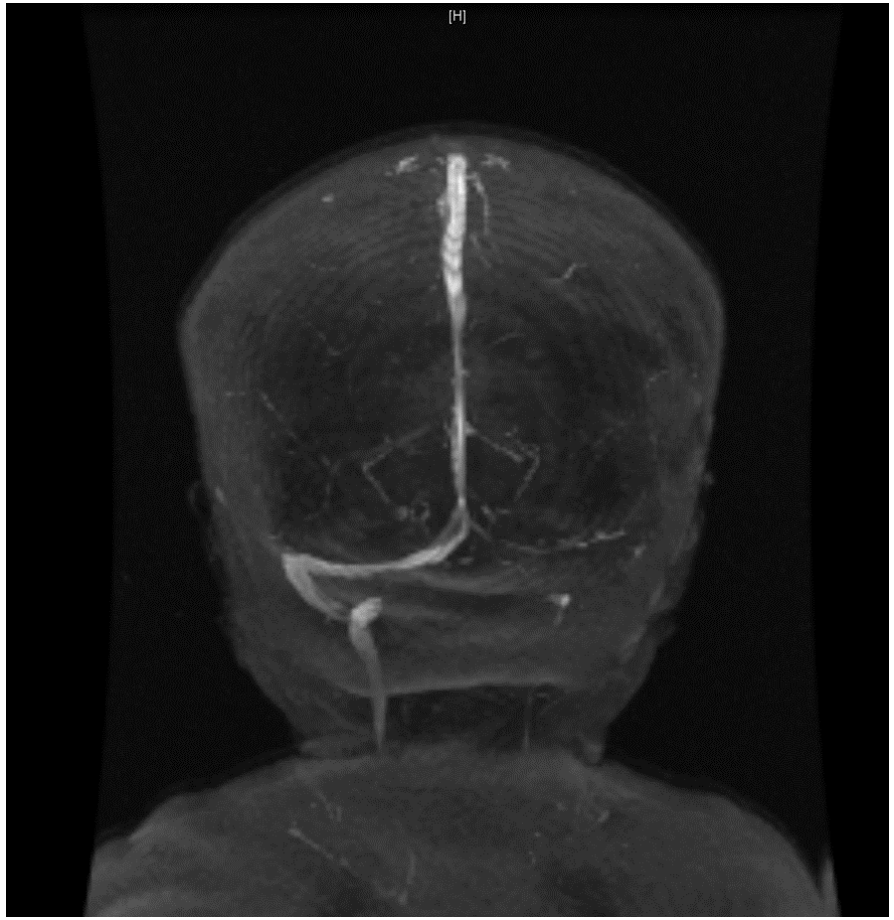
- Perinatal and presumed perinatal strokes are not rare with likely incidence even more common that past studies suggest
- Etiology of perinatal and presumed perinatal stroke is multifactorial with the main mechanism being emboli, arteriopathies or thrombosis.
- Risk factors can be maternal, fetal or placental
- The left middle cerebral artery is the most common area affected
- Seizures are a common presentation and epilepsy is a common outcome
- Perinatal and presumed perinatal strokes are a leading cause of cerebral palsy
- Children with history of perinatal and presumed perinatal strokes can have significant neurologic morbidity not only with motor deficits but also behavioral and cognitive concerns.
- Early intervention can improve future outcomes

# CSVT – Cerebral Sinovenous Thrombosis

Occurs when a blood clot develops in a venous sinus or larger deep veins of the brain

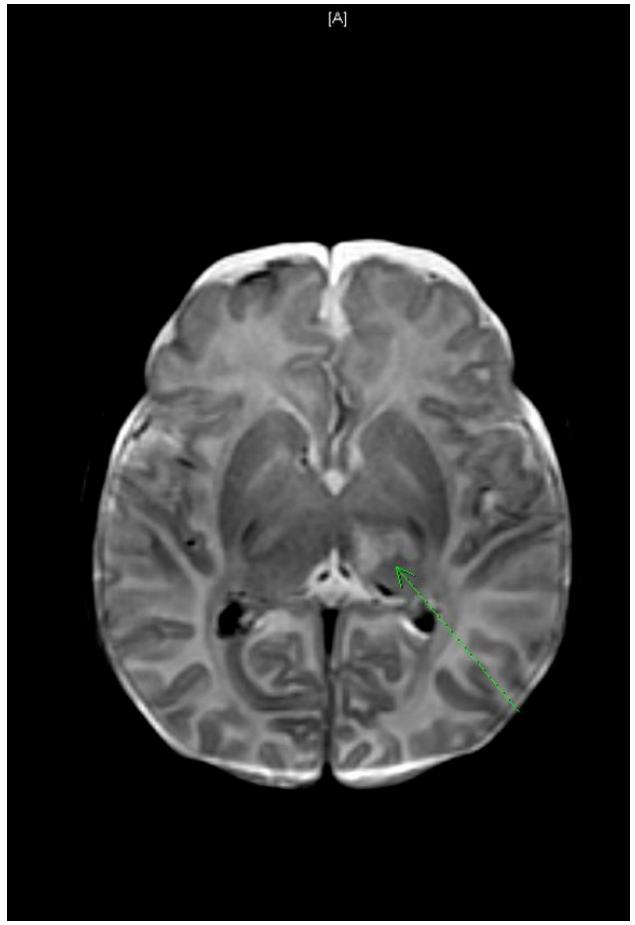
Smaller cortical veins can be involved but the mechanism can be the same.

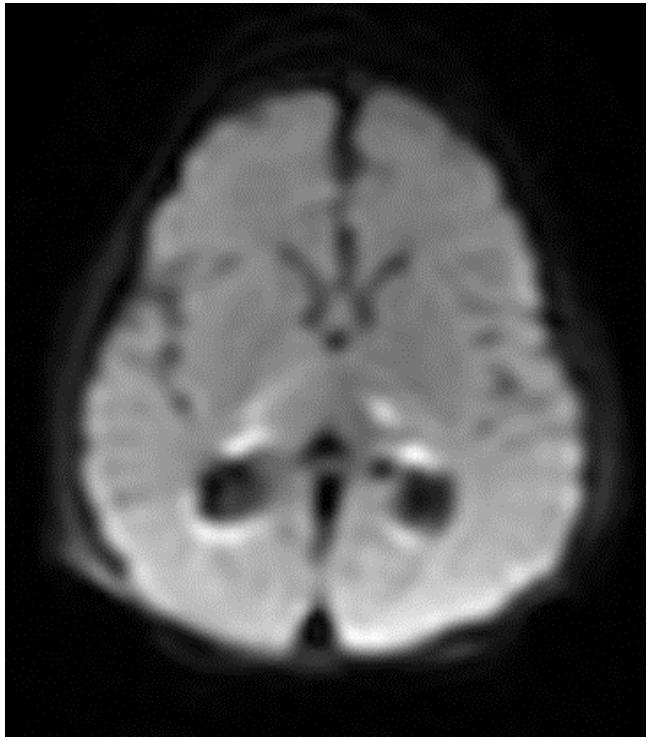
Sometimes the blood clot goes away before it causes permanent brain damage. However, sometimes the clot remains and causes a type of stroke called a venous infarct, or may cause bleeding into the brain.



