UCSF Pediatric Hyperacute Arterial Ischemic Stroke Guidelines

I. <u>Clinical Syndrome</u>: Acute onset focal deficit within 24 hours: face, arm or leg weakness, aphasia, ataxia, diplopia, dysarthria, with or without seizures or headache. *For children with sickle cell disease: Call hematology for emergent exchange transfusion.* For patients who will be admitted to an adult hospital, call Adult Transfer Center 353-9166.

II. Activate Pediatric Code Stroke response through Access Center

"Acute Stroke, pt. name and location, call Access Center at 415 353-1611 for consult" alert goes to:

- □ PICU fellow (intensivist is default MCP; clarify if PEM will be MCP at end of call).
- □ Child Neurology fellow and neurohospitalist
- □ PEM attending if ED to ED transfer or if stabilization anticipated in ED
- □ If inpatient outside of an ICU: primary service attending
- □ If heart disease or prior cardiac intervention: Peds cardiology fellow and PCICU attending/fellow

To minimize delay, begin when the intensivist is on the line. Additional providers are bridged in. *Location:* For inpatients outside of an ICU, activate RRT. For Gateway, transport to ED for neurology evaluation.

III. <u>Establish plan</u>

Stroke syndrome in window for hyperacute stroke treatment (see chart below)? If yes, establish emergent plans for imaging and potential hyperacute treatment. If no, patient can be stabilized first with urgent imaging as needed. If at outside hospital (as appropriate): accept patient, provide brief general medical recommendations, arrange emergent transport, make ED expect.

Treatment windows for ischemic stroke with arterial occlusion on vascular imaging		
Age range	IV tPA	Endovascular treatment
\geq 13 years	4.5 hours	discuss with NIR if < 24 hrs
\geq 1 year to < 13 years	none	discuss with NIR if < 24 hrs
< 1 year	none	none

After outside providers are off the call, UCSF providers use checklist to establish internal plan:

- Access adds Neuroradiology fellow to Access call to discuss emergent protocol and MRI availability. For MRI scans Saturday Monday, an MRI technologist will only be available on an on-call basis (see appendix). If heart disease, default CT/CTA (high frequency of metallic hardware). If MRI/MRA will be delayed, default to CT/CTA.
- \Box If thrombolysis candidate:
 - If at UCSF: call to alert pharmacist to prep alteplase for *potential* thrombolysis.
 - If at outside hospital: reasonable to administer available thrombolytic (Alteplase or Tenecteplase) to teenagers according to local adult protocol prior to transfer.
- □ If endovascular candidate: neurology contacts NIR fellow to prep for *potential* thrombectomy.
- □ Establish transport plan (if at OSH):
 - Where should the transport team deliver the patient? (ie ICU, ED, MRI, CT or NeuroIR). Access center specifies path of travel. If handoff to PICU will be done in ED, notify PEM
 - Which team (MD/NP and RNs) will receive handoff from transport team?
 - Will Access need to arrive the patient (if delivered to MRI, CT, NeuroIR)?

For patients of Benioff Children's Hospital, SF. Adapted from UCSF Adult NV Service and UCSF Hospital Wide Endovascular AIS Guidelines. Approved by BCHSF P&T Committee and Patient Safety Committee (June 2020), revised by Pediatric Neurocritical Care group (April 2022) with minor updates March 2024.

IV. <u>Workflows</u>

Child Neurology service

- □ Voalte "Neuroendovascular Surgery1st Call" early if suspected LVO and symptoms <24 hours
- □ Neuro Fellow documents exam including pediatric NIHSS, confirms time of onset (last normal)
- □ Review imaging with Neuroradiology/NIR, call appropriate teams to proceed with treatment

