

Neurocritical Care Guide 2020-2021



University of Pennsylvania

Mission Statement

The Penn Neurocritical Care Program aims to serve patients with severe acute injury to the nervous system through provision of exceptional, compassionate, cutting-edge care, to make important discoveries through innovative research that lessens the burden of suffering, and to train the next generation of international leaders in Neurocritical Care through a rigorous, multifaceted and comprehensive fellowship program.

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THE NEUROLOGIC EXAMINATION

MENTAL STATUS:

- Attention: Alert, Sleepy, Lethargic, Stuporous, Coma
 - Does patient open eyes to voice vs sternal rub vs deep pain
 - Can pt. spell WORLD backwards, count from 20 to 1, perform serial 7s
- Language: Fluent/nonfluent, repetition, naming, comprehension
 - Can p. repeat a phrase (e.g., no ifs ands or buts)
 - Can pt. name high frequency objects (e.g., watch, pen) and low frequency objects
 - Can pt. follow 1-step and 2-step commands, midline and appendicular commands?
- Memory: can pt. recall 3-5 objects at 1 minute, forward digit span (avg 7), story details
- Visuospatial: Organization of space (i.e., ability to draw clock, complex figure), Neglect
- Executive: organization of knowledge
 - Ask pt. to name as many animals as possible in 1 minute (>20 is normal)
 - Ask pt. to complete oral trails (A1, B2, 3C. ..)
 - Ask pt. to perform go/no go tasks

CRANIAL NERVES:

- Pupils OD/OS, size, reactivity, ptosis
- Visual acuity: Snellan eye chart (can use pinhole to correct refraction), color testing
- Visual fields: Test all four quadrants, central vision, neglect
- Fundus: Assess disc/vasculature/venous pulsations/retina
- Extraocular movements: Ab/adductions-both eyes, versions-one eye, alignment
- CN V / Face sensation: LT/PP/temp, V1-V3 dist, corneal reflex
- CN VII / Face strength— assess upper and lower facial symmetry, hyperacusis, dysgusia, corneal dehydration
- CN VIII: Hearing— hi/lo pitch, VOR, vestibular testing (past pointing, Fukuda step test—march in place with eyes closed, Dix-Hallpike, Frenzel lenses—nystagmus)
- Palate elevation—Aaaah, gag, uvula position, myoclonus
- CN XI: Sternocleidomastoid strength/bulk, trapezius strength/bulk
- CN XII -Tongue: position, bulk, fasciculations, strength (tongue against cheek)

MOTOR:

- Bulk: atrophy, fasciculations
- Tone: flaccid, spastic/clasp knife, rigid/lead pipe, cogwheeling, etc.
- Abnormal movement -- tremor, dystonia, chorea, athetosis, etc. Note frequency, amplitude and triggers (i.e., rest, postural, action) for tremors
- Strength: Pronator drift, 0-5 isolated muscles (3=antigravity), gait testing

SENSORY:

- Extremities/trunk/back/perineum, Romberg
- Anterolateral system/Spinothalamic tract (pain, temperature, some fine touch)
- Dorsal Columns (light touch/vibration/2 point discrimination/proprioception)

CEREBELLAR:

- Distal coordination: Finger-nose-finger, heel-knee-shin, titubation, optic ataxia, nystagmus, rhythm testing / rapid alternating movements
- Midline/vermis: Appendicular coordination

REFLEXES:

- DTRs: 0 to 4+ - note that 3 indicates spread of reflex, not amplitude of response
- Jaw jerk (can be used to distinguish between cord & brain lesions)
- Frontal release signs: glabellar, rooting, snouting, palmomentary, grasp, perseveration
- Hoffman and Babinski

GAIT:

- Ability to arise and sit (proximal movements), base of stance, stability of stance
- Also assess posture, initiation of gait, stepping, base of gait, arm swing, turning strength and balance (i.e., with tandem walk, heel/toe, deep knee bend)

EXAMINATION OF MENTAL STATUS

1. General Observations
 - Arousal Affect Communication
2. Attention
 - Count backwards: 20 19 18 17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
 - Digit span: 539 9703 59128 7681302 52081643
 - Vigilance: GFALTRNAJRPOANAGKILOPAWERZMALAKWOPTHAKFLA
3. Orientation:
 - Date , Time , Place
4. Speech/Language
 - Speech: dysarthric/hypophonic/spastic/scanning
 - Fluency: fluent/non fluent//paraphasias//circumlocutions
 - Repetition:
 - No ifs ands or buts
 - Methodist Episcopal
 - Comprehension:
 - one step
 - two-step
 - imbedded
 - Naming:
 - high frequency
 - low frequency
 - Reading/Writing:
 - irregular words
 - non-words
5. Memory:
 - Short term: Ball/flag/tree repeat: remember:
 - Long term: Presidents, historic events, current events
6. Praxis:
 - Oro buccal
 - Limb
 - Tool use
7. Visual spatial/Perceptual
 - Line bisection
 - Extinction: visual/auditory/tactile
 - Object recognition: Visually guided reaching
8. Emotion
 - Prosody
 - Expression
 - Comprehension
 - Executive/frontal function
 - Verbal fluency: Category (animals): Letter (F):
 - Oral trails: A1 B2 C3 D4 E5 F6 G7 H8 19 J10 KI I LI2 MI3 NI4
 - Go no go or contrasting programs
 - Crossed motor inhibition

MANAGING ELEVATED ICP

Elevated ICP is **bad** because:

- increased intracranial pressure reduces cerebral perfusion pressure (remember: **CPP = MAP-ICP**)
- increased intracranial pressure can lead to **herniation**.

The **Monro-Kellie doctrine** states that the skull has a fixed volume, so that any increase in volume of one intracranial compartment (e.g. blood, mass, etc.) will result in an increase in ICP. The increase in volume of one intracranial compartment can initially be offset by reductions in volume of other compartments, but after a certain point the brain's volume buffering capacity is exceeded and disastrous increases in ICP can occur. *The absolute ICP number is less important than the rate of rise and the pressure gradient between compartments. Patients can have a normal ICP and still herniate if their baseline is low, and patients with slow, longstanding increases in ICP may be asymptomatic such as patients with slow-growing tumors or idiopathic intracranial hypertension (IIH).*

All measures used to reduce ICP either reduce the volume of one of the intracranial compartments or change the total volume of the cranium

- CSF drainage → reduces CSF volume
- Hyperosmolar therapy → reduces brain tissue edema and brain tissue volume
- Hyperventilation → reduces cerebral blood flow (CBF), in turn reducing cerebral blood volume (CBV) - transient effect, can lead to rebound increase in CBF
- Metabolic therapy (e.g. barbiturate coma or hypothermia) → primary reduction in cerebral metabolic rate (CMRO₂), secondary reduction in CBF and CBV
- Removal of mass lesion/blood → reduces volume of mass/blood compartment
- Craniectomy → increases fixed volume of cranium

