Stroke Guideline

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Definition:

A pediatric stroke can be classified by stroke type, the age at which it occurred and the vessels involved. The three primary types are arterial ischemic stroke, cerebral sinovenous thrombosis and hemorrhagic stroke. As in adults, pediatric stroke can also be classified according to whether the underlying cause is ischemic or hemorrhagic[21]. The timing of the stroke is classified as i) perinatal stroke, where diagnosis occurred or is presumed to have occurred between 28 weeks gestation and 28 days of life or, ii) childhood stroke, which is defined by stroke occurring between 29 days and 18 years of age[2].

Ischemic stroke includes arterial ischemic stroke (AIS) and venous infarction caused by cerebral sinovenous thrombosis (CSVT) or cortical vein thrombosis.

An **arterial ischemic stroke (AIS)** is an injury to the brain or spinal cord caused by a lack of oxygen to the area affected. Usually arterial ischemic stroke results from obstruction of blood flow by blood clots, narrowed or damaged arteries or both. Acute ischemic stroke (AIS) is defined as rapidly developing signs of focal cerebral disturbance observed as cognitive, sensory and/or motor changes, with symptoms lasting ≥1 hour. In adults, ischemic stroke accounts for 75 to 85% of strokes. In children, arterial ischemic stroke is also the most common subtype, accounting for just over half of all strokes [3].

Cerebral sinovenous thrombosis (CVST) occurs when a blood clot forms in the brain's venous sinuses. The clot is in a vein that is carrying blood from the brain back to the heart. When the clot does not resolve, it can cause a type of stroke called a venous infarct, or may cause bleeding into the brain (brain hemorrhage). This type of clot is called a thrombus. It is a rarer type of stroke accounting for approximately 1 in 4 pediatric stroke cases, but is associated with significant morbidity and mortality.

Hemorrhagic stroke is the result of bleeding from a ruptured cerebral artery or bleeding into the site of an acute ischemic stroke. Hemorrhagic stroke can include intracerebral hemorrhage and less commonly subarachnoid or intraventricular hemorrhage. Hemorrhagic stroke is estimated to account for just under half of all childhood strokes [4], significantly more than the 6 to 15% reported in the adult population.

Guideline Inclusion Criteria:

Patient (≥ 1 month of age at time of presentation) with clinical presentation of sudden onset of Acute CNS Neurological Deficit, within 24 hours of symptom onset. (Ischemic Stroke, Primary Hemorrhagic Stroke, Cerebral Sinovenous Thrombosis)

Patients >18 years old treated at DCMC will be administered alteplase as the medication of choice.
There are no differences between any dose of tenecteplase and alteplase for either the efficacy or safety end points.[33,34]

Guideline Exclusion Criteria:

Perinatal Stroke: <1 month of age, traumatic brain injury, suspected stroke with symptom onset >24 hrs. Transient ischemic attack (TIA).

Incidence:

- Annualized pediatric stroke incidence rates, including both neonatal and later childhood stroke and both ischemic and hemorrhagic stroke, range from 3 to 25 per 100,000 children in developed countries. Newborns have the highest risk ratio: 1 in 4000 live births[21].
- Boys were at higher risk than girls, and black children were at higher risk than white and Asian children, even after adjustment for trauma and the presence of SCD.[13]
- Infants are disproportionately affected because of congenital heart disease and neonatal asphyxia.
    - If infants are excluded, the annual incidence is 1.25 cases per 100,000 children between 1 and 14 years.
- The incidence of childhood CVST is 0.3 per 100,000 children per year for term birth to 18 years of age, and neonates make up 43% of the patients
- Approximately 45% of strokes in children are hemorrhagic, and 55% are ischemic.
- The incidence among African-American populations is increased because of sickle cell disease (10%) and hemoglobin SC disease (2% to 5%).
- Stroke is one of the major complications of SCD. Rates of stroke in SCD are much higher than rates of stroke in children in general[13].
    - The Baltimore-Washington Cooperative Young Stroke Study was a retrospective study that identified all cases of ischemic and hemorrhagic stroke among children and young adults within a catchment area that totaled 46 hospitals over a 3-year period between 1988 and 1991. The overall incidence of AIS was 0.58 per 100,000 and ICH was 0.71 per 100,000. Conversely, for children with SCD, the incidence rates per 100,000 were 238 and 47.5 for AIS and ICH, respectively[13].

Differential Diagnosis:

- Seizures
- Meningitis
- Tumors and other space occupying lesions such as brain abscess
- Hypoglycemia
- Hypertensive encephalopathy
- Complicated or hemiplegic migraine
- Focal encephalitis including cerebellitis
- Traumatic extradural or subdural hemorrhage
- Demyelinating conditions e.g. acute disseminated encephalomyelitis (ADEM)
- Postictal paralysis (Todd's paresis)
- Idiopathic intracranial hypertension
- Musculoskeletal disorders

Risk Factors

In arterial ischemic stroke (AIS) the risk factors that predominate in children and young people are distinct from adults. The more commonly reported risk factors include nonatherosclerotic arteriopathies, cardiac disorders, infection, inherited or acquired coagulation abnormalities, malignancies, acute and chronic head and neck disorders (including trauma leading to extracranial arterial dissection), and haemoglobinopathies such as sickle cell disease [5, 6]. Importantly, multiple risk factors converge in more than 50% of children with stroke, however at least 10% remain idiopathic [1,7]. A vast number of factors have been associated with childhood stroke. As it

becomes increasingly clear that risk of childhood stroke is multifactorial the importance of high clinical suspicion and rapid diagnosis by neuroimaging cannot be understated.

For a more detailed list of risk factors see:
Table 1: Risk Factors for Ischemic Stroke and CVST
Table 2: Risk Factors for Hemorrhagic Stroke in Children

Diagnostic Evaluation

A detailed neurologic exam should be performed. The PediNIH Stroke Scale should be completed in the case of suspected (or confirmed) stroke. (Examiners should be staff certified in the administration of the National Institutes of Health Stroke Scale.)

The use of the PedNIHSS for children's stroke assessment

The pediatric adaptation of the National Institutes of Health Stroke Scale was developed by pediatric and adult stroke experts by modifying each item of the adult National Institutes of Health Stroke Scale for children, retaining all examination items and scoring ranges of the National Institutes of Health Stroke Scale[30].

- 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)

The PedsNIH Stroke Scale ideally should be performed upon arrival at the hospital, to determine eligibility for interventions.

Physical Examination:

There is moderate evidence to suggest that clinical presentation does not distinguish between AIS and HS. Signs and symptoms of acute stroke in children are similar to those in adults. The most common symptoms include hemiparesis and hemifacial weakness in 67% to 90%, speech or language disturbance in 20% to 50%, vision disturbance in 10% to 15%, and ataxia in 8% to 10%. Children present with nonlocalizing symptoms such as headache in 20% to 50% and altered mental status in 17% to 38%. Seizures at stroke onset are more common in children than adults, affecting 15% to 25%, especially in those <6 years of age[21].

Children with cerebral sinovenous thrombosis present with even more diverse and non-focal symptoms including headache, seizures, lethargy, nausea, vomiting or signs of increased intracranial pressure.

Children with hemorrhagic stroke can also present with non-specific symptoms. There are however, retrospective studies to suggest that vomiting and loss of consciousness are more common in hemorrhagic stroke in addition to headaches, altered mental status, whereas focal neurological deficits are more commonly seen in children with arterial ischemic stroke [8,9,10].