PICU/PCICU or ED service

- \Box Establish airway, ventilation, circulation
- □ Call radiology tech to coordinate imaging; MR Tech 476-1071; CT Tech 476-1262
- Determine sedation need for imaging or endovascular treatment (Anesthesia E1 Voalte 502-0442)
- □ For <u>cardiac patients CICU attending to notify</u>:
 - * Ventricular Assist Device (VAD) attending (when applicable)
 - * Pediatric Cardiac Surgery Attending for all VAD or post-surgery patients
 - * Pediatric Cardiac Anesthesia if prolonged, off-unit sedation is anticipated
- □ Place stroke orders (Apex Stroke orderset: "IP/ED Pediatric Hyperacute Stroke Orders")
 - □ Q15 minute VS (temp, HR RR, BP), continuous cardiac monitor & pulse oximetry
 - \Box Venous access (18 gauge preferred; 22 gauge ok for <30 kg)
 - □ Nasal cannula to maintain SaO2 >95%
 - \Box Weight in kg for tPA dosing.
 - □ Stat labs: CBC, platelets, PT/PTT, electrolytes, BUN/Cr, POC glucose, type & screen.
 - □ Pediatric Hyperacute Stroke imaging (MRI is preferred modality, but consider heart disease and imaging availability/speed):
 - MRI/MRA; write "focused stroke MRI/MRA" in comments
 - Pediatric CT Angiogram Brain/Neck for Stroke (include CT perfusion)
 - If prior cardiac surgery or VAD, default CT/CTA (high frequency of metallic hardware)
 - □ Blood pressure: Set range with neurology; generally, allow permissive hypertension. For patients with VAD, BP goals to be determined by VAD attending and neurology. Typical MAPs in 50-95% range for age norms (table below), consider increasing by 10% if arteriopathy.

Age Range	Typical MAP goals:	If tPA, treat for SBP above:
1-3	60-70	> 130
4-8	65-75	> 145
9-14	70-80	> 170
15-18	80-90	> 185

- □ NPO, IV fluids (normal saline) at 1 to 1.5 times calculated maintenance rate
- □ Bedrest, head of bed flat if ischemic stroke or unknown (30 degrees if vomiting)
- □ Point of care glucose; goal normoglycemia (65-100 mg/dl)
- \Box Temperature: prevent hyperthermia, goal temp <37.5°
- □ Stat Alteplase order as appropriate
- □ Neurointerventional radiology referral as appropriate
- □ Confirm access, eligibility criteria, MRI Safety checklist. Discuss treatment options with family.
- □ Second call to stroke pharmacist (502-6036) after imaging for yes/no emergent mixing of tPA, pharmacist will hand carry to bedside (get name of pharmacist and give patient location)
- □ Obtain consent (emergency verbal consent by phone ok).

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□ PICU/PCICU nurse releases order: 10% bolus at bedside ASAP, can be administered outside of PICU. Transfer to PICU/PCICU during remaining infusion.

Neuro-Interventional Radiology service

- □ Book case in OR and anesthesia when decision is made for endovascular procedure
- □ Obtain consent for endovascular procedure

Pharmacy service

- Designated pharmacist carries the Stroke Voalte (502-6036; same number as Seizure Voalte)
- □ 1st call, potential patients: verify STAT tPA orders, print tPA labels, set aside drug and supplies

 \Box Determine tPA dosing: 0.9 mg/kg of tPA (maximum dose=90 mg, final concentration 1 mg/ml). 2nd call, eligible patient confirmed: technician mixes tPA. Pharmacist hand delivers tPA to bedside.

V. Hyperacute stroke treatment

A. Endovascular therapy inclusion criteria :

- \Box Age \geq 1 year
- □ Acute arterial ischemic stroke syndrome: new onset neurological deficits attributable to an infarct in an arterial distribution (with diffusion restriction if MRI is performed)
- □ If groin puncture 0-6 hours since onset: Occlusion of intracranial ICA and/or MCA-M1 or basilar artery as evidenced by MRA, CTA or angiogram; MCA-M2 occlusions considered if major neurological or imaging deficit.
- □ If groin puncture 6-24 hours since onset: "mismatch" of presumed brain at risk and limited core infarct volume (CT ASPECTS >6 or MR-DWI< 1/3 MCA territory); for adults (age ≥ 18 years), clinical imaging mismatch is defined as one of the following on MR-DWI or CTP-rCBF maps (DEFUSE-3 and DAWN criteria, appendix):</p>
 - a. Core< 70 ml, penumbra: core ratio > 1.8, penumbra > 15 ml
 - b. less than 31 cc core infarct and NIHSS ≥ 10
 - c. 31 to 50 cc core infarct and NIHSS ≥ 20
- $\hfill\square$ Both Neurology and Neuro-interventional attendings agree to treat
- □ Equipoise cases not meeting all inclusions yet without exclusions may be treated with endovascular surgery, provided both the neurology attending and endovascular surgeon agree