# CSVT with infarction

- 6wk acutely ill with vomiting, decreased level of consciousness
- Found to have sodium 200, increased BUN & Creatinine
- Left transverse sinus thrombosis, with left thalamic infarction
- Deep medullary vein thrombosis
- Thrombophilia testing negative
- Concern for mixing of formula



# CSVT

0.4-0.7/100,000 children annually

Neonates 6.6/ 100,000

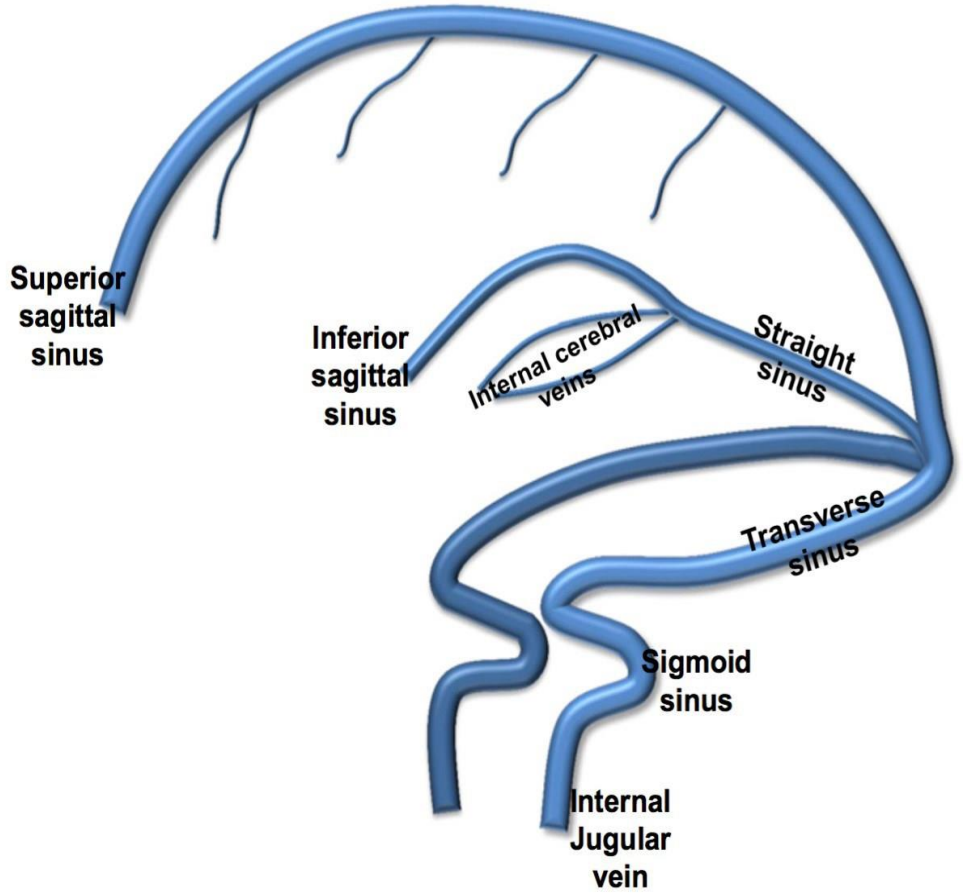
27-35% (up to 40%) of all CSVT's are neonates

Mortality 3-12% (9-29% in other cohorts)

Neurological sequelae – 62 % of survivors

60% of neonatal cases were premature

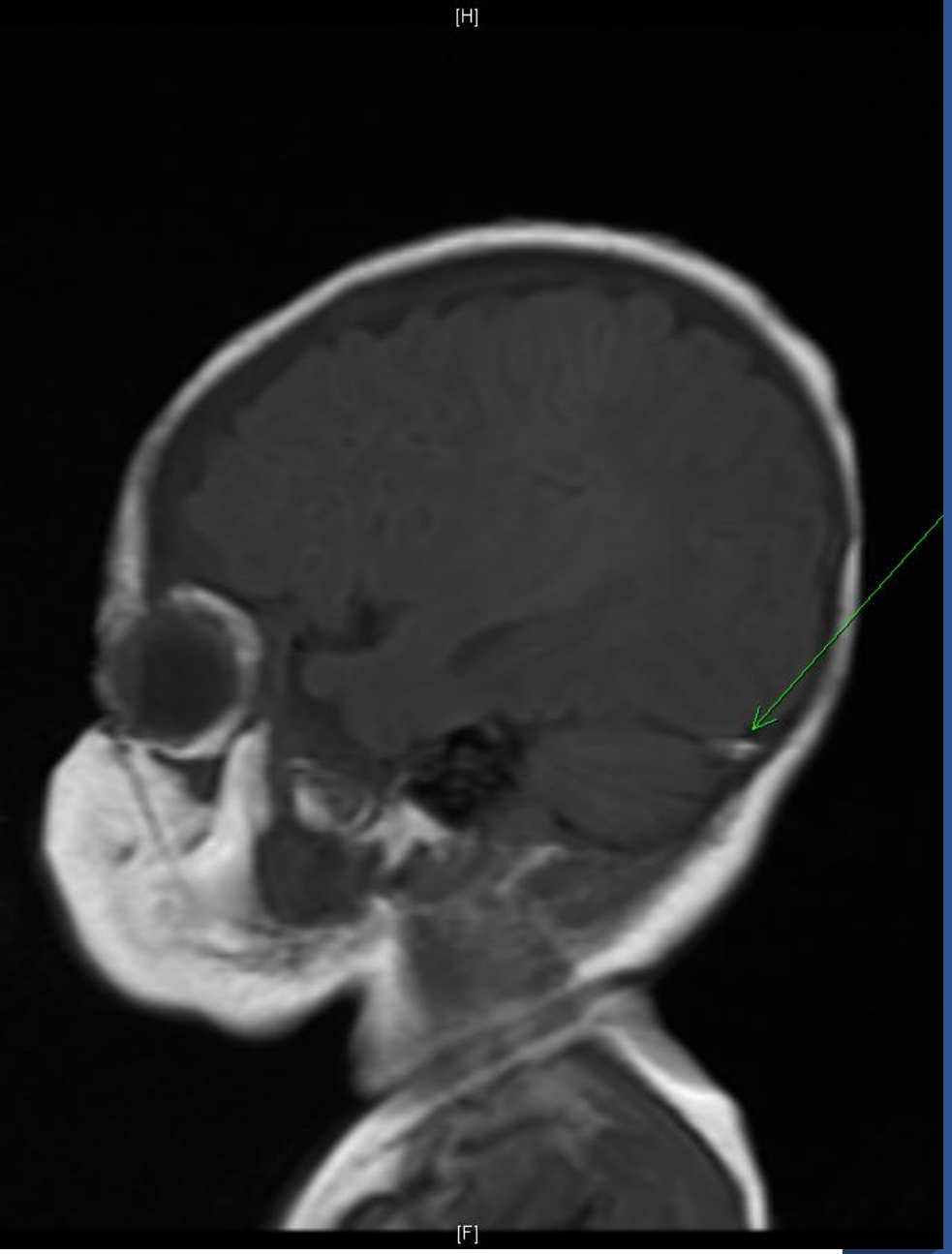
Median age 7.2 yrs. with 25% of children under the age of 3 yrs. (1 month –18 yrs.)



# CSVT – Risk Factors

- **Neonatal**
  - Delay in Diagnosis
  - Maternal condition - chorioamnionitis, diabetes, hypertension, emergency cesarean
  - Perinatal conditions
    - Asphyxia, hypoxia
    - Meconium aspiration
    - Apgar < 7 at 5 min
    - Neonatal infection
      - Meningitis
      - Sepsis
      - Pneumonia
      - DIC
    - Polycythemia
    - Severe dehydration
    - ECMO treatment
    - Congenital Heart disease
    - Congenital diaphragmatic hernia.