Infants <12 months of age: General signs and symptoms of a stroke in infants may be subtle and neurologic signs may be minimal. Seizures may accompany neurologic signs and symptoms.

Children > 12 months of age can present with:

Focal Motor deficits:

Monoparesis or hemiparesis

Focal Neurologic deficits:

Vision changes
Dysarthria (slurred or slow speech)
Aphasia (affecting ability to speak, write and understand language both verbal and written)
Numbness
Ataxia (lack of muscle control or coordination of voluntary movements)

Diagnostic Evaluation

History:

Because multiple factors are present in as many as 25% of children with stroke, which means further investigations are warranted even when one risk factor has been identified [28].

Assess for[28]:

- **Timing of onset** - when was patient last awake and symptom-free
- **Cardiac** - issues due to cardiac repair such as heart surgery or cardiac anomaly
- **Hematologic** - Sickle Cell Disease, family history of early onset AIS
- **Infection** - Recent viral infection (e.g., varicella infection or vaccination within the past year). Five to twelve percent of children with bacterial meningitis, TB meningitis, and viral encephalitis will have a stroke due to local vasculitis and thrombosis.
- **Vascular** - Arteriovenous malformations (AVM), Moyamoya
- **Syndromic and Metabolic Disorders** - Marfan syndrome, tuberous sclerosis, homocysteinuria, familial lipoprotein disorders.
- **Oncologic** - Children with cancer are at increased risk for AIS as a result of their disease, subsequent treatment, and susceptibility to infection.
- **Trauma** - head or neck trauma resulting from intraoral trauma, hypertension or rotational injuries experienced after motor vehicle collisions, sports, or even chiropractic manipulation.
- **Drugs** - drug use, both illicit and prescribed, are a concern in the adolescent population. Cerebral infarcts and hemorrhage have been reported in patients abusing drugs. Adolescent girls using oral contraceptives are at higher risk of cerebral venous thrombosis.

After physical examination and evaluation, the first step in assessing a stroke patient is to determine whether the patient is experiencing an ischemic or hemorrhagic stroke so that the correct treatment can begin. A MRI of the head (preferred) or CT scan (if MRI is unavailable) is typically the first test performed.

Critical Points of Evidence

Acute Arterial Ischemic Stroke:

Evidence Supports

Supportive Measures

- Supportive measures for AIS should include control of fever, maintenance of normal oxygenation, control of systemic hypertension, and normalization of serum glucose levels[13]. *(strong, low)*

IV-tPA

[≤2% of children with acute stroke are reported to have been treated with tPA in the United States[29]].

- Alteplase is the thrombolytic agent that is approved by the FDA for administration to adults with ischemic stroke. It has also been recommended by expert consensus for use in children and adolescents with acute ischemic stroke using the same per Kg dosing and similar inclusion criteria as those used to treat select adult patients[21-22].
- Children with AIS are being treated successfully with IV-tPA and mechanical thrombectomy. [11]
- Alteplase (IV r-tPA) within 4.5 hours of stroke onset remains the gold standard of care for most ischemic stroke patients[26].
- A patient with acute arterial ischemic stroke and still within 4.5 hours of symptom onset (but with sufficient time to allow for imaging and treatment) may be a candidate for IV alteplase (tissue plasminogen activator, tPA) infusion. See thrombolytic protocol.

Anticoagulation[31]

- The current AHA/ASA 2018 guidelines provide a grade-A recommendation against the use of anticoagulation with heparin regardless of the extent of stenosis[31,32]. In some patients, the need for anticoagulation therapy necessitates treatment despite contraindications. Consultation with a hematologist is recommended.
- Anticoagulation may be necessary for patients who are at substantial increased risk of recurrent embolism but are not candidates for TPA, such as congenital heart disease or those with severe hypercoagulable states[13]. *(strong, low)*
- Usually avoid anticoagulation with very large infarctions or infarction with hemorrhagic conversion.
- Consider transient anticoagulation if stroke etiology is unknown pending elimination of embolism and serious coagulopathy.
- Anticoagulation is no longer considered appropriate for arterial dissection. Aspirin is now recommended for arterial dissection.

Aspirin and other Antiplatelet agents

- Consider aspirin for intracranial vasculopathy or for idiopathic stroke.
- Anticoagulation is no longer considered appropriate for arterial dissection. Aspirin is now recommended for arterial dissection.

Sickle Cell Disease (SCD)

- Acute management of ischemic stroke resulting from SCD should include optimal hydration, correction of hypoxemia, and correction of systemic hypotension[13]. *(strong, low)*
- Periodic transfusions to reduce the percentage of sickle hemoglobin are effective for reducing the risk of stroke in children 2 to 16 years of age with an abnormal TCD resulting from SCD and are recommended[13]. *(strong, high)*
- Children with SCD and a confirmed cerebral infarction should be placed on a regular program of red cell transfusion in conjunction with measures to prevent iron overload[13]. *(strong, moderate)*

- Reducing the percentage of sickle hemoglobin with transfusions before performing catheter angiography (CA) is indicated in an individual with SCD[13]. *(strong, very low)*

Imaging [15-20]

- MRI is more sensitive than CT for the early detection of ischemic stroke as well as for the elimination of several stroke mimics in children. Consequently, cranial MRI is recommended for the initial evaluation for suspected ischemic stroke, especially when time-sensitive treatments such as thrombolysis or mechanical clot retrieval may be considered.
    - If an acute stroke is identified, then MRA brain and neck may be added to look for arterial dissection.
- MRI is more sensitive to acute diffusion changes, but may be contraindicated or limited in patients with dental braces, ferromagnetic implants, pacing or stimulator wires.
- CT is not as sensitive as MRI for the early identification of acute ischemic stroke, but later findings include:
    - Focal parenchymal hypodensity
    - Cortical swelling with sulcal effacement and loss of gray-white matter differentiation
    - Hyperdense MCA sign
- Brain CT with brain CTA can be used to evaluate vessel patency when considering acute intravascular thrombectomy.
- CTA has a high dose of radiation requirement

Mechanical Thrombectomy

- With severe arterial ischemic stroke (NIH stroke scale > 6) and occlusion of internal carotid artery or middle cerebral artery on CTA or MRA, the patient may be a candidate for mechanical thrombectomy. Time to catheter puncture should ideally be 6 hours, but longer times may be eligible: need to discuss w/ interventional radiologist on call for possible mechanical thrombectomy.

Evidence Lacking/Inconclusive

IV-tPA/Patient Management

- When feasible, shared decision-making between the patient (and/or his or her surrogate) and a member of the health care team should include a discussion of potential benefits* and harms** prior to the decision whether to administer intravenous tissue plasminogen activator (IV tPA) for acute ischemic stroke [consensus recommendation][27].
    - **Potential benefit of implementing the recommendation - Administration of IV tPA within 3 to 4.5 hours of stroke symptom onset increases the probability of better long-term functional outcome.*
    - ***Potential harm of implementing the recommendation - Administration of IV tPA within 3 to 4.5 hours of stroke symptom onset increases the risk of early Symptomatic Intracerebral Hemorrhage (sICH).*

Tenecteplase (TNK)

- Tenecteplase (TNK) is a genetically engineered form of tPA with slower plasma clearance, greater resistance to plasminogen activator inhibitor 1, and greater selectivity for clot-bound fibrin. Tenecteplase was approved by the FDA for use in individuals with myocardial infarction. The apparent safety and efficacy of TNK compare favorably with those reported in pediatric studies of tPA and adult studies of TNK. Because experience with tenecteplase is limited in children, it is suggested that further investigation is warranted in children, therefore, alteplase will be used for children with acute ischemic stroke[23].