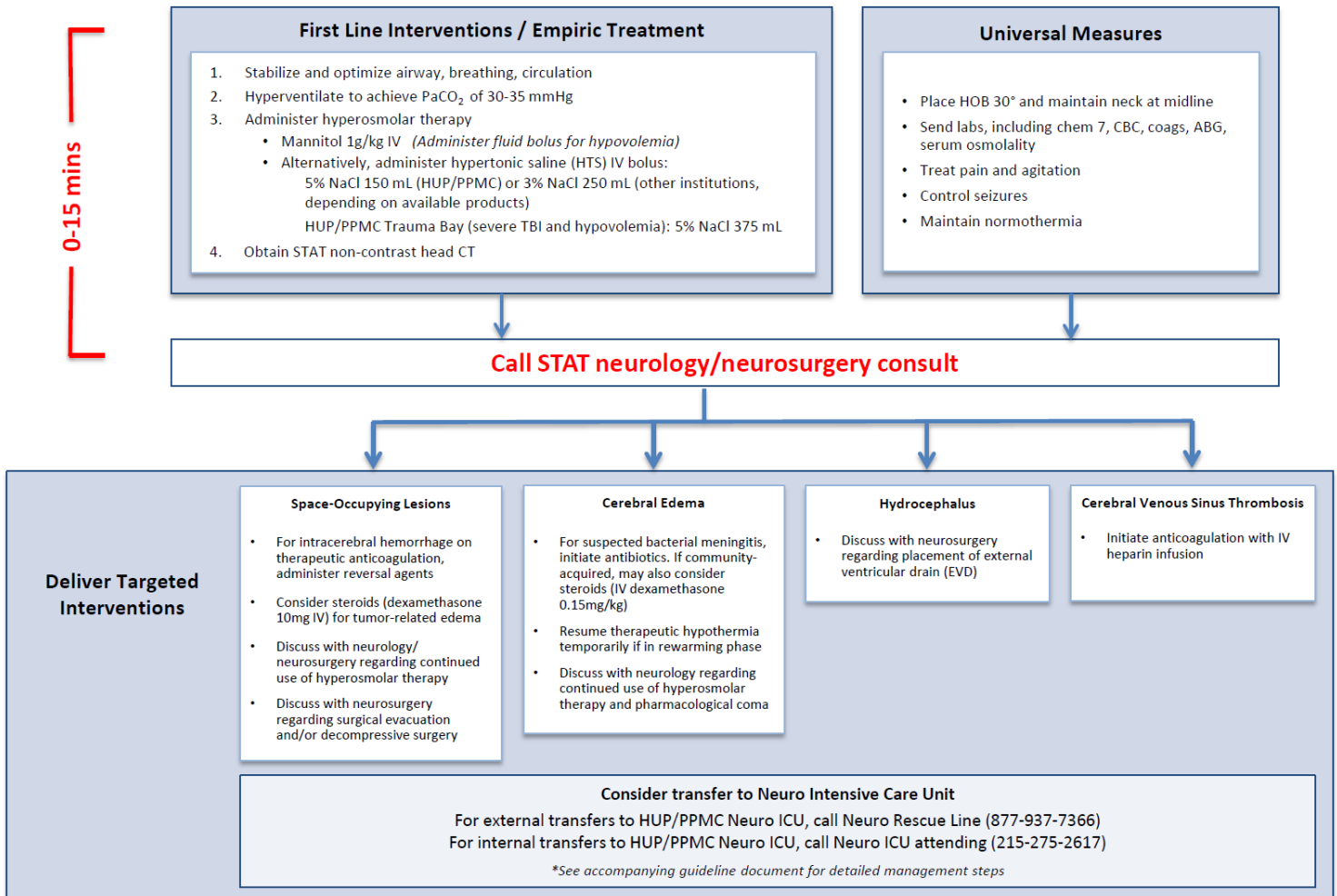
Symptoms of elevated ICP include:

- Headache
- Diminished level of consciousness
- VI nerve palsies
- Impaired upgaze
- Cushing's response (bradycardia, elevated BP, respiratory depression)

Herniation Syndromes

- Uncal herniation: ipsilateral pupillary dilation--> IIIrd nerve palsy --> contralateral or ipsilateral hemiparesis (Kernohan's notch phenomenon)
- Subfalcine herniation: weakness/increased tone in ipsilateral leg (due to contralateral ACA compression)
- Tonsillar herniation: respiratory arrest, downbeat nystagmus

UPHS GUIDELINE FOR EMERGENT MANAGEMENT OF CEREBRAL HERNIATION AND INTRACRANIAL HYPERTENSION



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Stepwise management of acute intracranial hypertension

A. Universal Measures:

1. HOB elevated above 30 degrees
2. Maintain head facing straight, consider exchanging c-collar for bolsters to stabilize c-spine (goal is to optimize jugular venous drainage)
3. Avoid hypotonic fluids
4. Minimize CNS metabolic needs: adequate sedation, control fevers, treat subclinical seizures
5. Appropriate monitoring of ICP and other physiologic parameters
6. Treat elevated intraabdominal and intrathoracic pressure

B. Hyperosmolar therapies

Mannitol:

Effects peak at 1 hour and last 4 – 24 hours. Complications include hypovolemia due to osmotic diuresis, hyperkalemia, acute renal failure

Relative Contraindications: renal failure/insuff., hypovolemia

To administer:

1. Give Mannitol 20% 1 g/kg bolus; maximum 150g
2. Give additional 1 g/kg in 6 hours
3. Check serum osmolality and basic chemistry in 5 hours:
4. If $Posm < 320$ give additional 1 g/kg
5. If $Posm > 320$, calculate the osmolar gap ($\text{measured } Posm - [2 \times \text{plasma Na} + \text{Glc}/18 + \text{BUN}/2.8]$); if < 20 AND $\text{Na} < 160$, give additional 1 g/kg
6. Repeat step 3 until $ICP < 20$, definitive therapy is performed or pathologic process is improved.
7. Maintain euvolemia to avoid hypotension and decreased CPP – replete urine output cc for cc with isotonic fluid

Hypertonic Saline (HTS):

For patients whose increased ICP is refractory to mannitol or for whom mannitol is contraindicated, consider hypertonic saline therapy. The primary complication is precipitation of CHF.

5% Bolus Therapy

1. $ICP > 20$ and mannitol is contraindicated or ineffective, AND HTS has not been administered within the past 4 hrs
2. Contraindications to HTS?
3. Obtain stat serum Na if none available in last two hours
4. Make sure $\text{Na} < 160$ mEq/L,
5. Bolus 150 mL 5% NaCl IV over 9 minutes

3% Infusion Therapy

1. $ICP > 20$ and 5% NaCl ineffective
2. Contraindications to HTS?
3. Obtain stat serum Na
4. Make sure $\text{Na} < 160$ mEq/L
5. Start continuous IV infusion 3% NaCl and adjust infusion rate per sliding scale (see below)
6. Check Na every 2 hours or as mandated by the clinical scenario.

HTS Infusion Sliding Scale

Serum Na+	ICP	3% NaCl Rate
<140	>20	Increase rate by 20ml/hr not to exceed 100ml/hr.
	<20	Continue current rate
141-150	>20	Increase rate by 10ml/hr not to exceed 100ml/hr.
	<20	Continue current rate
151-160	>20	Increase rate by 5ml/hr not to exceed 100ml/hr.
	<20	Continue current rate
> 160 Stop infusion; recheck serum Na+ in 2 hrs. Call MD.		

C. Other measures

CSF Drainage: Consider ventriculostomy for monitoring and controlling ICP when appropriate.