B. Endovascular therapy exclusion criteria:

- Suspected chronic arteriopathy (for example, imaging showing moyamoya arteriopathy or history of prior cranial radiation)
- □ Acute non-traumatic ICH or SAH on baseline imaging that is responsible for the presenting neurological syndrome
- □ Substantial irreversible infarction of the brainstem in the judgement of the treating physician
- \Box Premorbid mRS >3 in an adult, or severe disability in a child
- □ Neurological syndrome likely caused by a "stroke mimic" (e.g. seizure or migraine with aura is likely the cause of the neurological syndrome rather than stroke)
- □ Patient is physiologically unstable making transport to angiography risky
- □ History of severe head injury within past 90 days that increases risk of intraprocedure complications or makes it difficult to determine the clinical impact of the stroke
- \Box Platelet count < 25,000/uL

<u>C. Inclusion criteria for IV thrombolysis:</u>

- Clinical diagnosis of acute ischemic stroke
- \Box Last time normal without deficit < 4.5 hours
- \Box Age \geq 13 years
- □ Infarct and partial or complete arterial occlusion of the corresponding intracranial artery
- □ No evidence of intracranial blood on CT or MRI
- \Box < 1/3 MCA territory involved on MRI or CT ASPECTS >7
- \Box PedNIHSS <25

D. Exclusion criteria for IV thrombolysis; (advisable to withhold tPA administration)

- Any circumstance in which the treating physician assesses that tPA poses a significant hazard.
- □ Significant edema or midline shift on imaging
- □ Symptoms suggestive of subarachnoid hemorrhage or verified by imaging
- □ Prior intracranial hemorrhage from an untreated source
- \Box Sustained SBP >185 mm Hg, or > 125% above age norms or aggressive treatment to lower BP
- □ Coma, severe obtundation, fixed eye deviation with complete hemiplegia
- □ Minor or isolated stroke symptoms (NIHSS <4)
- □ Neurological syndrome likely caused by a "stroke mimic" (e.g. seizure not stroke is likely the cause of the neurological syndrome)
- \Box INR > 1.7 or suspected/known coagulopathy
- □ Low molecular weight heparin within 24 hours or a PTT>40 secs due to unfractionated heparin
- Caution with the use of dabigatran, rivaroxaban, or apixaban within the previous 5 days
- \Box Platelet count < 100,000; hematocrit < 25%; serum glucose < 50 or > 400 mg/dL
- □ Prior stroke or head injury within the preceding 3 months
- Arterial puncture at a noncompressible site or lumbar puncture within 7 days
- □ Major surgery or serious trauma within prior 14 days
- □ Known intracranial neoplasm, AVM, or aneurysm
- □ Presumed septic embolus
- History of pericarditis, ventricular thrombus or aneurysm related to MI in previous 3 months
- □ Pregnancy
- GI or urinary tract hemorrhage within previous 21 days
- Stroke related to sickle cell disease (emergent hematology consult for exchange transfusion)

E. Guidelines for the Use of IV tPA in Acute Stroke

- □ Bolus with 10% of total dose (= 0.09 mg/kg) infused over 1 minute, then administer remaining 90% of (=0.81 mg/kg) infused over 60 minutes.
- □ Flush line with NS bag at the same rate as the infusion (do not push)
- □ Maintain goal BP for age (or max 185/110) during tPA administration and for first 24 hours
 - Monitor BP every 15 minutes for first 2 hours, then
 - Every 30 minutes for 6 hours
 - Every 60 minutes for 24 hours
- \Box Avoid insertion of Foley catheter for at least 4 hours after infusion ends.

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- □ Avoid IM injections, insertion of IV, arterial line and NG tube, if possible, for first 24 hours.
- \Box Hold antithrombotic medications (aspirin, heparin) for 24 hours after infusion ends.
- □ If patient develops acute neurologic deterioration, significant bleeding, or other complications, immediately discontinue tPA infusion and treat complications urgently and appropriately

For suspected symptomatic hemorrhage after IV or IA tPA:

- □ STAT non-contrast head CT
- □ Consult neurosurgery if ICH
- Check CBC, PT, PTT, platelets, fibrinogen, d-dimer. Repeat q2h until bleeding controlled
- □ Factor IX (Bebulin) or FFP (adult protocol: 2 units q 6 hours for 24 hours after tPA).
- \Box Cryoprecipitate (adult protocol: 20 units; If fibrinogen <200 mg/dL at 1 hr, repeat dose.
- □ Platelets (adult protocol: 4 units).
- □ Adult protocol: May give aminocaproic acid (Amicar) 5 g in 250 cc 0.9% NS IV over 1 hour if all other measures are unsuccessful.
- □ Institute frequent neurochecks and therapy of acutely elevated ICP, as needed