    Note: For consistency in thrombolytic used at DCMC, alteplase will also be used to address adult stroke patients. Evidence shows that alteplase (ALT) is noninferior to tenecteplase (TNK) for acute ischemic stroke for either the efficacy or safety end points.

Mechanical Thrombectomy

- Mechanical thrombectomy may be considered for acute ischemic stroke due to large vessel occlusion (ICA terminus, M1, basilar artery) in patients aged 1-18 years[25].

Evidence Against

Imaging [15-20]

- The disadvantages of MRA are its lower vessel resolution than that of CTA, its incompatibility with certain ferromagnetic materials, and the longer imaging time and increased need for sedation[15-20].

Acute Cerebral Venous Sinus Thrombosis:

Evidence Supports

Anticoagulation

- Patients cerebral venous sinus thrombosis (CVST) should be anticoagulated to prevent thrombus propagation or embolism (but not isolated cortical vein thrombosis)[13]. *(strong, low)*
- Most acute CSVT patients (both neonates and older children) should be anticoagulated[13]. *(strong, low)*
    - Benefit even with secondary hemorrhage (unless large hemorrhage)
    - Do not anticoagulate patients with small medullary venous infarcts
    - Discuss exceptions with stroke neurologists and hematologists
        - In particular discuss management of CSVT in the setting of acute trauma
    - Treatment: unfractionated heparin (UFH) or low-molecular-weight-heparin (LMWH) initially
    - Treatment longer term: LMWH or warfarin for six months
    - If anticoagulation deferred because of large cerebral infarct or large hemorrhagic conversion, repeat imaging in 3-5 days; consider anticoagulation if the thrombus extends.

Complications

- Increased intracranial pressure (ICP) is a common complication, with pain and risk of blindness[13]. *(strong, low)*
    - Ophthalmology consultation to document disc Friesen scale, acuity, and visual fields
    - Consider acetazolamide and then furosemide
    - Optic nerve sheath fenestration for progressive visual loss

Imaging[15-20]

- Both CT and MRI can detect large cerebral venous sinus thrombosis.
- MRV time of flight can be used to screen for cerebral venous sinus thrombosis, but this technique may not reliably distinguish dural sinus hypoplasia from versus occlusion. If a prior CT or MRI has already demonstrated a thrombus, then MRV can be used to identify the extent of occlusion.
- To follow resolution of a thrombus or to confirm the presence of a cerebral venous sinus thrombosis, order CT venography (CTV) with contrast or MRI with and without contrast.
- Reimage in response to clinical deterioration (rule out clot propagation, hemorrhagic conversion)[13]. *(strong, low)*
- It is reasonable to repeat the neuroimaging studies in children with CVST to confirm vessel recanalization or recurrence of the thrombus (Class IIa, Level of Evidence C)[13]. *(strong, low)*

Treatment[13]

- Supportive measures for children with CVST should include appropriate hydration, control of epileptic seizures, and treatment of elevated intracranial pressure[13]. *(strong, low)*
- Children with CVST should have a complete blood count[13]. *(strong, low)*

- Children with a CVST and a suspected bacterial infection should receive appropriate antibiotics[13]. *(strong, low)*

Acute Hemorrhagic Stroke:

Evidence Supports

Imaging[15-20]

- Brain CT is sensitive to hemorrhage and is study of choice when intracranial hemorrhage is suspected. If the patient has an acute intracranial or subarachnoid hemorrhage, further cerebrovascular imaging (CTA, MRA, or catheter angiogram) may be needed to identify the source of bleeding. This follow-up study should be done soon, particularly with subarachnoid hemorrhage, but after the patient is stabilized.

Neurosurgical Consultation

- Patients with a subarachnoid or intracerebral hemorrhage or a large cerebral or cerebellar infarction should have an urgent neurosurgical consultation. Large (i.e. thick) subarachnoid hemorrhages have increased risk of vasospasm. *(weak, low)*

Management

- Children with nontraumatic brain hemorrhage should undergo a thorough risk factor evaluation, including standard cerebral angiography when noninvasive tests have failed to establish an origin, in an effort to identify treatable risk factors before another hemorrhage occurs [13].*(strong, low)*
- Children with a severe coagulation factor deficiency should receive appropriate factor replacement therapy, and children with less severe factor deficiency should receive factor replacement after trauma[13].*(strong, high)*
- Given the risk of repeat hemorrhage from congenital vascular anomalies, these lesions should be identified and corrected whenever it is clinically feasible. Similarly, other treatable hemorrhage risk factors should be corrected[13].*(strong, low)*
- Stabilizing measures in patients with brain hemorrhage should include optimizing the respiratory effort, controlling systemic hypertension, controlling epileptic seizures, and managing increased intracranial pressure[13]. *(strong, low)*
- Consult hematology for patients with known or suspected bleeding disorders.
- Basic homeostasis measures are similar to those for arterial ischemic stroke.
    - If hemorrhage is result of hemorrhagic conversion of arterial or venous infarction, manage as arterial ischemic stroke or cerebral sinovenous thrombosis
- Prevent seizures and treat seizures aggressively
- Primary ICH or SAH should prompt an early evaluation for a cerebrovascular cause or an underlying coagulopathy
- The aneurysm causing a subarachnoid hemorrhage should be identified quickly to assist early intervention and reduce risk of early re-hemorrhage.

Evidence Lacking/Inconclusive

Management

- There are no clear guidelines for the management of intracerebral hemorrhage in children without bleeding disorders.
- Manage as per neurosurgery recommendations.

Practice Recommendations and Clinical Management

Emergency Imaging

Brain imaging is a crucial step in the evaluation of suspected stroke and must be obtained on an emergent basis.

It is impossible to distinguish between AIS and HS and to differentiate symptoms of real stroke from 'stroke mimics' on clinical grounds, and therefore imaging is key to diagnosis. Predisposing risk factors should be considered, and, if present, should increase suspicion of the diagnosis of stroke.

Consider primary imaging using magnetic resonance imaging (MRI) in suspected stroke only if it is available within one hour of arrival at hospital. (**MRI is the preferred method if immediately available**)
(Consider adding magnetic resonance angiogram (MRA) at the time of undertaking MRI; this should cover the aortic arch to vertex in arterial ischamic stroke (AIS) and can be limited to the intracranial circulation in HS.)

Where access to an MRI may not be immediately available, an emergent computed tomography (CT) may be acceptable for suspected SAH or brain hemorrhage.

Ensure that a cranial computerised tomography (CT) scan is performed within one hour of arrival at hospital in every child with a suspected stroke; including computerised tomography angiography (CTA), if the CT scan does not show hemorrhage, OR CTA limited to intracranial vascular imaging, if hemorrhagic stroke (HS) is demonstrated.