- **Child**
  - Hematological abnormalities (prothrombotic, hematologic)
  - Acute provoking Illness – (head or neck infection, meningitis)
  - Acute Systemic illness or injury – Dehydration, acidosis, anoxia, shock, trauma
  - Central Venous Line
  - Immunological disease
  - Cardiac Disease
  - Extracranial solid tumor
  - Other Infection
  - Systemic Illness
  - Head and neck infections
  - Chronic Illnesses
  - Congenital heart disease
  - Nephrotic syndrome
  - Autoimmune disorders

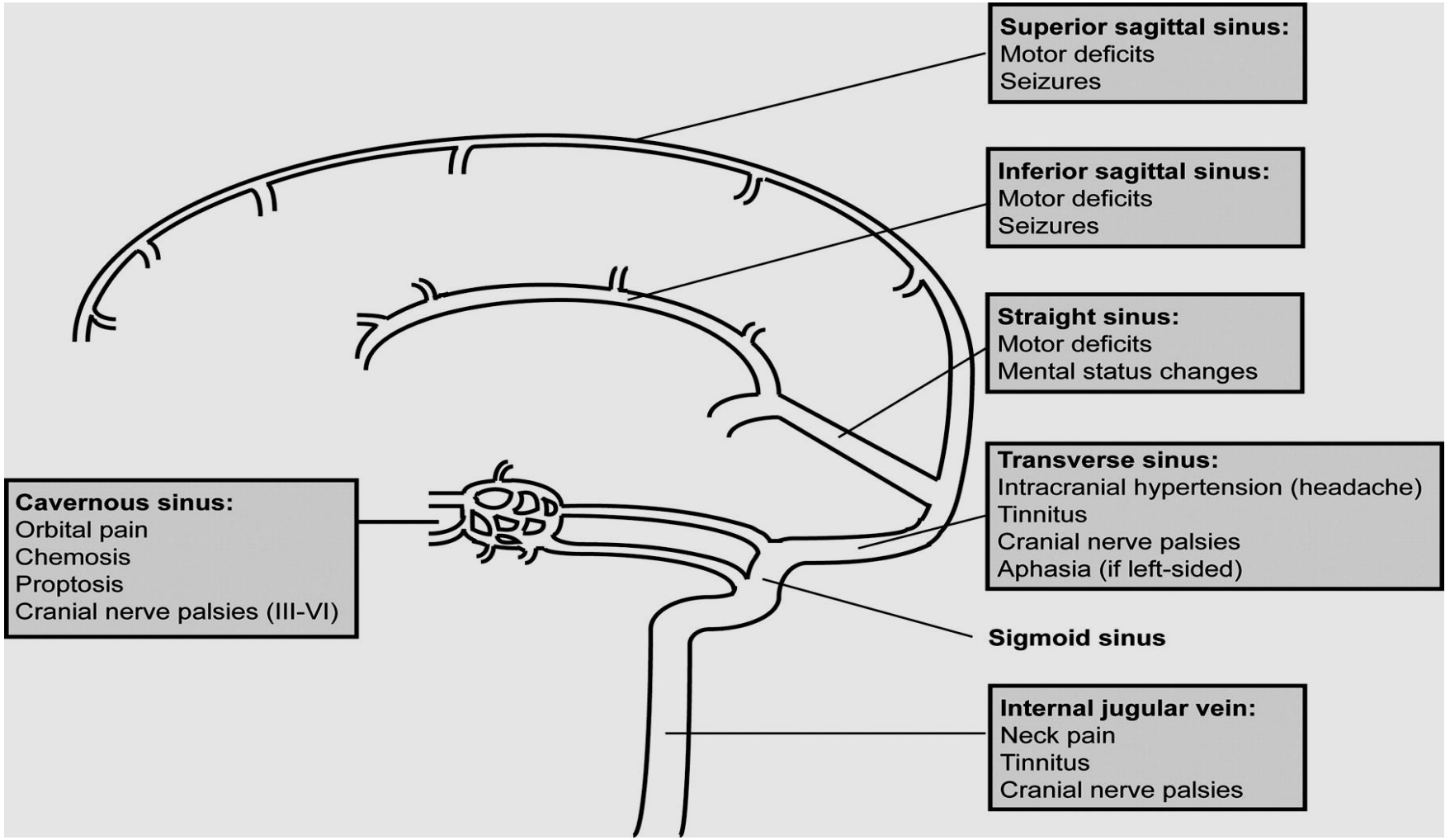



# Clinical Signs and Symptoms

- Symptoms can develop gradually
- Headache
- Nausea and vomiting
- Altered consciousness, lethargy
- Focal deficits – sixth nerve plasy
- Seizures – More in neonates
- Ringing or hearing other sounds in ears (IIH)
- Symptoms can vary depending on the location of CSVT
- Neonatal – can present with non-focal deficits

# CSVT AND CLINCAL SYNDROMES

Figure 1: Major Clinical Syndromes According to Location of Cerebral Venous Thrombosis




Zekja I, Mijo S, Grabova S, Shehu A, Vyshka G. Young Females and Cerebral Venous Thrombosis, WebmedCentral NEUROLOGY 2013: 4(6): WMC004294

# CSVT Outcomes

- Outcome
  - 84% went home with 7% going to rehab
  - Status at Discharge
    - Normal – 48%
    - Neurological deficits (43%)
    - Died (4%)
    - Unknown (5%)
  - Long term Neurological impairments and neurocognitive deficits in 40-60% of survivors
  - Overall tend to fare worse than adults

# Outcomes CSVT

Normal cognitive profile 20%

Less than expected compared with the normative population in at least one of the cognitive domains (80%)

6% performed below in all areas.

Overall IQ score lower

75.5 % had an individualized education plan

- Most prevalent impairments
  - Intellectual
  - Global executive functioning
  - Behavioral
  - Auditory attention
  - Memory function
  - Sustained attention
- Verbal ability spared
- Deficits can evolve over time

Slim M, Aziz A, Westmacott R, Dlamini N, Deveber G, Macgregor D, Yau I, Andres K, Moharir M Long-term cognitive outcomes after cerebral sinovenous thrombosis in childhood. Developmental Medicine and Child Neurology. 2020; 62: 1437-1443.

# CSVT Summary

- CVST is rare but clinically relevant in children.
- CVST generally presents as seizures in younger children and signs of increased ICP (headaches, change in consciousness) in older children.
- Diagnosis is made radiographically, with multiple possible modalities.
- A majority of episodes are associated with underlying medical issues (acute or chronic).
- Prothrombotic states have been associated with initial and recurrent thromboses.
- Treatment is currently at the discretion of the treating physician. There are no RCT to assess short or long-term efficacy.

# Recurrence – Arterial Ischemic Stroke

- Recurrence in 10-30%
- Can occur in the immediate post stroke period
- Dependent on Risk Factors
- Some may not have recurrence of stroke, but TIA symptoms.
- Preventive treatment varies depending on cause
- Secondary risk factors – smoking, physical activity, hypertension, dyslipidemias, obesity, diabetes, avoid recreational drugs (cocaine) increase risk for recurrence

# Recurrence – Perinatal stroke

Reccurrence rate is low, around 1% if no etiology identified (this includes future pregnancy risk)

- If congenital heart disease present then reccurence is around 14%

Follow up brain imaging is not recommended on a routine basis

# Diagnostic work up of pediatric stroke

## Imaging

- MRI brain with DWI (w/wo)
- MR angiogram with/without
- CT scan
- CT angiogram- radiation load
- Conventional angiogram
- Ultrasound

## Laboratory testing

- Thrombophilia
- Vasculitis
- Screening labs –
  - CBC
  - Inflammation - ESR, CRP, ANA

- Cardiac
  - ECHO
    - Transthoracic
    - Transesophageal
  - EKG
- Targeted
  - EEG
  - Transcranial Doppler

# Imaging

- Brain MRI – with and without contrast if needed
  - Preferred scan
  - No radiation
  - May be limited by braces
  - Sedation needed for younger children
  - Can obtain shorter scans for acute presentation
  - Need Diffusion weighted imaging with acute presentation
    - More sensitive than CT scan and other MRI sequences such as FLAIR
    - Diffusion weighted imaging can detect an infarct before it is seen on conventional MRI—looking at the rate of diffusion of water molecules. Presents as a bright signal on DWI

# Imaging

## MR angiogram

- Head and neck
- Assesses vessel integrity, looking for cervical and/or intracranial arteriopathy or obstruction

## MR venogram

- Useful in assessing thrombus when concern for CSVT

## Vessel wall imaging

- Useful to differentiate and monitor vasculopathies
- Shows inflammation in the vessel wall