VII. <u>References</u>

- 1. The National Institute of Neurological Disorders and Stroke t-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581-7.
- 2. Albers GW, Amarenco P, Easton D, et al. Antithrombotic and Thrombolytic Therapy for Ischemic Stroke: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126:483S-512S.
- 3. Adams H, Adams R, DelZoppo G et al. Guidelines for the early management of patients with ischemic stroke. 2005 Guidelines update. A scientific statement from the stroke council of the American Heart Association/American Stroke Association. *Stroke* 2005;36:916-921.
- 4. IMS II Investigators. Endovascular Therapy after Intravenous t-PA versus t-PA Alone for Stroke. NEJM 2013;368:893-903.
- 5. Synthesis Expansion Investigators. Endovascular treatment for acute ischemic stroke. NEJM 2013; 368:904-13.
- 6. MR RESCUE Investigators. A trial of imaging selection and endovascular treatment for ischemic stroke. NEJM 2013; 368:914-23.
- 7. Antithrombotic drugs for carotid artery dissection.Cochrane Database Syst Rev. 2010 Oct 6; (10)
- 8. Antiplatelets vs anticoagulation for dissection: CADISS nonrandomized arm and meta-analysis Neurology. 2012 Aug 14;79(7):686-9.
- 9. Analysis of the evidence for the lower limit of systolic and mean arterial pressure in children. Pediatr Crit Care Med. 2007 Mar;8(2):138-44.
- 10. Goyal M; ESCAPE Trial investigators. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372(11):1019–1030.
- 11. Campbell BC; EXTEND-IA Investigators. Endovascular therapy for ischemic stroke with perfusionimaging selection. N Engl J Med. 2015;372(11):1009–1018.
- 12. Saver JL et al. Primary results of Solitaire[™] with the intention for thrombectomy as primary endovascular treatment for acute ischemic stroke (SWIFT PRIME) trial. In: International Stroke Conference, Nashville TN, February 11, 2015.
- 13. Powers WJ, Derdeyn CP, Biller J, Coffey CS, Hoh BL, Jauch EC, et al. 2015 AHA/ASA Focused Update Of The 2013 Guidelines For The Early Management Of Patients With Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline For Healthcare Professionals From The American

Heart Association/American Stroke Association. Stroke. 2015¹

- 14. Rivkin MJ, Bernard TJ, Dowling MM, Amlie-Lefond C. Guidelines for urgent management of stroke in children. *Pediatr Neurol*. 2016;56:8-17.
- 15. Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, et al. Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct. The New England journal of medicine. 2018;378(1):11-21.
- 16. Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, et al. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. The New England journal of medicine. 2018;378(8):708-18.
- 17. Roman LS, et al. Imaging features and safety and efficacy of endovascular stroke treatment: a meta-analysis of individual patient-level data. The Lancet Neurology. 2018;17(10):895-904. doi: 10.1016/S1474-4422(18)30242-4. PMID: 30264728.
- Management of Stroke in Neonates and Children: A Scientific Statement From the American Heart Association/American Stroke Association. Ferriero DM, et al; American Heart Association Stroke Council and Council on Cardiovascular and Stroke Nursing. Stroke. 2019 Mar;50(3):e51e96. PMID: 30686119

Appendices

Contact list (also available through Access center):

PICU fellow (Voalte "PICU fellow BCH SF" or 502-0835) Child Neurology fellow (Voalte "Consult Peds Neuro 1st Call BCH SF") PEM attending (Voalte "ED BCH SF Attending 1" or 502-0635) Neuroradiology fellow: Day: 476-1220 (1st call), QC fellow 514-6522 (2nd call) Nights and weekends: On-call fellow (Voalte "Consult Neuroradiology 1st Call") CT/MRI tech (Voalte 476-8671) Neuro-Interventional Radiology: Voalte "Neuroendovascular Surgery 1st Call" or pager 443-2828 Stroke Pharmacist (Voalte 502-6036) Pediatric neurohospitalist (Voalte "Consult Peds Neuro Attg BCH SF") Pediatric cardiology fellow (AMION) PCICU attending/fellow (AMION)

MRI availability:

During times below, no on-site Mission Bay MRI technologist. Available on an on-call basis:

- Saturdays and Sundays from 1900-0700
- Mondays from 2300-0700

Call **415-476-1071** to reach the on-site MRI Hospital Assistant who will coordinate the on-call MRI Technologist. On-call tech expectations to arrive in 35 minutes. Escalate issues to Radiation MRI Management Ops On-Call leader (pager: 415-443-5408 or <u>radmrimanagement@ucsf.edu).</u>