Hyperventilation: Short-lived effects <24hrs; works by increasing vasoconstriction and decreasing cerebral blood volume. Effects achieved at the expense of CBF; **therefore should be used only as bridge to definitive therapy (generally urgent surgery).** Goal pCO₂ 25-35

Decompressive Craniectomy: definitive therapy for severe intracranial hypertension (especially consider for acute ischemic stroke with malignant brain swelling, see Acute Ischemic Stroke section below)

Hypothermia: a last tier treatment, not likely to improve outcome but does reduce ICP. **Use the “Hypothermia in the Neurocritical Care Patient” order set**

Barbiturate coma: Has been used for medically refractory increased ICP usually in the setting of SAH or head injury. **Recent evidence suggests worse outcomes in head injury.**

Combined ICP and brain tissue oxygen monitoring in TBI Patients

	ICP < 20	ICP ≥ 20
PbtO ₂ ≥ 20	A	B
PbtO ₂ < 20	C	D

Treatment is triggered by ICP > 20mmHg and/or PbtO₂ < 20 mmHg for > 5 min: Choose at least 1 intervention from a tier before progressing toward the subsequent tier.

Scenario B (good PbtO₂, high ICP)

- **Tier 1 (begin within 15 minutes of episode)**
 - Increase angle of HOB, straighten neck, loosen ETT tape, C-collar
 - Ensure core temp < 38°C
 - Treat agitation and pain with lowest necessary dose of sedative and analgesic
 - Adjust minute ventilation for target PaCO₂ 35 – 45 torr
 - CSF drainage
 - Mannitol per protocol
 - Hypertonic saline per protocol
- **Tier 2 (begin within 60 minutes of episode)**
 - Adjust minute ventilation for target PaCO₂ 30 – 35 torr
 - Higher dose of mannitol or administer more frequently
 - Repeat HCT – look for increased size of intracranial mass lesions
 - Treat surgically remediable lesions - craniotomy
 - Lower core temp to 35 – 37°C while treating rigors
- **Tier 3**
 - Decompressive craniectomy
 - Therapeutic hypothermia (32 – 34°C) per protocol
 - Barbiturate (pentobarbital) coma (if possible try test dose of thiopental)
 - Trial of neuromuscular blockade

Scenario C (good ICP, low PbtO₂)

- **Tier 1 (begin within 15 minutes of episode)**
 - Increase angle of HOB, straighten neck, loosen ETT tape, C-collar
 - Ensure core temp < 38°C
 - Increase CPP to maximum of 70 mmHg with fluid boluses (goal euvolemia)
 - Increase PaO₂ by increasing FiO₂ to maximum of 60 torr
 - Increase PaO₂ by increasing PEEP
 - Add EEG monitoring and treat seizures if present
- **Tier 2 (begin within 60 minutes of episode)**
 - Increase CPP to maximum of 70 mmHg with pressor
 - Transfuse PRBC for goal hgb ≥ 10
 - Decrease ICP to < 10 mmHg through CSF drainage and/or increased sedation
 - If significant hypoxemia then increase PaO₂ further by increasing FiO₂ to 100% and/or increasing PEEP
 - Adjust minute ventilation for goal PaCO₂ 45 – 50 torr

Scenario D (low PbtO₂, high ICP)

- **Tier 1 (begin within 15 minutes of episode)**
 - Increase angle of HOB, straighten neck, loosen ETT tape, C-collar
 - Ensure core temp < 38°C
 - Treat agitation and pain with lowest necessary dose of sedative and analgesic
 - Mannitol per protocol
 - Hypertonic saline per protocol
 - Increase PaO₂ by increasing FiO₂ to maximum of 60 torr
 - Add EEG monitoring and treat seizures if present
- **Tier 2 (begin within 60 minutes of episode)**
 - Higher dose of mannitol or administer more frequently
 - Increase CPP to maximum of 70 mmHg with pressor – however, consider evaluating for hyperemia as cause
 - If significant hypoxemia then increase PaO₂ further by increasing FiO₂ to 100% and/or increasing PEEP
 - Transfuse PRBC for goal hgb ≥ 10
 - Repeat HCT – look for increased size of intracranial mass lesions
 - Treat surgically remediable lesions - craniotomy
 - Lower core temp to 35 – 37°C while treating rigors
- **Tier 3**
 - Barbiturate (pentobarbital) coma (if possible try test dose of thiopental to see if ICP and PbtO₂ respond appropriately)
 - Decompressive craniectomy
 - Lower core temp to 32 – 34.5°C while treating rigors
 - Trial of neuromuscular blockade

ACUTE ISCHEMIC STROKE

GENERAL MEASURES

- Assess if patient is eligible for endovascular thrombectomy or tPA (see below)
- CALL THE STROKE TEAM (**215-452-2793**)
- Neuro and BP checks q 1-2 hrs x 24 hrs if unstable or in unit bed; q 4 hrs if stable (Not the same frequency if s/p tPA or endovascular thrombectomy; see separate section)
- Head of bed flat especially if perfusion dependent exam.
- IV fluids- Normal Saline or LR at 80-100 cc/hr, NO D5 solutions. Watch for fluid overload. Allow BP autoregulation: goal MAP > 100 (Mean Arterial Pressure = Diastolic BP + 1/3 (Systolic BP - Diastolic BP); MAP 120-140 is not uncommon after large MCA strokes- unless on t-PA, do not aggressively manage for first 10 days.
- For MAP > 140, SBP > 220 or signs of end-organ damage, try labetalol prn first, then nicardipine gtt. Can also try low-dose IV enalaprilat.
- For MAPs < 100 and fluctuating symptoms, give IV fluid bolus and increase rate if tolerated by cardiac status. May also consider pressors.
- Keep NPO if perfusion-dependent or low level of arousal. Otherwise can start on appropriate diet if speech and swallowing intact. If unsure, keep NPO and order speech and swallow evaluation for AM. Patient will need NG tube in a few days if still NPO.
- Keep on sliding scale with FSBG checks q 6 (regardless of whether pt has DM).
- Avoid fevers - if febrile, pan-culture, then start on round-the-clock tylenol for 24 hours.
- Start antiplatelet therapy (usually aspirin) if ischemic stroke and not on t-PA or heparin.
- ALMOST NEVER use IV heparin in acute stroke. (See exceptions below).

WORKUP

- Order fasting lipids, CBC, coags, LFTs, basic metabolic panel, and U/A.
- If appropriate, consider ordering ESR, RPR, TSH (for new onset a-fib), type and screen, cardiac enzymes, or CXR. Remember, if RPR+, patient WILL need a lumbar puncture to r/o neurosyphilis.
- Consider ordering D-dimer (elevated in associated cancer/hypercoagulability)
- Order TTE for AM; keep NPO past midnight (in case of TEE).
- Order CUS if anterior circulation stroke and pt is a CEA candidate (even if known afib).
- If posterior circulation stroke, order MRA or CTA of head and neck to evaluate vertebral/basilar/PCA vessels.
- Order TCDs if not ordering MRA or CTA to evaluate for intracranial stenosis.
- If stroke in an unusual location/posterior circulation/hemorrhage, t/c MRI as an inpatient.
- May consider cerebral angiogram to evaluate vessels, esp if exam deteriorating despite maximal medical therapy
- T/C labs for hypercoagulability state if all above studies negative and no stroke etiology identified yet.