Management - *Acute Stroke*

I. Imaging Protocol - Emergency MRI or CT imaging of the brain is necessary before beginning specific treatment for acute stroke.
II. Determine stroke type and identify stroke mimics.
    A. Identify any process that can lead to acute worsening (e.g. pending herniation, hemorrhagic infarction, vasculopathy, hydrocephalus).
III. *First Line Therapy* - Eligible patients should receive Intravenous Alteplase (tPA) for acute arterial stroke.
    A. Because the benefit of alteplase is time dependent, it is critical to treat patients as quickly as possible. Eligible patients should receive intravenous alteplase without delay even if mechanical thrombectomy is being considered.
        1. Addendum 1: Selection criteria for IV tPA in children
        2. Addendum 1: Exclusion criteria for IV tPA in children

        **Because the use of thrombolytic drugs carries the real risk of major bleeding, the risks of potential benefits of alteplase should be discussed whenever possible with the patient and family before treatment is initiated.*
    B. Intravenous Alteplase Dosing
    C. Medical Management Following Alteplase Administration
    D. Management of bleeding complications after tPA
IV. *Second Line Therapy* - Mechanical Thrombectomy
    A. Mechanical Thrombectomy is indicated for patients with acute ischemic stroke due to an emergent large vessel occlusion in the anterior circulation who can be treated within 24 hours of

the time last known to be well (i.e., at neurologic baseline), regardless of whether they receive intravenous alteplase for the same ischemic stroke event[24].

1. Addendum 2: Selection criteria for Mechanical Thrombectomy
2. Addendum 2: Exclusion criteria for Mechanical Thrombectomy

Laboratory

	Initial Labs (send STAT)	Secondary Labs
Thrombotic or Hemorrhagic Stroke	Complete metabolic panel CBC w/ platelet count and peripheral smear PT (prothrombin time) aPTT (activated partial thromboplastin time) Fibrinogen Urinalysis Quantitative d-dimer BHCG in menarcheal females Hgb electrophoresis for individuals at risk for hemoglobinopathy (if status unknown) Type and cross if anticipate exchange transfusion or IV tPA	Thrombin time (as deemed necessary) POC Glucose EKG *(For unexplained Hemorrhagic Stroke - Discuss with Consulting Hematologist)* Clotting factor Levels ● von Willebrand studies ● Platelet function screen <u>Metabolic:</u> when clinically suspect inborn error of metabolism as cause of infarction ● Lactic acid- plasma (CSF as suspected) ● Mitochondrial disease evaluation <u>Autoimmune disease screen:</u> when clinically suspect autoimmune disorder, but discuss with Rheumatology ● ESR, CRP, C3, C4, CH50, ANA <u>Infection:</u> ● Varicella titer (varicella exposure may have been up to 12 months prior to ischemic infarct) Drug Screen in at risk individuals
Ischemic Stroke	Complete metabolic panel CBC w/ platelet count and peripheral smear PT (prothrombin time) aPTT (activated partial thromboplastin time) Fibrinogen Urinalysis Quantitative d-dimer BHCG in menarcheal females Hgb electrophoresis for individuals at risk for hemoglobinopathy (if status unknown) Type and cross if anticipate exchange transfusion or IV tPA INR	*(Discuss with Consulting Hematologist)* Factor V Leiden Prothrombin 20210 Homocysteine Anti-Phospholipid Antibody Studies Panel StaClot LA Anticardiolipin Antibodies dRVVT (dilute Russell's Viper Venom Time) β2-Glycoprotein 1 Antibodies Protein C Activity Protein S Activity Anti-Thrombin Hemoglobin electrophoresis (in at risk individuals) Lipid panel Lipoprotein a

	Chem 10 (Electrolytes, glucose, BUN, creatinine, Calcium, Magnesium, Phosphorus) Blood Glucose check by Accu-Chek® at time of blood draw Type and Screen Hemoglobin profile (if indicated)	Drug Screen in at risk individuals

Stroke Alert Protocol

See "The 'pit-crew' model for door to needle times (DTN) in Pediatric Stroke" workflow.
See Stroke Alert Protocol - description of roles and responsibilities in the management of a stroke alert

Consults/Referrals

Numerous other specialties are involved in the care of the child with AIS and should be consulted during the first 72 hours

Social Work
Child Life

Outcome and rehabilitation after childhood stroke

Between 20% and 40% of children die after a stroke. The mortality is higher for hemorrhagic (about a third) than for ischemic stroke (up to 20%, with about half related to underlying systemic illness rather than the stroke itself). Recurrent stroke occurs in 6% to 15%, and mortality is higher in this group. Between 50% and 80% of surviving children have neurological sequelae, most commonly hemiparesis. Neurological outcome appears to be better for those with hemorrhage, CVST, and posterior circulation stroke. Early evaluation of physical and cognitive disability is the key to preventing avoidable complications and to planning rehabilitation, which should involve a multidisciplinary team[(13)].

Outcome Measures

- Door to Physician: Time from ED arrival to first contact with physician conducting physical assessment
- Door to CT/MRI Initiation: Time from ED arrival to neuroimaging
- Door to Interpretation: Time from ED arrival to imaging interpretation/confirmation of stroke type
- Door to Needle Time: Time from ED arrival to administration of tPA (when eligible)
- Patients missing thrombolytic therapy due to delay in:
    - initial patient assessment
    - Imaging (CT or/and MRI)
    - lab studies

Methods

Existing External Guidelines/Clinical Pathways

Existing External Guideline/Clinical Pathway	Organization and Author	Last Update
Suspected Acute Stroke	Children's Hospital and Medical Center	January 2020
Management of Acute Ischemic Stroke	MD Anderson Center	June 2019
ED Clinical Pathway for Stroke Management	CHOP - Children's Hospital of Philadelphia	October 2019

Any published clinical guidelines have been evaluated for this review using the **AGREE II criteria**. The comparisons of these guidelines are found at the end of this document. **AGREE II criteria** include evaluation of: Guideline Scope and Purpose, Stakeholder Involvement, Rigor of Development, Clarity of Presentation, Applicability, and Editorial Independence.

Review of Relevant Evidence: Search Strategies and Databases Reviewed

Search Strategies	Document Strategies Used
Search Terms Used:	AIS, Stroke, CVST, pediatric stroke management, acute ischemic stroke, thrombolytic stroke, mechanical thrombectomy, NIHSS, pediatric, stroke, tPA, and combinations of the key words/phrases.
Years Searched - All Questions	1998-2021
Language	English
Age of Subjects	0-18 years old
Search Engines	PubMed, Scholar Google, Cochrane
EBP Web Sites	
Professional Organizations	www.stroke.org American Stroke Association ninds.nih.gov National Institute of Neurological Disorders and Stroke
Joint Commission	
Government/State Agencies	None
Other	

Evidence Found with Searches

Check Type of Evidence Found	Summary of Evidence – All Questions
x	Systematic Reviews
x	Meta-analysis articles
x	Randomized Controlled Trials
☐	Non-randomized studies
x	Review articles
☐	Government/State agency regulations
x	Professional organization guidelines, white papers, ect.

Evaluating the Quality of the Evidence

The GRADE criteria were used to evaluate the quality of evidence presented in research articles reviewed during the development of this guideline. The table below defines how the quality of evidence is rated and how a strong versus a weak recommendation is established.

