UCSF Pediatric Hyperacute Arterial Ischemic Stroke Guidelines (Revised April 2022)

I. Clinical Syndrome: 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 443-COMA.

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. Establish plan

If at outside hospital, accept patient and provide brief medical recommendations (if appropriate) and arrange emergent transport. If appropriate, make ED expect.

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

- □ Stroke syndrome in window for hyperacute stroke treatment (see chart below)? If yes:
- □ Access pages Neuroradiology fellow to discuss emergent protocol and MRI availability. If heart disease, default CT/CTA (high frequency of metallic hardware). If MRI/MRA will be delayed, default to CT/CTA
- □ If IV tPA candidate: PICU makes first call to pharmacist to prep for *potential* tPA
- □ 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)?

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

IV. Workflows

Child Neurology service

- Page NIR fellow (443-2828) early if suspected large vessel occlusion and symptoms <24 hours
- Fellow sees pt, 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

- 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 cardiac patients CICU attending to notify:
  * 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
  - ☐ Venous access (18 gauge preferred; 22 gauge ok for <30 kg)
  - ☐ Nasal cannula to maintain SaO2 >95%
  - ☐ 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)
  - ☐ Temperature: prevent hyperthermia, goal temp <37.5^{o}
  - ☐ Stat Alteplase order as appropriate
  - ☐ Neurointerventional radiology referral as appropriate
- While awaiting imaging: Confirm access, eligibility criteria, MRI Safety checklist as needed. 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).
- 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
- 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 :

- Age ≥ 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):
  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
- 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
- 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
- Platelet count < 25,000/uL

C. Inclusion criteria for IV thrombolysis:

- Clinical diagnosis of acute ischemic stroke
- Last time normal without deficit < 4.5 hours
- Age ≥ 13 years
- Infarct and partial or complete arterial occlusion of the corresponding intracranial artery
- No evidence of intracranial blood on CT or MRI
- < 1/3 MCA territory involved on MRI or CT ASPECTS >7
- 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
- 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)
- 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
- 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
- Avoid insertion of Foley catheter for at least 4 hours after infusion ends.
- Avoid IM injections, insertion of IV, arterial line and NG tube, if possible, for first 24 hours.
- 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).
- 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

VI. Contact list (also available through Access center):

PICU fellow (Voalte 502-0835)
Child Neurology fellow (415-443-4707)
PEM attending (Voalte 502-0635)
Neuroradiology fellow:
Day: 476-1220 (1st call), QC fellow 514-6522 (2nd call)
Nights and weekends: On-call fellow 443-1465.
CT/MRI tech (Voalte 476-8671)
Stroke Pharmacist (Voalte 502-6036)
Pediatric neurohospitalist (AMION)
Pediatric cardiology fellow (AMION)
PCICU attending/fellow (AMION)

VII. References

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Appendices. Full DEFUSE-3 and DAWN Eligibility (reference for adults, ≥ 18 years)

DEFUSE-3 Criteria

A. DEFUSE-3 Clinical Inclusion Criteria:

1. Signs & symptoms consistent w/ the diagnosis of acute anterior circulation ischemic stroke
2. Age 18-90 years
3. Baseline NIHSSS is ≥ 6 and remains ≥6 immediately prior to randomization
4. Endovascular treatment can be initiated (femoral puncture) between 6 and 16 hours of stroke onset. Stroke onset is defined as the time the patient was last known to be at their neurologic baseline (wake-up strokes are eligible if they meet the above time limits).
5. modified Rankin Scale less than or equal to 2 prior to qualifying stroke (functionally independent for all ADLs)
6. Patient/Legally Authorized Representative has signed the Informed Consent form.

B. DEFUSE-3 Clinical Exclusion Criteria:

1. Other serious, advanced, or terminal illness (investigator judgment) or life expectancy is <6 months.
2. Pre-existing medical, neurological or psychiatric disease that would confound the neurological or functional evaluations
3. Pregnant
4. Unable to undergo a contrast brain perfusion scan with either MRI or CT
5. Known allergy to iodine that precludes an endovascular procedure
6. Treated with tPA >4.5 hours after time last known well
7. Treated with tPA 3-4.5 hours after last known well AND any of the following; age >80, current anticoagulant use, history of diabetes or prior stroke, NIHSS >25
8. Known hereditary or acquired hemorrhagic diathesis, coagulation factor deficiency; recent oral anticoagulant therapy with INR > 3 (recent use of one of the new oral anticoagulants is not an exclusion if estimated GFR > 30 ml/min).
9. Seizures at stroke onset if it precludes obtaining an accurate baseline NIHSS
10. Baseline blood glucose of <50mg/dL (2.78 mmol) or >400mg/dL (22.20 mmol)
11. Baseline platelet count < 50,000/uL
12. Severe, sustained hypertension (Systolic BP >185 mmHg or Diastolic BP >110 mmHg)
13. Current participation in another investigational drug or device study
14. Presumed septic embolus; suspicion of bacterial endocarditis
15. Clot retrieval attempted using a neurothrombectomy device prior to 6 hrs from symptom onset
16. Any other condition that, in the opinion of the investigator, precludes an endovascular procedure or poses a significant hazard to the subject if an endovascular procedure was performed.