Heparin

When may IV heparin be possibly indicated in an acute stroke setting?

- Central venous sinus thrombosis
- Extracranial carotid or vertebral artery dissection (although no randomized study to support this) - anticoagulation in intracranial dissections can lead to subarachnoid hemorrhage
- Stuttering TIA (although no randomized study to support this)
- Basilar artery thrombosis (although no randomized study to support this)
- Stump emboli from carotid occlusion (based on TOAST subgroup analysis)

Endovascular thrombectomy for acute ischemic stroke

- Many studies have demonstrated superior survival and functional outcomes with endovascular therapy with or without standard care (i.e. intravenous thrombolysis)
- The DEFUSE-3 and DAWN trials showed that mechanical thrombectomy can improve outcomes in select patient populations up to 16 and 24 hours, respectively
- Inclusion criteria:
 - DEFUSE-3 (up to 16 hours after last known well)
 - Age 18-90, NIHSS >6, occlusion of proximal MCA or ICA, infarct volume <70cc, ischemic tissue:infarct volume ratio >1.8, penumbra volume >15cc
 - DAWN (up to 24 hours after last known well)
 - NIHSS >10, pre-stroke mRS <3, <1/3 MCA territory involvement via CT or MRI, occlusion of intracranial ICA or M1, favorable core infarct size on MR-DWI or CTP (0-20cc if age >80 and NIHSS >10, 0-30cc if age <80 and NIHSS >10, and 31-50cc if age <80 and NIHSS >20)
- In any patient with suspected acute ischemic stroke, CALL THE STROKE TEAM (**215-452-2793**). They will decide on need for Endovascular thrombectomy.

Sequence of events on recognition of potential endovascular AIS patient: www.pennstroke.org

1. Stroke fellow will contact stroke attending, Neuro IR fellow, R2 clinical lead nurse, Neuro consult JAR, CT, transfer center, NCC team to coordinate care
2. Patient will undergo endovascular therapy, if applicable (see inclusion criteria above)
3. Patient will be transported to Neuro ICU, possibly after dual energy CT en route
4. Neuro IR fellow, Stroke fellow, and Anesthesia resident will provide handoff to NCC team via telephone or at bedside
5. Begin post-endovascular therapy care. Use **EPIC order set "Acute Ischemic Stroke Post Thrombolysis and Endovascular Thrombectomy Order Protocol."**

Supportive measures following endovascular therapy

- Vital signs: q15 min x8 times, then q30 min x12 times, then q1 hour x16 times
 - Temperature q4 hours
- Neurochecks: q15 min x8 times, then q30 min x12 times, then q1 hour x16 times
- Bed rest with head of bed flat x24 hours
- If femoral access, leg immobilization per protocol and groin checks (pulse and visual assessment) q15 min x4 times, then q30 min x2 times, then q1 hour x4 times.
 - If bleeding appears significant or loss of pulses, call NCC or Neuro IR fellow
- Hemodynamic parameters and interventions:
 - Goal SBP < 180 and > 110, goal DBP < 105 and > 60
 - Use labetalol 20mg IVP q2 hours PRN as 1st line
 - If continues to be hypertensive, use nicardipine gtt
 - SpO2 > 92%
- Avoid fevers, culture if temp > 101.4
- Accuchecks q4 hours, goal normoglycemia
- STAT CXR for endotracheal tube placement if patient not extubated post EVT
- Standard acute ischemic stroke work up (see previous page)
- Repeat head CT in 24 hours or sooner if clinical change
- No antithrombotics including chemical DVT prophylaxis x24 hours or longer at discretion of NCC/Stroke team
- NPO, dysphagia screen with consult to Speech if concerns
- Physical/occupational therapy

Guidelines for recombinant tPA administration

CALL THE STROKE TEAM AT 215-452-2793 FOR ANY rt-PA QUESTIONS and do NIH stroke scale on all tPA patients!

Indication/ eligibility: Age \geq 18; clinical diagnosis of ischemic stroke with measurable neurological deficit; onset of symptoms less than 4.5 hours ago

Strong Contraindications:

- Symptoms minor or rapidly improving
- Other stroke or serious head trauma within past 3 months
- Major surgery within last 14 days
- Known history of intracranial hemorrhage
- Uncontrolled hypertension at the time of treatment (>185 mm Hg systolic or >110 mm Hg diastolic)
- Aggressive treatment needed to lower BP
- Suspicion of subarachnoid hemorrhage
- Gastrointestinal or urinary tract hemorrhage within 21 days
- Arterial puncture at noncompressible site within 7 days
- Administration of heparin within 48 hours preceding the onset of stroke and an elevated aPTT at presentation
- Platelet count $< 100,000$
- INR > 1.7

Relative Contraindications:

- Seizure at the onset of stroke
- Serum glucose <50 mg/dL or >400 mg/dL
- Hemorrhagic eye disorder
- Myocardial infarction in the prior six weeks
- Suspected septic embolism
- Infective endocarditis

Additional indications for extended window tPA

- Age < 80 years
- No history of prior stroke or diabetes
- No active anticoagulation
- NIHSS <25
- CT hypodensity $<1/3$ cerebral hemisphere

Pretreatment:

- Clearly establish time of onset of symptoms
- Obtain two IV accesses
- Monitor BP every 15 min. If over 185/110, BP may be treated with nitroglycerin paste and/or one or two 10-20 mg doses of labetalol given IV within one hour. If these measures do not keep BP below 185/110, do not give t-PA
- STAT platelet count, CBC, panel-7, PT/PTT, type and screen, t/c pregnancy test in young women

Dosing and Administration:

- 0.9 mg/kg; maximum dose not to exceed 90 mg
- 10% of the total dose administered as an IV bolus over 1 minute
- Remaining 90% infused over 60 minutes

After t-PA Treatment:

*Use EPIC orderset "Acute Ischemic Stroke Post Thrombolysis and Endovascular Thrombectomy Order Protocol"

- Monitor BP (maintain <180/105) and neuro exam:
 - -q 15 min for 2 hours after starting the infusion, then
 - -q 30 min for 6 hours, then
 - -q hour for 18 hours
- Head of bed flat
- No heparin, warfarin, aspirin, or other antiplatelet therapy for 24 hours.
- Repeat CT scan 24 hours post infusion to exclude intracerebral hemorrhage before initiating any anticoagulants or sooner if any neurologic changes occur.
- NO invasive procedures (i.e. no central lines, no blood draws, no NG tubes, no foley insertion) for 24 hours after tPA
- Bleeding precautions: check puncture sites for hematomas. Apply digital pressure or pressure dressing to active compressible bleeding sites. Evaluate urine, stool and emesis for blood. Monitor patient for evidence of gingival bleeding.
- Unexplained hypotension should prompt a thorough workup: GI bleed, tamponade from pericardial bleed etc.
- Order repeat CT scan (should be done 24 hrs after tPA was given)
- If post-24 hour CT scan is negative for bleed, can give ASA, start sub-Q heparin, do invasive procedures, get blood tests, etc; refer to section on acute stroke for relevant studies. (See below for management of positive CT scans)

Blood Pressure management post initiation of rt-PA:

- If diastolic BP >140 mm Hg:
 - Start an IV infusion of sodium nitroprusside; begin at 0.25-0.5 mcg/kg/min and titrate until diastolic decreases by 20%
- If systolic BP >230 mm Hg and/or diastolic BP 121-140 mm Hg:
 - Give labetalol 20 mg IV over 1-2 min. The dose may be repeated and/or doubled every 10 minutes up to 150 mg. Alternatively, after the first bolus of labetalol, an IV infusion of 2-8 mg/min of labetalol may be initiated and continued until the desired BP is reached. If satisfactory response is not achieved, use nitroprusside
- If systolic BP 180-230 mm Hg and/or diastolic BP 105-120 mm Hg on two readings 5 minutes apart:
 - Give labetalol 10 mg IV over 1-2 min. The dose may be repeated or doubled every 10-20 min, up to 150 mg. Alternatively, after the first bolus of labetalol, start an IV infusion of 2-8 mg/min of labetalol and continue until the desired BP is reached.