Recommendation	
Strong	Desirable effects clearly outweigh undesirable effects or vice versa
Weak	Desirable effects closely balanced with undesirable effects
Type of Evidence	
High	Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies
Moderate	Evidence from RCTs with important limitations (e.g., inconsistent results, methodological flaws, indirect evidence, or imprecise results) or unusually strong evidence from unbiased observational studies
Low	Evidence for at least 1 critical outcome from observational studies, from RCTs with serious flaws or indirect evidence
Very Low	Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence

Table 1: Risk Factors for Ischemic Stroke and CVST*

Congenital Heart Disease
- Ventricular septal defect
- Atrial septal defect
- Aortic stenosis
- Mitral stenosis
- Coarctation of aorta
- Cardiac rhabdomyoma
- Complex congenital heart defects

Acquired Heart Disease
- Rheumatic heart disease
- Prosthetic heart valves
- Libman-Sacks endocarditis
- Infectious endocarditis
- Cardiomyopathy
- Myocarditis
- Atrial myxoma
- Arrhythmia

Systemic Vascular Disease
- Arterial hypertension
- Familial hyperlipidemias
- Volume depletion or hypotension
- Hypernatremia
- Diabetes mellitus

Vasculitis and Inflammatory
- Acquired immunodeficiency syndrome
- Behçet disease
- Meningitis
- Systemic infection
- Systemic lupus erythematosus
- Polyarteritis nodosa
- Granulomatous angiitis
- Takayasu's arteritis
- Rheumatoid arthritis
- Drug abuse (cocaine, amphetamines)
- Hemolytic-uremic syndrome
- Varicella infection

Vasculopathy
- Ehlers-Danlos type 4
- Moyamoya disease
- Fabry disease
- Malignant atrophic papulosis
- Neurofibromatosis type 1
- Post-irradiation
- Progeria
- Pseudoxanthoma elasticum
- Transient cerebral arteriopathy
- Williams syndrome

Hematologic/Coagulation Disorders
- Hemoglobinopathy (e. g. sickle cell disease)
- Fanconi anemia
- Thrombotic thrombocytopenic purpura
- Thrombocytosis
- Polycythemia
- Disseminated intravascular coagulation (DIC)
- L-asparaginase
- Leukemia or other neoplasm
- Oral contraceptives
- Pregnancy/postpartum period
- Antithrombin III deficiency
- Factor V Leiden mutation
- Hyperhomocysteinemia
- Nephrotic syndrome
- Protein S deficiency
- Protein C deficiency
- Prothrombin mutation
- Antiphospholipid antibodies
- Inflammatory bowel disease

Structural Vascular Anomalies
- Arterial fibromuscular dysplasia
- Arterial agenesis or hypoplasia
- Sturge-Weber syndrome
- Intracranial arterial aneurysm

Trauma
- Fat or air embolism
- Foreign body embolism
- Carotid ligation (e.g., with ECMO)
- Chiropractic manipulation
- Traumatic arterial dissection
- Blunt cervical or intraoral trauma
- Catheter angiography
- Carotid cavernous fistula
- Coagulation defect with minor trauma
- Amniotic fluid/placental embolism

Vasospastic Disorders
- Migraine
- Ergot poisoning
- Vasospasm & subarachnoid hemorrhage

Metabolic Disorders
- Homocystinuria
- Isovaleric acidemia
- MELAS
- Methylmalonic and propionic acidemia
- NADH-CoQ reductase deficiency
- Ornithine transcarbamylase deficiency

*Table 1 adapted from E.S. Roach, et al. Pediatric Stroke and Cerebrovascular Disorders, Third Edition. Demos Medical. New York, 2011, 364 pp.

Table 2: Risk Factors for Hemorrhagic Stroke in Children*

Arteriovenous malformation or fistula
Cavernous malformation
Aneurysm
Arterial hypertension
Arteritis of cerebral vessels
Infectious endocarditis
Brain tumor
Diabetic ketoacidosis
Hypernatremia
Hematologic disorders
Sickle cell disease
Thrombocytopenia
Bone marrow transplantation
Disseminated intravascular coagulation
Leukemia
Coagulopathies
Afibrinogenemia
Hemophilia (Factor VIII or factor IX deficiency)
Factor VII deficiency
Factor XIII deficiency
Coagulopathy due to hepatic failure
Liver transplantation
Vitamin K deficiency
Maternal medications (e.g. phenobarbital, phenytoin)
Anticoagulant, antiplatelet, or thrombolytic agents
Hemorrhagic infarction
Venous sinus thrombosis
Intracranial arterial dissection
Moyamoya disease (more in adolescents and adults)
Drug related (amphetamines, cocaine, etc.)

*Table 2 adapted from E.S. Roach, et al. Pediatric Stroke and Cerebrovascular Disorders, Third Edition. Demos Medical. New York, 2011, 364 pp.

Table 3: Potential Stroke Mimics in Children*

Complicated migraine
Post-ictal deficit
Focal ictal deficit
Acute disseminated encephalomyelitis (ADEM)
Encephalitis (e.g. herpes simplex, autoimmune encephalitis)
Cerebral abscess
Brain tumor
Labyrinthitis
Paraneoplastic disorder
Somatoform disorder

Addendum 1: IV Alteplase (tPA)

Selection criteria for IV Alteplase (tPA) in children[21-22]

- Patient presents with a known arterial ischemic stroke and can receive IV alteplase within 4.5 hours of symptom onset. (Symptom onset time is calculated from the point at which the patient was last known to be normal, but with sufficient time to allow for imaging and treatment.)
- Clinically significant deficit that is not improving as defined by a PedNIHSS score of > 4 or severe global aphasia at the time of alteplase administration.
- Neuroimaging findings confirming a diagnosis of arterial ischemic stroke consisting of EITHER;
    - Restricted MRI diffusion within a neuro-vascular territory consistent with clinical syndrome PLUS MRA showing absent flow signal consistent with occlusion in a cerebral artery corresponding to the clinical and parenchymal infarct
      OR
    - CT findings with early ischemic infarct and a CT angiogram showing occlusion in a cerebral artery corresponding to the clinical and parenchymal infarct.
- Patients with an extensive clinical deficit AND thrombo-embolic occlusion of the internal carotid artery, proximal middle cerebral artery, or basilar artery (large vessel occlusions, LVOs) are less likely to respond to IV alteplase.
- If a patient has an LVO and a major clinical deficit within 24 hours of symptom onset, evaluate the feasibility of intra-arterial alteplase administration or mechanical thrombectomy.

Exclusion Criteria for IV Alteplase (tPA) in children[21-22]

- > 4.5 hours from onset of symptoms (i.e. last known to be normal) before alteplase can be started.
- Rapidly improving symptoms or mild deficit. PedNIHSS score of ≤ 4 is a relative contraindication.
- Isolated mild neurological deficits, such as ataxia alone, sensory loss alone, dysarthria alone, or minimal weakness.
- Caution is advised before giving intravenous r-tPA to persons with NIH Stroke Scale >22
- Symptoms suggestive of subarachnoid hemorrhage.
- Stroke due to subacute bacterial endocarditis, sickle cell disease, meningitis, bone marrow or fat embolism, or moyamoya disease.
- Stroke or major head trauma within the past three months.
- Any prior intracranial hemorrhage or known arterial venous malformation, aneurysm, or neoplasm
- Arterial puncture at a non-compressible site or lumbar puncture within the prior seven days
- Persistent systolic blood pressure > 2 standard deviations of the mean for age
- Bleeding diathesis including platelets < 100,000, INR > 1.4 (PT > 15 sec) or elevated PTT > 40 sec
- Glucose <50 or > 400 mg/dl
- Pregnancy (obtain urine for b-HCG in all females of child-bearing age)
- Intracranial hemorrhage on pretreatment head CT or MRI
- CT with hypodensity / sulcal effacement > 33% of MCA territory or Alberta stroke program early CT score (ASPECTS) score ≤ 7 (relative contraindication; this suggests a longer interval between stroke onset and neuroimaging and time of onset of neurological symptoms must be confirmed)
- Current use of oral anticoagulants or a prolonged prothrombin time
- Use of heparin in the previous 48 hours and a prolonged partial thromboplastin time
- Recent myocardial infarction