# Imaging

## CT scan-

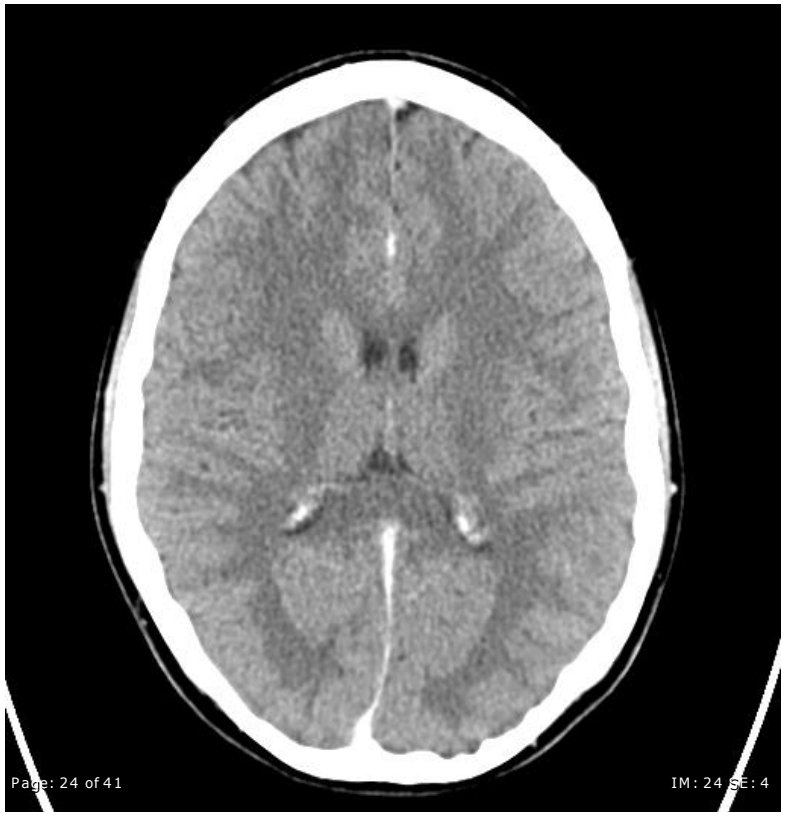
- not as sensitive in children for assessing acute ischemia
  - Fails to identify diagnosis in more than 40% of children
- Used as initial screening if brain MRI is not available
- Useful for ruling out intracranial hemorrhage
- Exposure to radiation

## CT angiogram

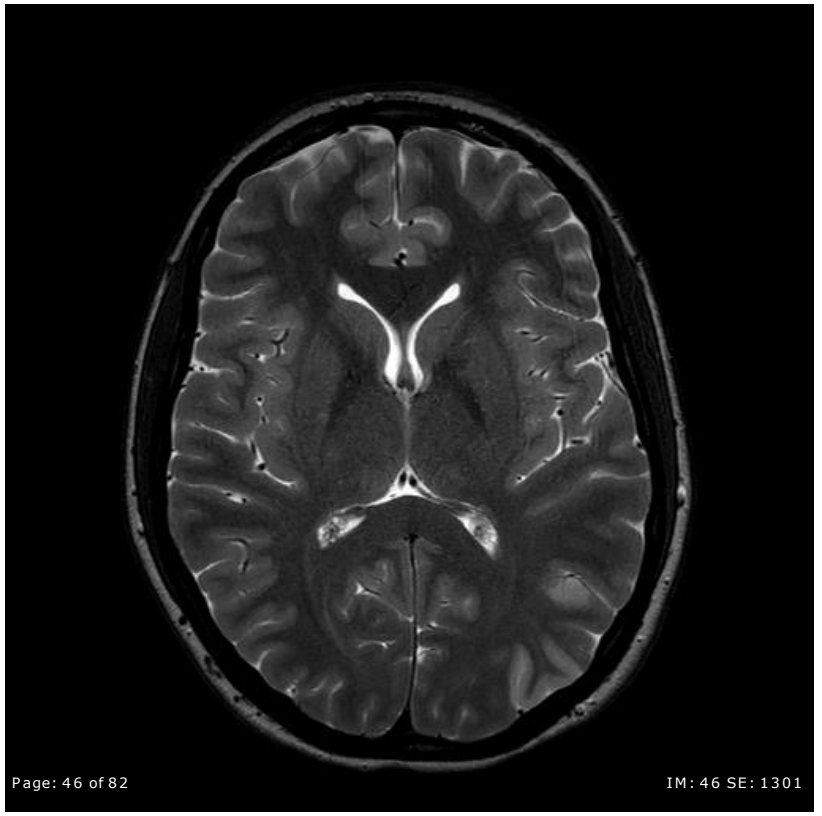
- Used to assess vessels
- Same radiation as with CT scan

## CT venogram

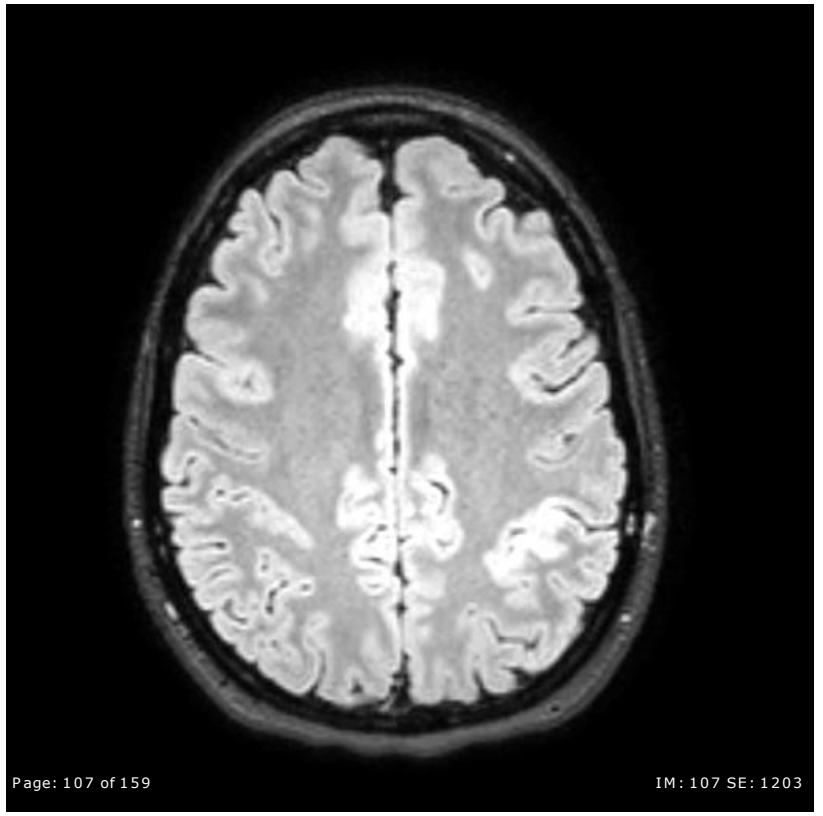
- May be equivalent in sensitivity to MR venogram for CSVT diagnosis