Monitor BP every 15 min during the antihypertensive therapy. Observe for hypotension.

Management of suspected intracranial hemorrhage: (Suspicion of intracranial hemorrhage prompted by neurologic deterioration, new headache, acute hypertension, new onset or increase in nausea/vomiting. If suspect intracranial bleed:)

- Discontinue rt-PA infusion if still on-going.
- Obtain a STAT CT scan; take patient down yourself.
- If CT shows bleed: draw blood: PT, aPTT, platelet count, fibrinogen
- Prepare to give 6-8 units cryoprecipitate containing Factor VIII and/or 6-8 units platelets. Consult neurosurgery if indicated.

Management of tPA associated intracranial hemorrhage

(See Pennstroke.org - password = silver9)

Primary goal is to give back fibrinogen and clotting factors, which are found in plasma and cryoprecipitate. tPA has a poorly understood antiplatelet effect, so we also give platelets.

One unit of cryoprecipitate has the same amount of clotting factors as one unit of FFP.

Cryoprecipitate is much more concentrated than FFP and so has a much smaller volume. As a result, cryoprecipitate can be used to deliver a large amount of clotting factors in a short period of time. HOWEVER, cryoprecipitate must be thawed prior to use, which takes time. FFP also has to be thawed and takes longer since the volume is greater.

HUP will almost always have several units of **thawed plasma** ready to be infused, so although it has a lower concentration of clotting factors, plasma can be given much faster than cryoprecipitate. You have to specifically ask for "thawed plasma."

Our suggested protocol for reversal of tPA-associated ICH is to give:

2 units of thawed plasma (available from blood bank in 5-15 minutes)

Can give unmatched if T&S not back

2 bags (5 units per bag) of cryoprecipitate

If the cryo becomes available after the first unit of plasma, stop the plasma and give the cryo

2 doses of platelets

One dose is equivalent to 4 units of pooled donor platelets

These blood products can be ordered verbally by calling the blood bank at 215-662-3448 and informing them that you need blood for the "tPA Reversal Protocol"

You will need the name of the neurology attending, patient name, patient MRN, and patient location to order.

If there is a problem, call the transfusion medicine attending on call at 215-838-8449.

Consider checking fibrinogen after completion of cryo infusion - if persistently < 100 mg/dl, give addit

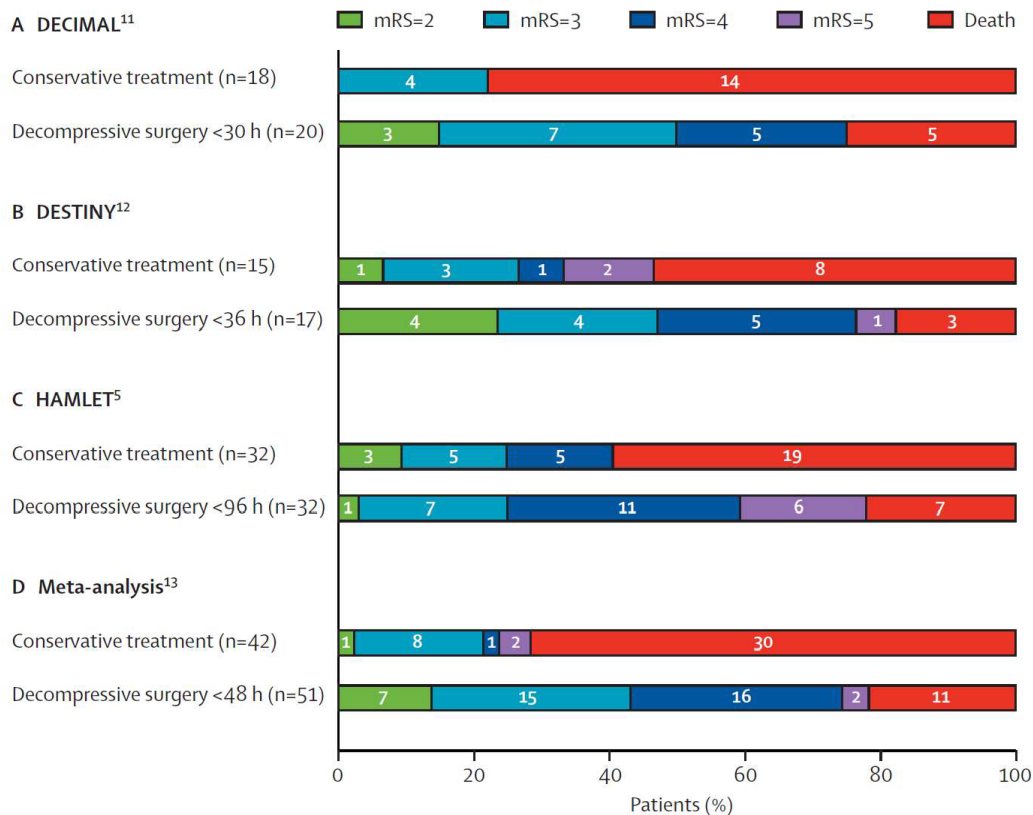
Decompressive Hemicraniectomy for Malignant MCA Territory Ischemic Stroke

Complete MCA territory stroke has a high (80%) mortality because cytotoxic edema can cause life threatening herniation. Decompressive hemicraniectomy can be a life-saving (and function saving) procedure for patients with malignant MCA territory infarction.