- Because the use of thrombolytic drugs carries the real risk of major bleeding, the risks of potential benefits of alteplase should be discussed whenever possible with the patient and family before treatment is initiated.
- Relative contraindications include:
    - Neurosurgery within the prior 90 days
    - Major surgery or parenchymal biopsy within 10 days
        - (Perioperative cardiac stroke)
- Gastrointestinal or urinary bleeding within 21 days

Intravenous Alteplase (tPA) dosing[21-22]

- There is no age-specific data to guide dosing for children with stroke. However, adult patients are dosed per Kg, and the same dose per Kg is usually recommended for children.
- An alteplase dose of 0.9 mg/kg to max of 90 mg is recommended for adults, with 10% given as bolus and the remainder given as continuous infusion over 60 minutes.
- Treatment must be given within 4.5 hours of onset of ischemic stroke, but administration earlier within the 4.5-hour window is desirable. Onset is defined as the time at which the patient was neurologically intact unless there is clear evidence of a favorable perfusion status.
- Based on expert consensus, individuals who have taken aspirin are eligible for treatment with alteplase if they meet all other criteria for therapy. There is limited information about the safety of alteplase administration to individuals who have taken other antiplatelet agents.
- Persons given intravenous alteplase should not receive aspirin, heparin, warfarin, ticlopidine, or other antithrombotic or antiplatelet aggregating drugs within 24 hours of treatment.

Medical Management Following Alteplase Administration[21-22]

- The patient should be managed in the Pediatric Intensive Care Unit.
- Careful management of arterial BP is critical during the administration of alteplase and the ensuing 24 hours. Excessively high blood pressure might predispose to bleeding; excessively low blood pressure may worsen ischemic symptoms.
- Central venous access and arterial punctures are restricted during the first 24 hours after alteplase
- Placement of an indwelling bladder catheter should be avoided during the period of drug infusion and for at least 30 minutes following the end of the infusion.
- Insertion of a nasogastric tube should ideally be avoided during the first 24 hours after alteplase administration.

Management of bleeding complications after tPA[21-22]

- Hemorrhage affecting the brain or other organs can be fatal.
- Treatment of thrombolysis-related bleeding is guided by:
    - the location and size of the hematoma
    - the likelihood that the bleeding can be controlled mechanically
    - the risk of neurological worsening or death

  - the interval between administration of the drug and the onset of hemorrhage
  - the specific thrombolytic drug used. There is a paucity of information to guide treatment of hemorrhagic complications of thrombolytic therapy.

- If bleeding is suspected, blood should be drawn to measure the patient's hematocrit, hemoglobin, partial thromboplastin time, prothrombin time/INR, platelet count, and fibrinogen.
  - Blood should be typed and crossed in preparation (for adults at least 4 units of packed red blood cells, 4-6 units of cryoprecipitate or fresh frozen plasma, and 1 unit of single donor platelets)
- Bleeding should be considered the likely cause of neurological worsening following use of a thrombolytic drug until a CT is available.
  - The study should be obtained on an urgent basis whenever worsening of the neurological status follows the administration of rt-PA.
- Any life-threatening hemorrhagic complication, including intracranial bleeding, should lead to the following sequential steps:
  - Discontinue infusion of thrombolytic drug if still being given;
  - Obtain blood samples for coagulation tests (see above);
  - Obtain surgical consultation, as necessary.

The antidote for alteplase is aminocaproic acid.

Addendum 2: Mechanical Thrombectomy

Selection criteria for Mechanical Thrombectomy in children[21-22]

- Embolic or thrombotic occlusion of internal carotid artery (ICA), proximal MCA, or basilar artery (unlikely to respond to IV alteplase)
- The child must weigh more than 40 kgs/88 lbs
- If the patient is a potential candidate for mechanical thrombectomy and the procedure can be performed before 24 hours from onset of symptoms, discuss with a neurosurgery attending on call.

*STROKE INTERVENTIONS **< 6 HOURS***

Inclusion Criteria:
- NIHSS ≥ 6
- Large vessel occlusion seen on CTA or MRA
- Premorbid mRS ≤ 2
- **CBF (< 30 %) volume ≤ 70 ml**

Exclusion criteria for Mechanical Thrombectomy in children[21-22]

- Life expectancy ≤ 90 days
- Intracerebral hemorrhage (ICH) or completed infarction on CT
- INR ≥ 3
- Platelets ≤ 40,000
- Aortic dissection or subclavian/brachiocephalic dissection
- Weight < 40 kgs/88 lbs

*STROKE INTERVENTIONS **6-24 HOURS***

Inclusion Criteria:
- NIHSS ≥ 6
- ICA or M1 occlusion seen on CTA or MRA; M2 occlusions w/ cut-off is considered on a case-by-case basis
- Premorbid mRS ≤ 2
- **CBF (< 30 %) volume ≤ 70 ml or ASPECTS ≥ 6 AND**
- **Mismatch ratio ≥ 1.8 AND**
- **Mismatch volume ≥ 15 ml**

Exclusion Criteria: paediatric
- Life expectancy ≤ 90 days
- **CBF (< 30 %) volume ≥ 70 ml or ASPECTS ≤ 6**
- ICH or completed infarction on CT
- INR ≥ 3
- Platelets ≤ 40
- Aortic dissection or subclavian/brachiocephalic dissection
- Weight < 40 kgs

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APPENDIX A. PEDIATRIC NIH STROKE SCALE (PedNIHSS)

Pediatric NIH Stroke Scale (PedNIHSS) – R. Ichord, 2004 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.

Case ID# _____EXAMINER _____Onset symptoms: Date_____ Time_____

Instructions	Scale Definition	Date/Time	Date/Time	Date/Time
1a. Level of Consciousness: For children age 2 yrs and up, 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. **For infants age 4 months up to age 2 years, multiply the score for this item by three, and omit scoring items 1b and 1c.**	**0 =** Alert; keenly responsive. **1 =** Not alert, but arousable by minor stimulation to obey, answer, or respond. **2 =** Not alert, requires repeated stimulation to attend, or is obtunded and requires strong or painful stimulation to make movements (not stereotyped). **3 =** Responds only with reflex motor or autonomic effects or totally unresponsive, flaccid, areflexic.	_____	_____	_____
1b. LOC Questions: The patient is asked the month and his/her age. The answer must be correct - there is no partial credit for being close. Aphasic and stuporous patients who do not comprehend the questions will score 2. Patients unable to speak because of endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier or any other problem not secondary to aphasia are given a 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. Omit this item for infants age 4 months up to age 2 years. See comment under item 1a.	**0** = Answers both questions correctly. **1** = Answers one question correctly. **2** = Answers neither question correctly.	_____	_____	_____
1c. LOC Commands: The patient is asked to open and close the eyes **(For children > age 2 years, this command to open and close the eyes is suitable and can be scored as for adults.)** and then to grip and release the non-paretic hand. **For children > age 2 years, substitute the command to grip the hand with the command "show me your nose" or "touch 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 to command, the task should be demonstrated to them (pantomime) and score the result (i.e., follows none,	**0** = Answers both questions correctly. **1** = Answers one question correctly. **2** = Answers neither question correctly.	_____	_____	_____