C. DEFUSE-3 Neuroimaging Inclusion Criteria:

1. ICA or MCA-M1 occlusion (carotid occlusions can be cervical or intracranial; with or without tandem MCA lesions) by MRA or CTA, AND
2. Target Mismatch Profile on CT perfusion or MRI (ischemic core volume is < 70 ml, mismatch ratio is >/= 1.8 and mismatch volume* is >/= 15 ml)

Alternative neuroimaging inclusion criteria (if perfusion imaging or CTA/MRA is technically inadequate):

1. If CTA (or MRA) is technically inadequate: Tmax>6s perfusion deficit consistent with an ICA or MCA-M1 occlusion AND Target Mismatch Profile (ischemic core volume is < 70 ml, mismatch ratio is >1.8 and mismatch volume is >15 ml as determined by RAPID software)
2. If MRP is technically inadequate: ICA or MCA-M1 occlusion (carotid occlusions can be cervical or intracranial; with or without tandem MCA lesions) by MRA (or CTA, if MRA is technically inadequate and a CTA was performed within 60 minutes prior to the MRI) AND DWI lesion volume < 25 ml
3. If CTP is technically inadequate: Patient can be screened with MRI and randomized if neuroimaging criteria are met.

D. DEFUSE-3 Neuroimaging Exclusion Criteria:

1. ASPECTS score <6 on non-contrast CT (if patient is enrolled based on CT perfusion criteria)
2. Evidence of intracranial tumor (except small meningioma) acute intracranial hemorrhage, neoplasm, or arteriovenous malformation
3. Significant mass effect with midline shift
4. Evidence of internal carotid artery dissection that is flow limiting or aortic dissection
5. Intracranial stent implanted in the same vascular territory that precludes the safe deployment/removal of the neurothrombectomy device
6. Acute symptomatic arterial occlusions in more than one vascular territory confirmed on CTA/MRA (e.g., bilateral MCA occlusions, or an MCA and a basilar artery occlusion).

DAWN Criteria:

A. DAWN General Inclusion Criteria:

1. Clinical signs and symptoms consistent with the diagnosis of an acute ischemic stroke, and subject has failed IV t-PA therapy (defined as a confirmed persistent occlusion 60 min after administration) or is contraindicated for IV t-PA administration
2. Age ≥18
3. Baseline NIHSS ≥10 (assessed within one hour of measuring core infarct volume)
4. Subject can be randomized between with 6 to 24 hours after time last known well
5. No significant pre-stroke disability (pre-stroke mRS must be 0 or 1)
6. Anticipated life expectancy of at least 6 months

B. DAWN Imaging Inclusion Criteria:

1. < 1/3 MCA territory involved, as evidenced by CT or MRI
2. Occlusion of the intracranial ICA and/or MCA-M1 as evidenced by MRA or CTA
3. Clinical Imaging Mismatch (CIM) defined as one of the following on MR-DWI or CTP-rCBF maps:
    a) 0-<21 cc core infarct and NIHSS ≥ 10 (and age ≥ 80 years old)
    b) 0-<31 cc core infarct and NIHSS ≥ 10 (and age < 80 years old)
    c) 31 cc to <51 cc core infarct and NIHSS ≥ 20 (and age < 80 years old)

C. DAWN General Exclusion Criteria:

1. History of severe head injury within past 90 days with residual neurological deficit, as determined by medical history
2. Rapid improvement in neurological status to an NIHSS <10 or evidence of vessel recanalization prior to randomization
3. Pre-existing neurological or psychiatric disease that would confound the neurological or functional evaluations, e.g. dementia with prescribed anti-cholinesterase inhibitor (e.g. Aricept)

4. Seizures at stroke onset if it makes the diagnosis of stroke doubtful and precludes obtaining an accurate baseline NIHSS assessment
5. Baseline blood glucose of <50mg/dL (2.78 mmol) or >400mg/dL (22.20 mmol)
6. Baseline hemoglobin counts of <7 mmol/L
7. Baseline platelet count < 50,000/uL
8. Abnormal baseline electrolyte parameters as defined by sodium concentration <130 mmol/L, potassium concentration <3 mEq/L or >6 mEq/L
9. Renal failure as defined by a serum creatinine >3.0 mg/dL (264 μmol/L) NOTE: subjects on renal dialysis may be treated regardless of serum creatinine levels
10. Known hemorrhagic diathesis, coagulation factor deficiency, or on anticoagulant therapy with INR > 3.0 or PTT > 3 times normal. Patients on factor Xa inhibitor for 24-48 hours ago must have a normal PTT.
11. Any active or recent hemorrhage within the past 30 days
12. History of severe allergy (more than rash) to contrast medium
13. Severe, sustained hypertension (Systolic Blood Pressure >185 mmHg or Diastolic Blood Pressure >110 mmHg) NOTE: If the blood pressure can be successfully reduced and maintained at the acceptable level using medication the subject can be enrolled
14. Female who is pregnant or lactating at time of admission
15. Current participation in another investigational drug or device study
16. Presumed septic embolus, or suspicion of bacterial endocarditis
17. Treatment with any cleared thrombectomy devices or other intra-arterial (neurovascular) therapies prior to randomization

D. DAWN Imaging Exclusion Criteria:

1. Evidence of intracranial hemorrhage on CT/MRI
2. CTA or MRA evidence of flow limiting carotid dissection, high-grade stenosis, or complete cervical carotid occlusion requiring stenting at the time of the index procedure (i.e., mechanical thrombectomy).
3. Excessive tortuosity of cervical vessels on CTA/MRA that would likely preclude device delivery/deployment
4. Suspected cerebral vasculitis based on medical history and CTA/MRA
5. Suspected aortic dissection based on medical history and CTA/MRA
6. Intracranial stent implanted in the same vascular territory that would preclude the safe deployment/removal of the Trevo device
7. Occlusions in multiple vascular territories (e.g., bilateral anterior circulation, or anterior circulation/vertebrobasilar system) as confirmed on CTA/MRA, or clinical evidence of bilateral strokes or strokes in multiple territories
8. Significant mass effect with midline shift as confirmed on CT/MRI
9. Evidence of intracranial tumor (except small meningioma) as confirmed on CT/MRI