Initial CT scan, read as normal




T2



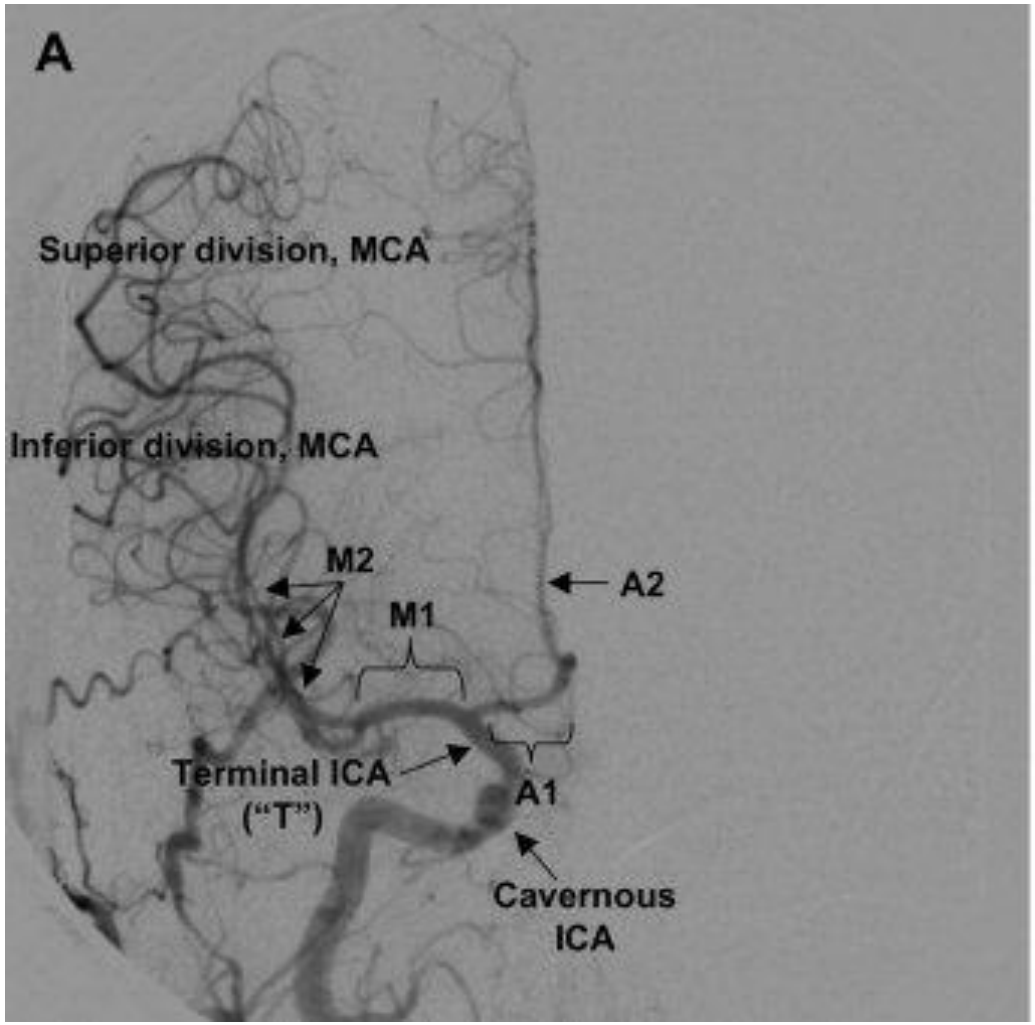

Flair

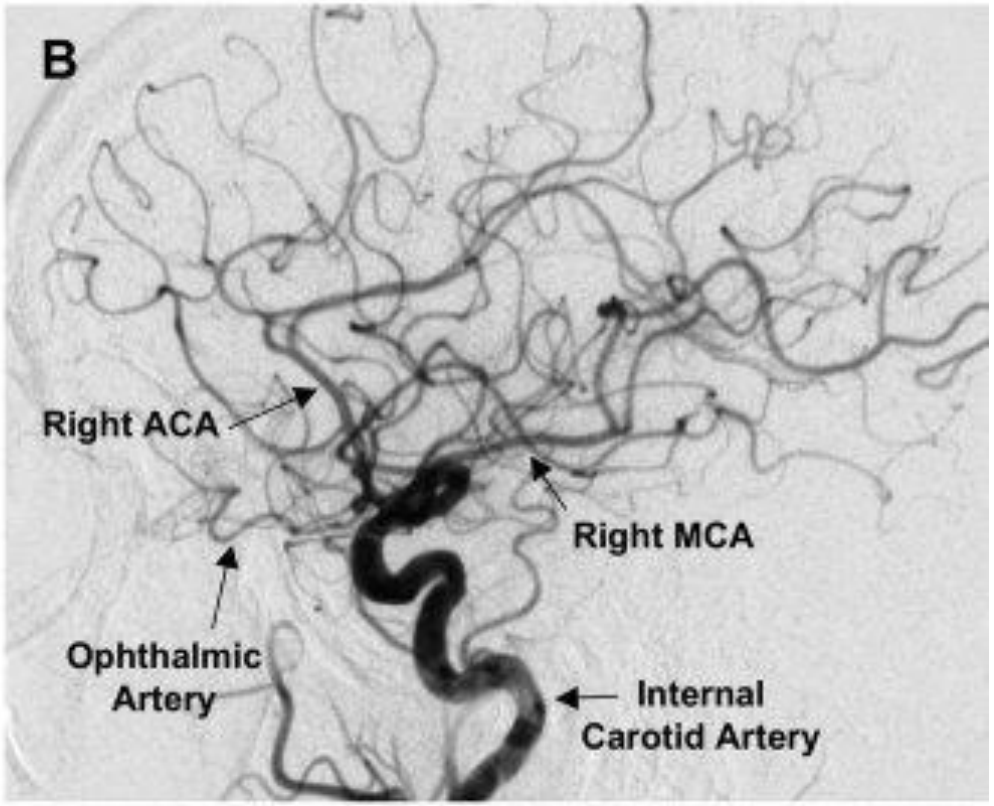
Initial MRI showing

Small areas of infarcts in the left parietal lobe with a wedge-shaped area at the parieto-occipital junction and a smaller region more superiorly. There is corresponding cortical T2 intense signal