Consider **early** (< 48 hrs) decompressive hemicraniectomy if

- Patient age less than 60
- Radiologic signs suggestive of “malignant” MCA territory infarction
 - > ½ MCA territory infarcted
 - DWI infarct volume > 145 cm³ on MRI

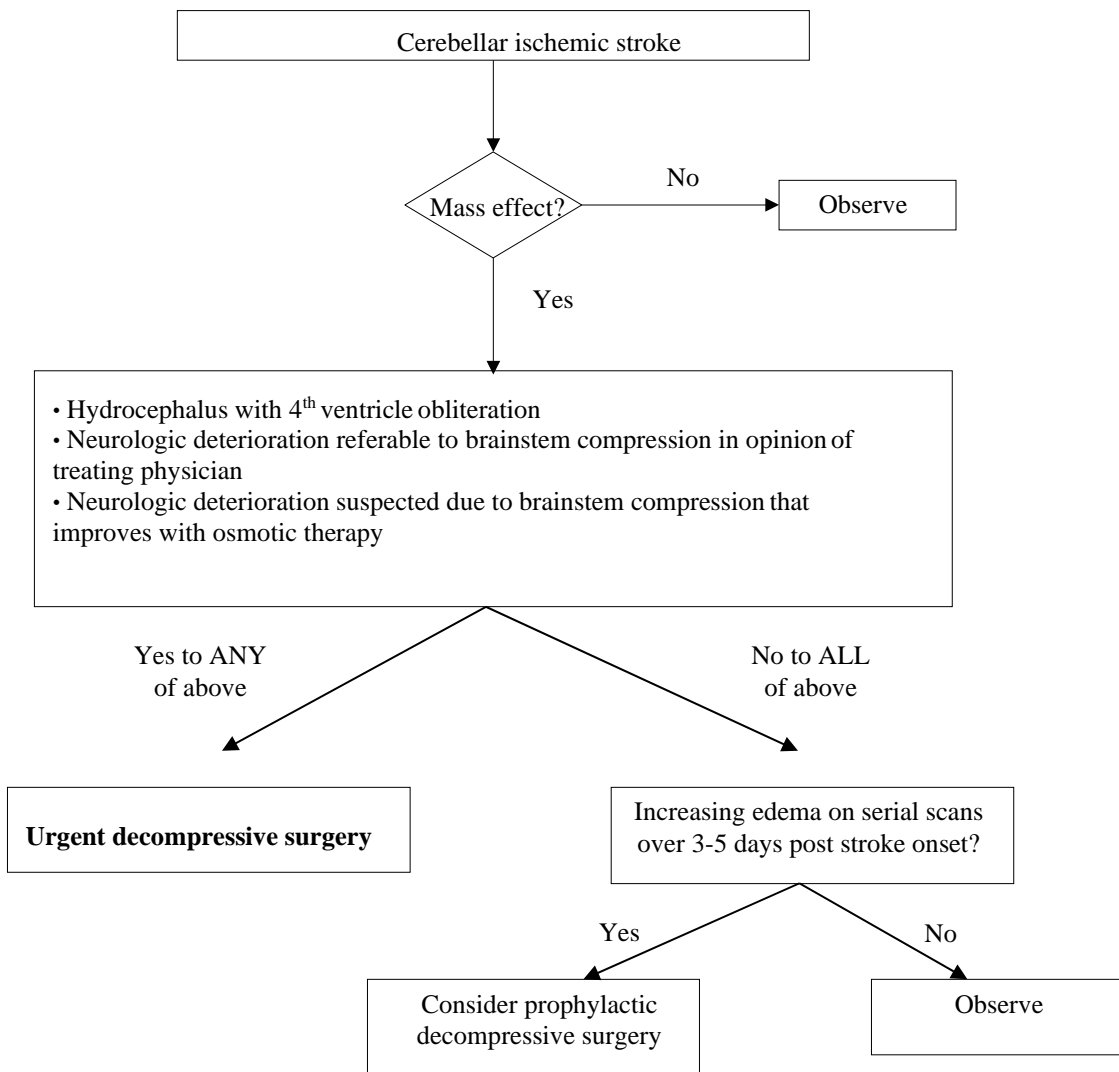
Results of randomized trials evaluating decompressive hemicraniectomy:



Important points when talking to families:

- Decompressive hemicraniectomy is life saving
- A significant proportion of patients who get DHC and survive have Modified Rankin Scales (MRS) of 3 or better (able to walk without assistance)
- However, a significant proportion of patients who get DHC and survive have MRS of 4 or worse (unable to walk, dependent on others for assistance with bodily needs)
- Left versus right hemispheric stroke does not impact outcome

Protocol for cerebellar stroke/posterior fossa syndrome



Notes:

- Above applies only to patients who are suitable candidates for surgery
- Involvement of vermis is associated with increased risk of neurologic deterioration and should lower threshold for surgery
- For uncomplicated cases, single anti-platelet therapy or IV heparin may be started 3 days post-op if there is a strong clinical indication

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Secondary Stroke Prevention

- Antiplatelet agent
 - ASA 81-325 mg or Plavix 75mg daily as soon as it is safe
 - ASA and Plavix ONLY if patient has acute coronary syndrome (CURE) or has just been stented.
- Statin
 - Preferably Lipitor 80 mg daily or simvastatin 40 mg daily if total cholesterol > 135 (Heart Protection Study, 2004)
- ACE-inhibitor (i.e. ramipril) or ARB
 - Within 1-2 weeks after D/C (HOPE, PROGRESS, LIFE)
- Hypertension:
 - Patients with flow dependent lesions may need higher BP acutely
 - Chronically hypertensive patients may have a shifted cerebral autoregulation curve and rapid lowering > 25% may compromise cerebral perfusion
- Long-term anticoagulation:
 - For A fib, EF < 30%, or cardiac thrombus, hypercoagulable state, mechanical valve in the setting of acute ischemic stroke (multiple refs).
 - No good data exist about when to start--our practice is generally to start ASA within 48 hours, and warfarin in 1-2 weeks.
 - No benefit to warfarin over aspirin for symptomatic intracranial stenosis (WASID, 2005).
- Carotid endarterectomy or stent:
 - Remember, even lacunes may be due to emboli (20%), so rule out carotid disease.
 - Consider CEA in >70% stenosis & +/- 50-69% (NASCET, 1997).
 - Symptomatic patients with poor surgical risk patients benefit from carotid stenting (SAPPHIRE), but more widespread use is not yet established.
- Intracranial stenting and interventional neuroradiology:
 - Limited evidence, but option for patients with multiple events due to symptomatic stenoses > 50% despite medical therapy.
- Intracranial hemorrhages:
 - If ICH, no antiplatelet/anticoagulant therapy x 3 months in general.
 - If ICH in the face of atrial fibrillation/ cardiac thrombus, can try ASA in 2 weeks, reconsider warfarin in a month after deep ICH if BP controlled, and monitor VERY closely.
 - Do not resume anticoagulation in amyloid angiopathy or most lobar ICHs.
- PFO and IASA
 - About 25% of people have PFOs.
 - Ensure there is no other source for a stroke before attributing it to the PFO. Get a complete hypercoag workup.
 - Recent studies show long term outcomes support PFO closure in cryptogenic stroke in patients < 60 yo (RESPECT, CLOSE, REDUCE studies)
 - There are no FDA approved PFO closure devices although cardiologists will close them with devices approved for other purposes. The decision is largely a matter of personal preference for the patient. Offer them enrollment in a trial if appropriate.
- Atrial flutter vs. fib:
 - Some cardiac studies suggest that patients in atrial flutter may be going in and out of atrial fibrillation.
 - Consider outpatient Holter monitor if suspicion of AF.
 - CHADS2VAS2C scoring system
- Glucose:
 - Screen for diabetes with fasting glucose, HbA1c
- Smoking cessation:
 - Screen and counsel on smoking cessation
 - Consider nicotine replacement products