one or two commands). Patients with trauma, amputation, or other physical impediments should be given suitable one-step commands. Only the first attempt is scored. **Omit this item for infants age 4 months up to age 2 years. See comment under item 1a.**trauma, amputation, or other physical **impediments should be given suitable one-step commands. Only the first attempt is scored.**				
2. Best Gaze: Only horizontal eye movements will be tested. Voluntary or reflexive (oculocephalic) eye movements will be scored but caloric testing is not done. If the patient has a conjugate deviation of the eyes that can be overcome by voluntary or 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, preexisting 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.	**0** = Normal **1** = Partial gaze palsy. This score is given when gaze is 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 4 months 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 degrees (always tested supine). Drift is scored if the arm falls before 10 seconds or the leg before 5 seconds. **For children too immature to follow precise directions or uncooperative for any reason, power in each limb should be graded by observation of spontaneous or elicited movement according to the same grading scheme, excluding the time limits.** The aphasic patient is encouraged using urgency in the voice and pantomime but not noxious stimulation. Each limb is tested in turn, beginning with the non-paretic arm. Only in the case of amputation or joint fusion at the shoulder or hip, **or immobilization by an IV board,** may the score be "9" and the examiner must clearly write the explanation for scoring as a "9".	**0** = No drift, limb holds 90 (or 45) degrees for full 10 seconds. **1** = Drift, Limb holds 90 (or 45) degrees, but drifts down before full 10 seconds; does not hit bed or other support. **2** = Some effort against gravity, limb cannot get to or maintain (if cued) 90 (or 45) degrees, drifts down to bed, but has some effort against gravity. **3** = No effort against gravity, limb falls. **4** = No movement **9** = Amputation, joint fusion explain:_____			

	5a. Left Arm	_____	_____	_____
	5b. Right Arm	_____	_____	_____
	_____			
	0 = No drift, leg holds 30 degrees position for full 5 seconds. **1** = Drift, leg falls by the end of the 5 second period but does not hit bed. **2** = Some effort against gravity; leg falls to bed by 5 seconds, but has some effort against gravity. **3** = No effort against gravity, leg falls to bed immediately. **4** = No movement **9** = Amputation, joint fusion explain:_____			
	6a. Left Leg	_____	_____	_____
	6b. Right Leg	_____	_____	_____
7. Limb Ataxia: This item is aimed at finding evidence of a unilateral cerebellar lesion. Test with eyes open. In case of visual defect, ensure testing is done in intact visual field. The finger-nose-finger and heel-shin tests are performed on both sides, and ataxia is scored only if present out of proportion to weakness. **In children, substitute this task with reaching for a toy for the upper extremity, and kicking 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.	**0** = Absent **1** = Present in one limb **2** = Present in two limbs	_____	_____	_____
	If present, is ataxia in			
	Right arm **1** = Yes **2** = No **9** = amputation or joint fusion, explain _____	_____	_____	_____
	Left arm **1** = Yes **2** = No **9** = amputation or joint fusion, explain _____	_____	_____	_____
	Right leg **1** = Yes **2** = No **9** = amputation or joint fusion, explain _____	_____	_____	_____
	Left leg **1** = Yes **2** = No **9** = amputation or joint fusion, explain _____	_____	_____	_____
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. The patient with brain stem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic score 2. Patients in coma (item 1a=3) are arbitrarily given a 2 on this item.	**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.	_____	_____	_____
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**	**For Children age 2 years and up:** **0** = No aphasia, normal			

up with normal language development before onset of stroke: The patient is asked to describe what is happening in the attached, to name the items on the attached naming sheet (see pictures used in the STOP study, attached), and to read from the attached list of sentences (see the list of words/phrases from the STOP study; or who premorbid were known to be unable to read). Comprehension is judged from responses here as well as to all of the commands in the preceding general neurological exam. If visual loss interferes with the tests, ask the patient to identify objects placed in the hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in coma (question 1a=3) will arbitrarily score 3 on this 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 disability), score this item based on observations of language comprehension and speech during the preceding examination. For infants age 4 months to 2 years, score for auditory alerting and orienting responses.**	**1** = Mild to moderate aphasia; some obvious loss of fluency or facility of comprehension, without significant limitation on ideas expressed or form of expression. Reduction of speech and/or comprehension, however, makes conversation about provided material difficult or impossible. For example, in conversation about provided materials examiner can identify picture or naming card from patient's response. **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 comprehension. **For Infants age 4 months to 2 years:** **0 =** alerts to sound and orients visually or by behavior toward the location of origin of sound **2 =** alerts to sound, but does not have spatial orientation to sound **3 =** does not alert or orient to sound	_____	_____	_____
10. Dysarthria: If patient is thought to be normal an adequate sample of speech must be obtained by asking patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. Only if the patient is intubated or has other physical barrier to producing speech, may the item be scored "9", and the examiner must clearly write an explanation for not scoring. Do not tell the patient why he/she is being tested.	**0** = Normal **1** = Mild to moderate; patient slurs at least some words and, at worst, can be understood with some difficulty. **2** = Severe; patient's speech is so slurred as to be unintelligible in the absence of or out of proportion to any dysphasia, or is mute/anarthric. **9** = Intubated or other physical barrier, explain_____	_____	_____	_____
11. Extinction and Inattention (formerly Neglect): For children age 2 years and up: Sufficient information to identify neglect may be obtained during the prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosognosia may also be taken as evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable. **For children age 4 months to 2 years, score as "1" if there is either a sensory or motor deficit, score as a "2" if there are both sensory and motor deficits on the general neurological examination.**	**0** = No abnormality. **1** = Visual, tactile, auditory, spatial, or personal inattention or extinction to bilateral simultaneous stimulation in one of the sensory modalities. **2** = Profound hemi-inattention or hemi-inattention to more than one modality. Does not recognize own hand or orients to only one side of space.	_____	_____	_____