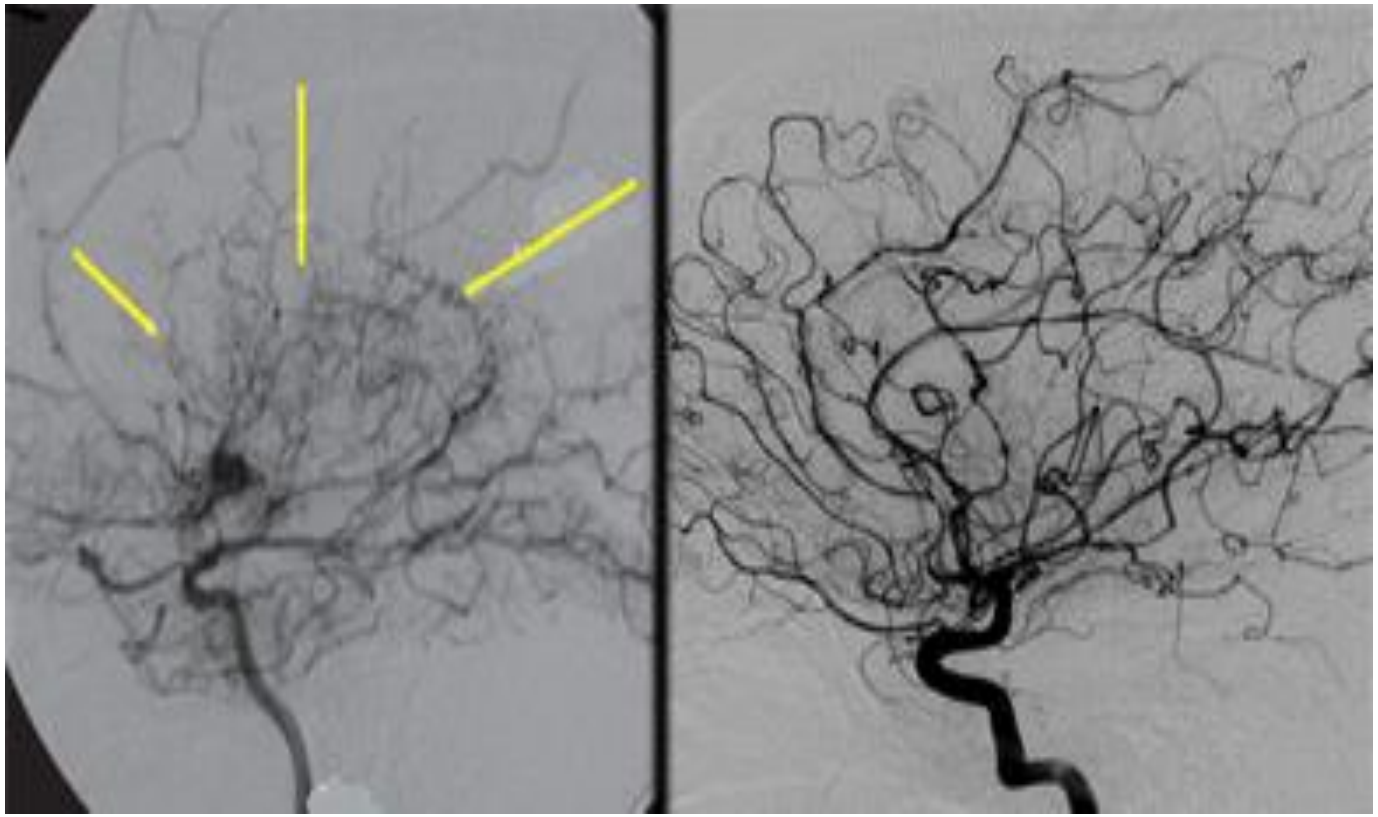
# Imaging

- Conventional angiogram
  - minimally invasive diagnostic procedure using a catheter
  - Ability to see very small arteries and veins
  - Done in real time
  - Useful in diagnosing aneurysms, malformations and assessing vessels




Example of conventional angiogram with vessels marked



Moyamoya vessels on Left  Normal cerebral vasculature on Right

# Cardiac

- EKG
  - Checking for cardiac concerns
- ECHO (echocardiogram)
  - Transthoracic ECHO with bubble study
    - Agitated saline contrast-provides contrast in the right heart and enables detection of right-to-left shunts.
      - The saline makes bubbles and this is watched to see if they move from one side of the heart to the other.
    - This is looking for cardiac source of potential embolic
  - Transesophageal ECHO
    - If high suspicion of cardioembolic source and TTE normal
    - Produces much clearer images to evaluate heart
    - Minimally invasive, transducer with tube swallowed until resting behind heart

# Targeted testing

- EEG
  - Done if there is concern regarding epileptic seizures
- Transcranial Doppler
    - Looks at velocity of blood flow through the brains blood vessels
    - Used to predict stroke in children with sickle cell disease

# Multi-disciplinary Stroke Management – Neuroprotection is Key

- Barriers
  - Delay in diagnostic neuroimaging
  - Need assisted sedation for neuroimaging
  - Need to transfer to tertiary center
  - Non-availability of intensive care unit beds
- Prevention of secondary injury caused by pathological change in BP, oxygenation, temperature, impaired glucose regulation is needed for neuroprotection even before stroke is diagnosed

# Recanalization Therapy

Limit consideration of this intervention to children meeting these criteria

Persistent disabiling neurological deficts (peds NIH stroke scale) > or = 6 at the time of intervention

Radiographic confirmed cerebral large artery occlusion

- Intravenous tissue type plasminogen activator (tPA)
  - IV tPA – risk of symptomatic hemorrhage after tx tPA 4.5 hours is low 2.1 % efficacy is unknown. Optimal IV tPA dose is unknown – developmental hemostatic changes
  - 4.5 hr of symptom onset
- Intra-arterial tPA
  - 6 hrs of symptom onset

# Mechanical Thrombectomy

Guidelines extrapolated from Adult trials

Up to within 24 hr of symptom onset

Only for larger vessel occlusion strokes

Adult populations had greater improvement with thrombectomy versus IV tPA

- Administered in 2% of children with stroke
- Treated in a dedicated Pediatric Stroke Center
- Stentretriever versus aspiration dependent on size of patient
- Should not be used if arteriopathies are suggested

# Therapies

## Need for rehabilitation depending on deficits

- Early onset of therapy is beneficial
  - Occupational therapy
  - Physical Therapy
  - Speech Therapy
  - Recreational Therapy
  - Constraint Therapy

## Re-entry to school or accommodations at school

- IEP or 504 plan
- Neuropsychological testing

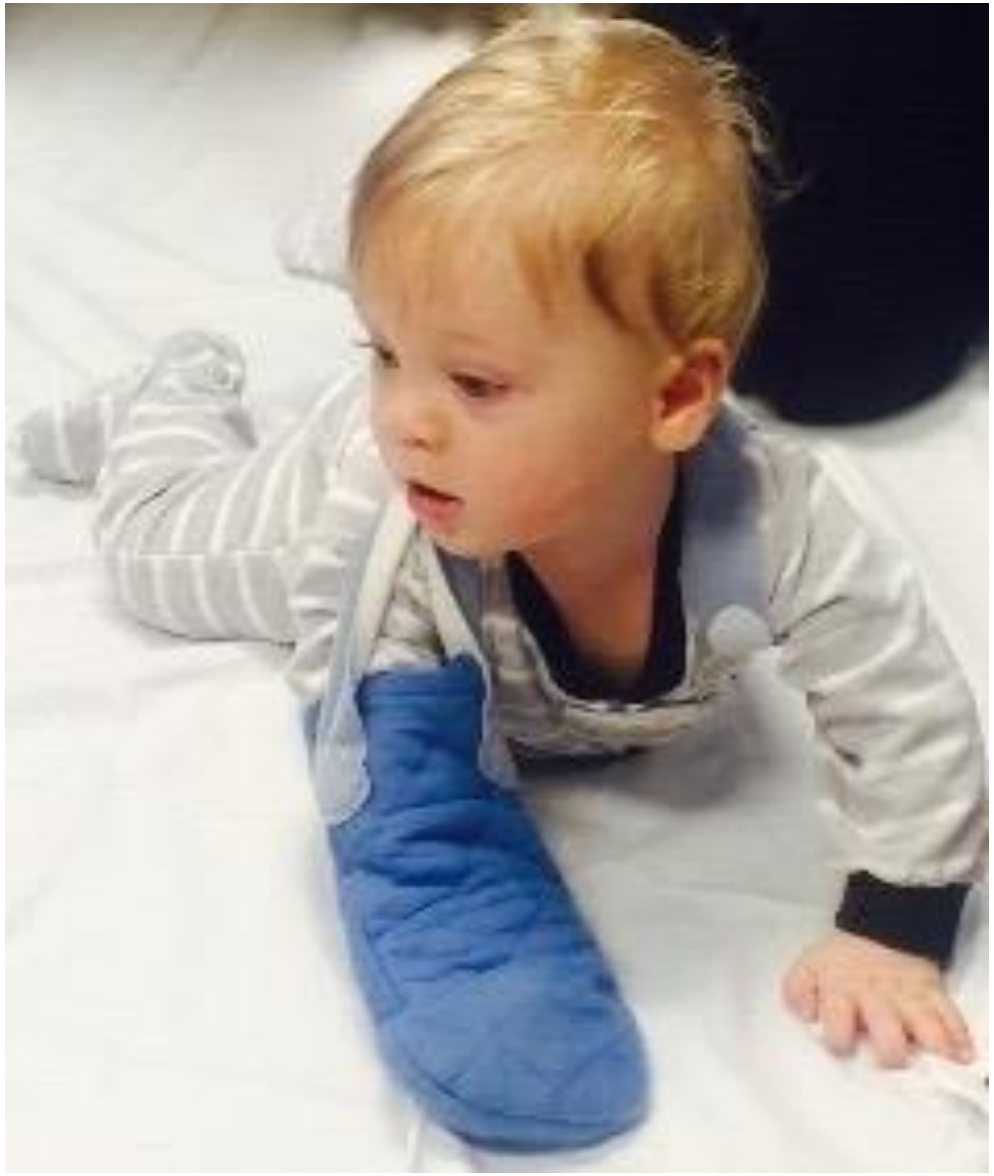
# Constraint Induced Movement Therapy

- Constraint Movement Therapy
  - Constraint of the unimpaired or less impaired upper extremity
  - A high and concentrated dosage of the therapy (hrs per day for at least 10 days)
  - Systematic application of principles of reinforcement, behavioural shaping and massed practice to elicit and improve neuromotor control of the hemiparetic upper extremity.
- Modified Constraint Movement Therapy
  - Does not include all of the components of typical constraint
  - This has been tested more often with children
- One of the few therapies that produces clinically meaningful and sustained benefit for children with hemiparesis