Stroke Syndromes

Eponym/artery	Anatomy	Signs and symptoms
ACA	Medial frontal and parietal	Contralateral leg > arm weakness Abulia
Recurrent artery of Huebner (A branch off A1 segment)	Anteroinferior caudate Putamen Anterior limb of internal capsule	Contralateral face weakness (Huebner) Contralateral leg weakness (A1 segment)
MCA - Superior M2 (anterior)		Face and arm > leg weakness / numbness Expressive aphasia (dominant, Broca's) Hemineglect (nondominant)
MCA - Inferior M2 (posterior)		Homonymous hemi / upper quadrantanopsia Receptive aphasia (dominant Wernicke's) Constructional apraxia (non-dominant)
Gerstmann syndrome (Partial MCA)	Dominant inferior parietal lobe (angular gyrus)	Alexia / agraphia Finger agnosia R-L confusion Acalculia
Unilateral PCA	Occipital and infero-medial temporal lobes, posterior thalamus	Homonymous hemianopsia with macular sparing +/- alexia without agraphia / anomia
Balint syndrome (bilateral PCA)	Bilateral parieto-occipital lobe	Optic ataxia Ocular apraxia Simultanagnosia
PCA Callosal branch	Dominant occipital lobe with splenium of corpus callosum	Alexia without agraphia, or "pure word blindness"
Dejerine-Roussy or "thalamic pain syndrome" (PCA branches)	Thalamus	Contralateral hemisensory loss Contralateral hemibody pain
Weber (PCA penetrators)	Midbrain, anterior	Contralateral weakness, ipsilateral CN III palsy
Claude (PCA penetrators)	Midbrain, tegmentum	Contralateral rubral tremor, ipsilateral CN III palsy +/- contralateral weakness and numbness
Benedikt (PCA penetrators)	Midbrain, tegmentum	Contralateral rubral tremor, ipsilateral CN III palsy, ipsilateral ataxia, contralateral hemisensory loss
Raymond (basilar paramedian branches)	Pons, ventral-medial	Ipsilateral CN VI (saves CN VII) Contralateral weakness
Millard-Gruber (basilar short and paramedian branches)	Pons, basis pontis and VI and VII fascicles	Ipsilateral CN VI and VII palsies Contralateral weakness
Foville (basilar shorts and paramedian branches)	Pons, tegmentum and caudal third	Ipsilateral VI / PPRF (gaze) and VII palsies Contralateral weakness and sensory loss (ML)
Marie-Foix (basilar/AICA)	Pons / lateral	Ipsilateral ataxia, contralateral weakness and numbness
Locked-in syndrome (basilar) "de- efferented state"	Bilateral ventral pons	Bilateral face/arm/leg weakness Bilateral VI palsies Aphonia
Wallenberg of lateral medullary syndrome (vertebral artery > PICA)	Medulla, lateral	Ipsilateral facial sensory loss (CN V) Ipsilateral ataxia, nystagmus, N/V Vertigo, hoarseness, dysphagia Ipsilateral Homer's, contralateral body sensory loss
Anterior spinal artery (Dejerine syndrome)	Medulla, medial	Contralateral weakness Contralateral vibration/proprioceptive loss (ML) Ipsilateral tongue deviation (CN XII nucleus)

PRIMARY INTRACEREBRAL HEMORRHAGE

Despite aggressive efforts, mortality from ICH is high. Scoring systems have been devised to calculate in-hospital mortality risk and functional outcome based on patient age, initial neurologic examination, hematoma size and site of bleeding (see appendix). It is, however, important to use these scores judiciously when making treatment decisions, since they can provide a “self-fulfilling prophecy”.

Most ICHs are secondary to **hypertension**. These tend to be in deeper structures (thalamus, basal ganglia, brainstem, cerebellum). The (distant) second most common cause in the elderly is secondary to **cerebral amyloid angiopathy**. Amyloid bleeds tend to be superficial and lobar.

Don't forget other potential causes:

- Iatrogenic secondary to systemic anticoagulation
- Hemorrhagic conversion of an ischemic infarct
- AVM or aneurysm rupture
- Trauma
- Cerebral Venous Sinus Thrombosis
- Vasculitis
- Cavernous Malformations
- Hemorrhagic Metastases/Primary Tumor
- Infection/endocarditis

The principles of ICH management involve:

- management of intracranial pressure (ICP) and cerebral perfusion pressure (CPP)
- correction of underlying coagulopathies that may exacerbate bleeding
- aggressive blood pressure control to limit hematoma expansion
- prevention of other medical complications

General Approach to ICH Management

- CT scan shows acute blood: is it in a pattern that suggests a **hypertensive hemorrhage** or **amyloid hemorrhage**, or something else atypical?
- Consider CTA to look for underlying vascular malformation and for “spot sign”
 - The “spot sign” is a bright spot within the hematoma on contrast enhanced CT angiography
 - It suggests active bleeding and is strongly associated with hematoma expansion
- Are there any correctable coagulopathies? (Also refer to reversal guidelines on page 82)
 - **Aspirin** – no clear benefit from platelet transfusion (Sansing et al., Neurology 72:1397, 2009). Do not transfuse platelets.
 - **Plavix** – unclear if platelet transfusion beneficial. Do not transfuse platelets.
 - **Warfarin** – For ICH or life threatening hemorrhage with elevated INR consider **activated Prothrombin Complex Concentrate (PCC)**. First dose can be given without hematology approval (**50 units/kg**). Also give intravenous **10 mg vitamin K stat**. (Watch for anaphylactoid reaction) FFP is a lot of volume and takes time to thaw.
 - **Heparin** – follow PTT and correct with **protamine sulfate**. Dose for protamine is **1 mg** for every **100 units** unfractionated heparin given in the last 2 hours. Dose

changes depending on when heparin infusion stopped. Pharmacy can help you calculate the dose (maximum = 50mg).

- **Low Molecular Weight Heparin (e.g. enoxaparin, dalteparin)** – cannot follow PTT effectively but can use protamine for partial reversal. Pharmacy will help you calculate the dose (1mg per 100 anti-Xa units).
- **Dabigatran and newer oral direct thrombin inhibitors (e.g. rivaroxaban, apixaban).** PTT can be elevated, but not always. SEE REVERSAL PROTOCOLS BELOW.
- **tPA** – reverse with 2 bags cryoprecipitate (5 units/bag), thawed plasma (2 units – must call blood bank) and platelets (2 doses to start). Follow fibrinogen q6 hr
- **Uremic Platelet Dysfunction** – Can give one time **desmopressin (ddAVP)** (0.3 - 0.4 ug/kg IV bolus) and **conjugated estrogens** (0.6 mg/kg IV slow bolus over 30 min daily X 5 days). Hemodialysis is definitive treatment. (Nat Clin Pract Nephrology, 3:138, 2007)
- Note: **Recombinant Factor VIIa limits hematoma expansion but should not be used due to increased thrombotic complications!** (Mayer et al., NEJM, 358:2127, 2008)
- Keep platelet count greater than 50,000 or >100K if neurosurgical candidate.
- Aggressive blood pressure control – target systolic < 160, MAP < 110 at least, lower BP target if patient has lower baseline BP. Use **labetalol** IV bolus (10-20 mg) first and then **nicardipine** infusion if needed. Avoid nitroprusside and nitroglycerin as these can increase ICP due to prominent venodilation
- Consider surgical evacuation for large superficial lobar hemorrhage. STICH I and II trials give evidence that earlier intervention may be life-saving especially in those who are clinically declining.
- Place EVD if evidence for early hydrocephalus
- If prominent intraventricular hemorrhage, consider **Intraventricular tPA**. This should be a discussion with attending, pharmacy, neurosurgery, etc., since this is still investigational. Data for this extends from MISTIE and CLEAR-IVH trials. Consider if prominent intraventricular hemorrhage with intraparenchymal hematoma < 30 cc, and patient has existing EVD for treatment of hydrocephalus. Current protocol at HUP:
 - 1 mg tPA followed by saline flush into EVD
 - Clamp EVD for 1 hour
 - Open EVD at 0 cm above tragus, can repeat every 12 hours until resolution of clot for 5 days
 - Get CT scan 8 hours after each tPA treatment