TOTAL SCORE	Tally up each individual column			

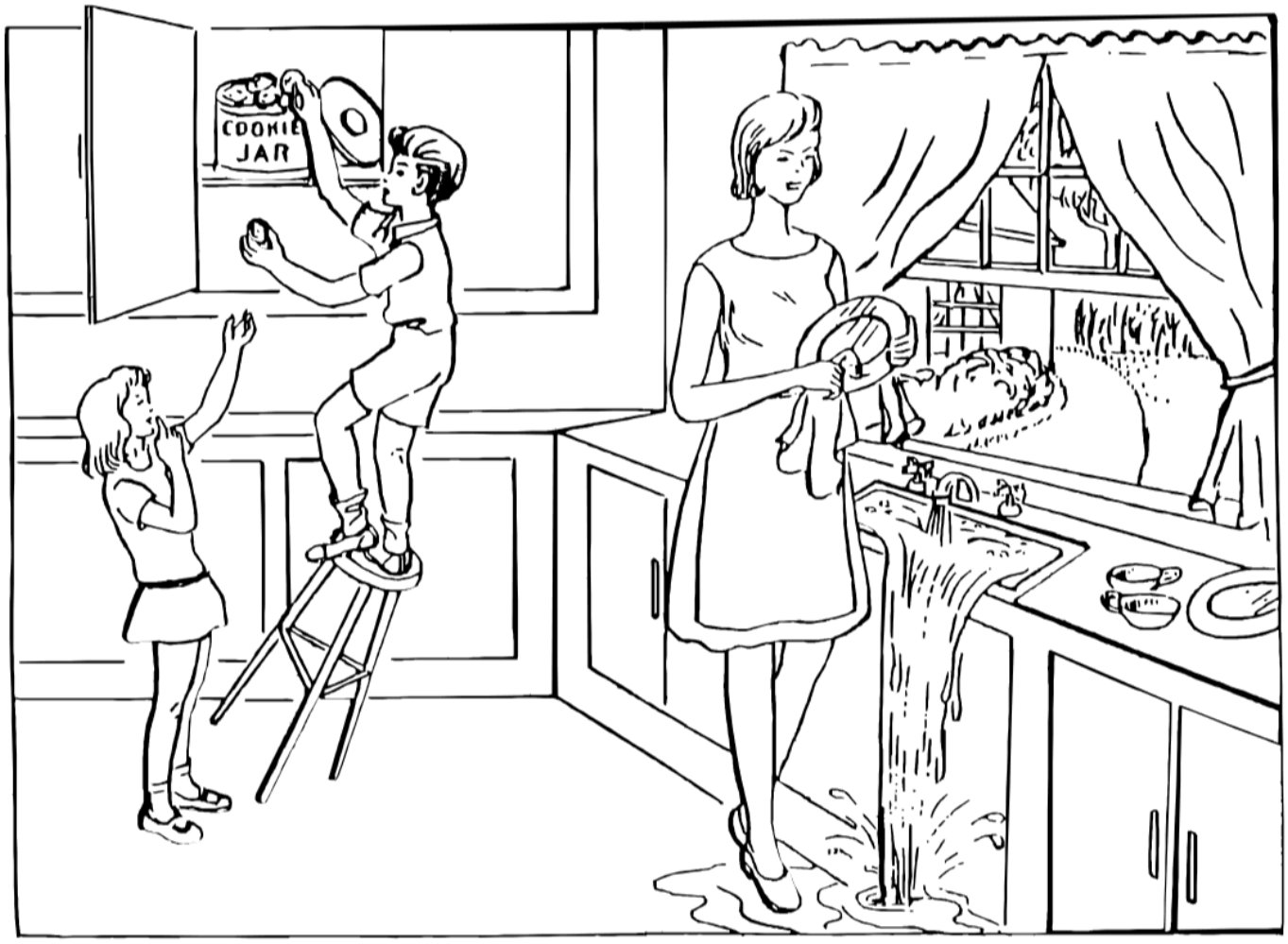
Comments (e.g. confounders, clarifications on scores):_____

_____

NIHSS Scoring

Score	Description
0	No stroke symptoms
1 - 4	Minor Stroke
5 - 15	Moderate Stroke
15 - 20	Moderate/severe stroke
21 - 42	Severe stroke

Picture to test story-telling for Item 9 Best Language of PedNISS



Pediatric NIH Stroke Scale: Picture for Item 9 "Best Language"

*Items from the STOP neurologic exam:

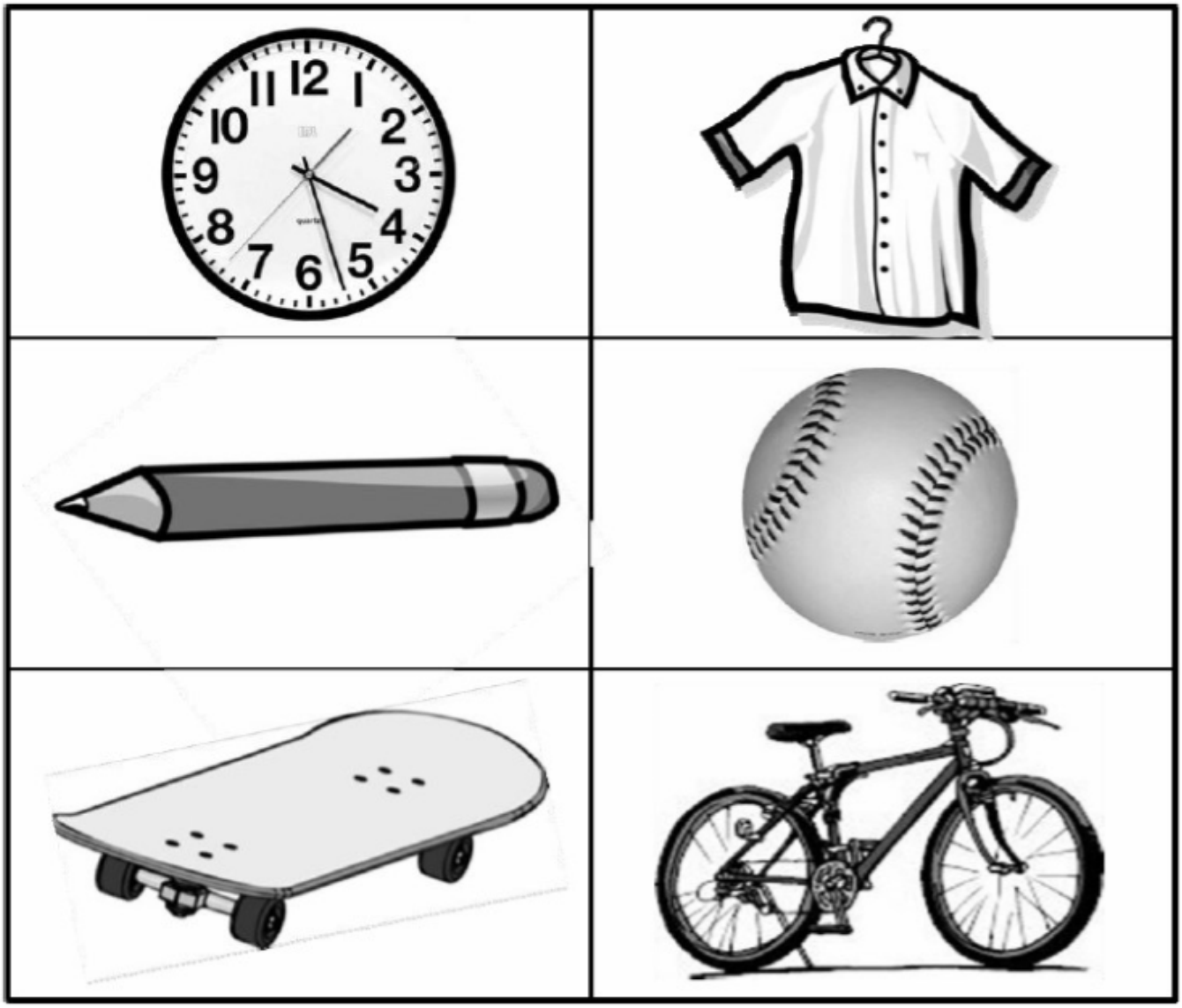
1. Naming – pictures are of a clock, pencil, skateboard, shirt, baseball, bicycle (see end of document for pictures).
2. Repetition – each of 4 word-repetition tasks is presented:
    a. Stop
    b. Stop and go
    c. If it rains we play inside
    d. The President lives in Washington
3. Reading – each of 3 items is presented for the child to read (adjust expectations according to child's age/school level): See below for printed stimulus.
    a. Stop
    b. See the dog run
    c. Little children like to play outdoors

1. Stop.

2. See the dog run.

3. Little children like to play outdoors.

Pictures to test naming for Item 9 Best Language of PedNIHSS. Ask patient to identify:



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Approved by the Pediatric Evidence-Based Outcomes Center Team

Revision History
Original Date Approved: August 27, 2021
Next Review Date: 2024
Update: 7/5/22 Changed the wording Inclusion criteria to "within 24 hours of symptom onset" instead of 72 hours to narrow down the time window to help prevent unnecessary activation of resources.

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