# Constraint Induced Movement Therapy

- Limitations
  - Specific treatment protocols are varied
  - Children treated are variable
  - Type of constraint applied to the more functional, less impaired upper extremity (how it is constructed and the amount of time)
  - Dosage or amount of CIMT measured in terms of the treatment hours per session and total number of treatment sessions

- Current Trials – I-ACQUIRE
  - 8-36 months of age
  - Stroke early in life, now showing motor weakness or poor control of movements
  - 5 days a week for 4 weeks
  - 3 groups – with varying amount of time for constraint. One group continue current therapy. (will have opportunity to participate in trial after 6 months)
  - 12 locations across USA
  - Therapy in home or homelike setting.
  - Free of charge
  - Cast – removed once a week




Pediatric Constraint Induced Movement Therapy or CIT is a type of treatment that **teaches the brain to "rewire" itself** following a brain injury.

# Special Circumstances

# Moya Moya Syndrome

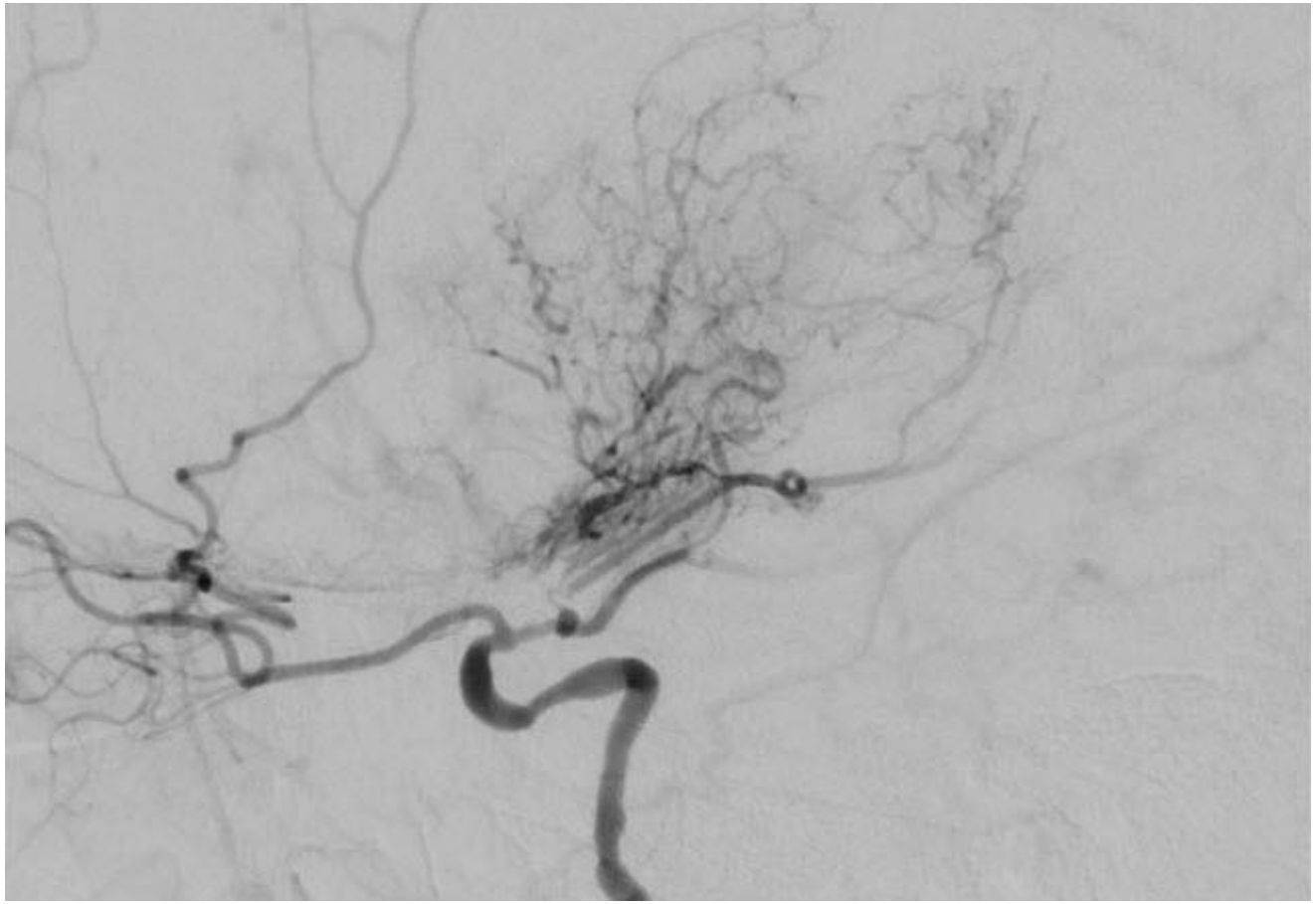
- Characterized by a progressive stenosis of the terminal portion of the intracranial internal carotid arteries, and/or proximal portion of Anterior cerebral artery (ACA)and/or middle cerebral artery (MCA) and the development of a network of abnormal collateral vessels
- “Puff of smoke” look of the tangled vessels formed to compensate for the blockage

- **Suzuki Classification**
  - **Grade I  Narrowing of ICA bifurcation**
  - **Grade II  Initiation of the moyamoya  collateral vessels**
  - **Grade III Progression of moyamoya collateral vessels**
  - **Grade IV  Minimization of the moyamoya, tenuous ACA nad MCA**
  - **Grade V  Reduction of the moyamoya with occlusion of ICA, ACA and MCA**
  - **Grade VI  Disappearance of the moyamoya – ICA disappeared with supply of brain from ECA**

Guey S, Tournier-Lasserve E, Herve D, Kossorotoff M. (2015) Moyamoya disease and syndromes:  from genetics to clinical management.  The Application of Clinical Genetics 8: 49-68.

# Moyamoya

- **Causes or associations**
  - **Idiopathic**
  - Neurofibromatosis I
  - Asian heritage
  - Cranial Therapeutic Radiation
  - **Down Syndrome**
  - **Sickle Cell**
- Congenital Cardiac anomaly – previously operated
- Renal Artery Stenosis
- **Hemoglobinopathy**
- Giant cervicofacial hemangiomas
- Shunted hydrocephalus
- Idiopathic hypertension – Med
- Hyperthyroidism



# Sickle Cell Disease

More at risk for silent infarctions, strokes, seizures with strokes, SCVT, Cerebral hemorrhages and hyperviscosity syndrome

Key is stroke prevention

Concern is for development of Moya Moya disease

Silent infarctions – treated with exchange transfusions

- Those with abnormal TCD measurements should have exchange transfusions- 92% reduction of risk
- Some switched to Hydroxyurea if stable and no silent infarctions
- Continue to monitor for worsening of arteriopathy

# Thrombosis and COVID-19 Infection

Marked predisposition to thrombosis

Cytokine storm described in COVID-19 is a major pathophysiological bridge between inflammation and thrombosis.

MIS-C can arise weeks after infection

Thrombotic or thromboembolic events are rare in children with COVID-19 infection especially in those with comorbidities predisposing to a thrombotic event.

- MIS-C
  - persistent fever
  - inflammation
  - symptoms of Kawasaki
  - shock

Multiple organ failure

Death in the severely ill.

# Pediatric COVID-19 Infection and MIS-C-Thrombotic Risk

- Coagulopathy associated with multisystem inflammatory syndrome in children (MIS-C)
- 71%  had thrombosis despite thromboprophylaxis
- Overall mortality  with MIS-C 2.3 %
- Mortality associated with thrombotic event – 28 %

- Significant factors
  - Age > or = 12 years of age
  - Cancer
  - Presence of a central venous catheter
  - MIS-C
- 2.1% COVID-19 infection with thrombotic event
- 6.5% MIS-C with thrombotic event
- Most common DVT, Stroke and CSVT occurred rarely

# Future Directions for pediatric stroke

- Perinatal – search for disease biology
- Childhood – better definition and treatment for cerebral arteriopathy
- Treatment dilemmas – Which guidelines to follow ???Canadian Best Practice Guidelines 2010.  Chest guidelines 2012
- Neonatal CSVT – Earlier diagnosis and treatment
- Rehab – harnessing the plasticity of the developing brain
- Translation of research into practice

# Children and Teens – Symptoms of a Stroke


- **Remember FAST (R)**
  - **Face Drooping**
  - **Arm weakness (or weakness on one side of the body)**
  - **Speech difficulty**
  - **Time to call 9-1-1**
  - **Remember Kids have Strokes Too**

# Warning signs and Symptoms of stroke

- Sleepiness – trouble staying awake and alert
- Dizziness and coordination problems.
- Severe Headache
- Nausea/vomiting
- Waking from sleep
- Altered Consciousness
- Seizures

# STROKES CAN HAPPEN AT ANY AGE

**Pediatric stroke can happen in infants, children and even before birth.**

## PERINATAL STROKE
**Last few months of pregnancy to 1-month-old**

## CHILDHOOD STROKE
**1-month-old to 18 years**

### Risk Factors

**The cause in most perinatal strokes remains unknown.**

**Risk factors that could lead to stroke include:**
- Congenital heart disease
- Disorders of the placenta
- Blood clotting disorders
- Infections (e.g. Meningitis)

**Risk factors in children ≠ Risk factors in older adults**
**Risk factors for children include:**
- Congenital heart disease
- Diseases affecting the brain's arteries
- Infections affecting the brain or other organs
- Head trauma
- Sickle cell disease
- Autoimmune disorders

**No previous risk factor is identified in about half of childhood stroke cases.**

### Warning Signs

**Signs of a perinatal stroke may go unrecognized for months or years because the signs can be subtle.**

**Newborns:**

Seizures may be an early sign:
- Repetitive twitching of face, arm or leg
- Apnea (pauses in breathing) associated with staring

**Developing Children:**
- Decreased movement or weakness on one side of the body
- Showing a hand preference, or consistently reaching out with only one hand before 1 year of age

**Signs are often missed in children because there is a lack of awareness that strokes can happen in this age group.**

**F. A. S. T.**

Face Drooping | Arm Weakness | Speech Difficulty | Time to Call 911

**Additional Signs in Children Include:**
- Severe sudden headache, especially with vomiting and sleepiness
- Weakness or numbness on one side of the body
- Difficulty speaking or understanding others
- Vision loss or double vision
- Severe dizziness or loss of coordination
- New-onset of seizures usually on one side of the body

### Time is Brain at Any Age

**Newborns:**
Quick recognition → Prompt medical evaluation and treatment

**Babies:**
Early diagnosis → Rehabilitation treatment can start while a young brain is still developing

**Don't delay!**

Prompt diagnosis and treatment of stroke in children is as critical as it is in adults.

**Learn more at:**
**iapediatricstroke.org**
**StrokeAssociation.org**



International Alliance for Pediatric Stroke

American Heart Association | American Stroke Association

*Together* to End Stroke™

# Resources

- Stroke and Vascular Anomalies clinic at Nationwide Children's Hospital.
- Nationwidechildrens.org/stroke
- Children's Hemiplegia and Stroke Association: **www.chasa.org**
- Pediatric Stroke Warriors: **www.pediatricstrokewarriors.org**
- Sickle Cell disease Association of America: **www.sicklecelldisease.org**
- United 4 Pediatric Stroke
- International Alliance for Pediatric Stroke: **www.iapediatricstroke.org**

# References


Ferriero DM, Fullerton HJ, Beonard TJ, etal. Management of Stroke in Neonates and Children: A Scientific Statement from the American Heart Association/American Stroke Association. Stroke 2019, 50(3) e51-e96.

Fragata I, Morais T, Silva R, Nunes AP, Loureiro P, Diogo Martins J, Pamplona J, Carvalho R, Baptista M, Reis J. Endovascular treatment of pediatric ischemic stroke: A single center experience and review of the literature. Interv Neuroradiol. 2021 Feb;27(1):16-24.

Guey S, Tournier-Lasserve E, Herve D, Kossorotoff M. (2015) Moyamoya disease and syndromes: from genetics to clinical management. The Application of Clinical Genetics 8: 49-68.

Jiang B, Hills NK, Forsyth R, Jordan LC, Slim M, Pavlakis SG, Freidman N, Dlamini N, Farooq O, Li Y, Zhu G, Fullerton H, Wintermark M, Lo WD; VIPS Investigators*. Imaging Predictors of Neurologic Outcome After Pediatric Arterial Ischemic Stroke. Stroke. 2021 Jan;52(1):152-161.

Lehman LL, Khoury JC, Taylor JM, Yeramaneni S, Sucharew H, Alwell K, Moomaw CJ, Pearlso K, Flaherty M, Khatri P, Broderick JP, Kissela BM, Kleindorfer DO. Pediatric Stroke Rates Over 17 Years: Report From a Population-Based Study.J Child Neurol. 2018 Jun;33(7):463-467.

Mackay MT, Chua ZK, Lee M, Yock-Corrales A, Churilov L, Monagle P, Donnan GA, Babl, FE Stroke and non stroke brain attacks in children. Neurology 2014: 82 1434-1440.

Mackay, MT, Yock-Corrales A, Churilov L, Monagle P, Donnan GA, Babl FE .Differentiating Childhood Stroke From Mimics in the Emergency Department, Stroke: 47: 2476-2481, 2016.

# References


Mastrangelo M, Giordo L, Ricciardi G, De Michele M, Toni D, Leuzzi V. Acute ischemic stroke in childhood: a comprehensive review. Eur J Pediatr. 2022 Jan;181(1):45-58.

Ramey SL, DeLuca S, Stevenson RD, et al Children with Hemiparesis Arm and Movement Project (CHAMP): protocol for a multisite comparative efficacy trial of paediatric constraint-induced movement therapy (CIMT) testing effects of dosage and type of constraint for children with hemiparetic cerebral palsy BMJ Open 2019;9:e023285. doi: 10.1136/bmjopen-2018-023285

Slim M, Aziz A, Westmacott R, Dlamini N, Deveber G, Macgregor D, Yau I, Andres K, Moharir M Long-term cognitive outcomes after cerebral sinovenous thrombosis in childhood. Developmental Medicine and Child Neurology. 2020; 62: 1437-1443.

Sun LR, Harrar D, Drocton G, etal Mechanical Thrombecomty for Acute Ischemic Stroke: Considerations in Children. Stroke 2020: 51(10), 3174-3181

Whitworth H, Sartain S, Kumar R, Armstrong K (et al) Rate of Thrombosis in Children and Adolescent Hospitalized with COVID-19 or MIS-C. Blood 2021; 138(2), 190-198.

Zaffanello M, Piacentini G, Nosetti L, Ganzarolli S. Thrombotic Risk in children with COVID-19 Infection: A Systematic Review of the Literature. Thrombosis Research: 205, 92-98

Zekja I, Mijo S, Grabova S, Shehu A, Vyshka G. Young Females and Cerebral Venous Thrombosis, WebmedCentral NEUROLOGY 2013: 4(6): WMC004294