Anticoagulant Reversal Guidelines

All guidelines can be assessed from Penn Medicine Formulary link in the Upenn homepage

Dabigatran (Pradaxa)

- Hold dabigatran dosing
- Assess nature and severity of hemorrhage; timing and dose of last taken; assess need for surgery to control bleeding; presence or absence of dialysis access
- Collect aPTT, thrombin time (TT), PT, dilute thrombin time (dTT), fibrinogen, CBC, serum Cr, LFTs
- The presence of severe bleeding is the primary determinant of therapeutic intervention
 - The aPTT, when prolonged, tends to predict residual dabigatran effect well
 - Thrombin time (TT) is highly sensitive to Pradaxa. A normal TT level rules out clinically significant drug level.
- In mild to moderate bleeding, use general measures to control bleeding. Follow renal function closely
- Fresh frozen plasma (FFP) should not be used
- Activated charcoal can be used (12.5g x1) if ingestion was within 2h
- **Praxbind (idarucizumab) 5mg IV (2 infusions of 2.5g IV within 15 minutes of each other)** is the preferred first reversal agent and does not need Hematology approval for severe or life threatening bleeding
- **In severe bleeding, hemodialysis should be considered. Consult renal fellow for hemodialysis**
 - If bleeding persists in spite of multiple doses of Praxbind, consider hemodialysis
- Hematology consult is required for multiple doses of Praxbind
- Do not give Activated Prothrombin Complex Concentrate (APCC - FEIBA), rFVIIa (Factor VIIa-NovoSeven RT), or Prothrombin Complex Concentrate (PCC – Kcentra)

Anti Xa drugs: Rivaroxaban (Xarelto), and Apixaban (Eliquis)

- Hold Factor Xa inhibitor
- Assess nature and severity of hemorrhage; timing and dose of last taken; need for surgery to control bleeding
- Collect PT, INR, Anti-Xa level, aPTT, fibrinogen, CBC, serum Cr, LFTs
- A prolonged PT/INR may suggest residual Factor Xa inhibitor effect
- Normal anti-Xa assay rules out significant anti-Xa drug levels. Anti-Xa levels are available at HUP weekdays from 8:00 am to 4:00 pm. Contact hematology for guidance
- Activated oral charcoal (12.5g x1) can be used if drug was ingested within 2 hours
- Reversal of anti-coagulation has increased risk for thrombosis; always balance risk-benefit ratio
- Andexanet alfa (Andexxa) is the preferred agent for patients on rivaroxaban or apixaban with intracranial or immediate life-threatening or limb/organ-threatening bleeding
- Prothrombin Complex Concentrate (PCC-Kcentra) (50U/kg x1) is an alternative agent that may be used for Factor Xa inhibitor reversal in patients who do not meet criteria for Andexanet alfa.
- Fresh frozen plasma (FFP) should not be used
- Hematology consult required for Activated Prothrombin Complex Concentrate (APCC- FEIBA), rFVIIa (Factor VIIa-NovoSeven RT), or subsequent doses of PCC and should be considered only if bleeding persist after first dose of PCC
 - aPCC dosing: 50-100 U/kg x1
 - rFVIIa dosing 20-40 mcg/kg or weight-based (2 mg if weight <100kg, 4 mg if >100kg) x1

Antithrombotic	Reversal agent
Vitamin K antagonists for urgent surgery or other invasive procedures	<p>If INR >1.5, no signs of bleeding and reversal required in >24h: Vit K 2.5-5 mg PO or, 0.5-1mg IV</p> <p>If INR >1.5, no signs of bleeding and reversal required in <24h: Vit K 2.5-5 PO or 0.5-1 mg IV PLUS FFP and/or 4F-PCC</p>
Direct factor Xa inhibitors (andexanet alfa -Andexxa)	<p>Activated charcoal (50 g) within 2 h of ingestion, For andexanet alfa: If last dose (<5 mg of apixaban) less than 8 hours or unknown: 400mg, then 4mg/min x120min If last dose (>5 mg/unknown of apixaban) less than 8 hours or unknown: 800mg, then 8mg/min x120min If last dose (<10 mg of rivaroxaban) less than 8 hours or unknown: 400mg, then 4 mg/min x120min If last dose (>10 mg of rivaroxaban) less than 8 hours or unknown: 800mg, then 8mg/min x120min</p>
Direct thrombin inhibitors	<p>For dabigatran reversal: Activated charcoal (12.5 g x1) if within 2 h of ingestion Idarucizumab 5 g IV (2 infusions of 2.5 g within 15 minutes) Consider hemodialysis for refractory bleeding after repeated infusions For other DTIs: Activated PCC (FEIBA) 50 units/kg IV OR 4 factor PCC 50 units/kg IV</p>
Unfractionated heparin	<p>Protamine 1 mg IV for every 100 units of heparin administered in the previous 2–3 h (up to 50 mg in a single dose)</p>
Low-molecular weight heparins	<p>Enoxaparin: Dosed within 8 h: Protamine 1 mg IV per 1 mg enoxaparin (up to 50 mg in a single dose) Dosed within 8–12 h: Protamine 0.5 mg IV per 1 mg enoxaparin (up to 50 mg in a single dose) Minimal utility in reversal >12 h from dosing Dalteparin, Nadroparin and Tinzaparin: Dosed within 3–5 half-lives of LMWH: Protamine 1 mg IV per 100 anti-Xa units of LMWH (up to 50 mg in a single dose) OR rFVIIa 90 mcg/kg IV if protamine is contraindicated</p>
Danaparoid	<p>rFVIIa 90 mcg/kg IV</p>
Pentasaccharides	<p>Activated PCC (FEIBA) 20 units/kg IV or rFVIIa 90 mcg/kg IV</p>
Thrombolytic agents (plasminogen activators)	<p>Cryoprecipitate 10 units IV OR Antifibrinolytics (tranexamic acid 10–15 mg/kg IV over 20 min or e-aminocaproic acid 4–5 g IV) if cryoprecipitate is contraindicated</p>
Antiplatelet agents	<p>DDAVP 0.4 mcg/kg IV 9 1 If neurosurgical intervention: Platelet transfusion (one apheresis unit)</p>

ANEURYSMAL SUBARACHNOID HEMORRHAGE

I. INTRODUCTION:

Subarachnoid hemorrhage (SAH) is a disorder where bleeding occurs between the arachnoid membrane (the middle membrane covering the brain) and the brain itself, with bleeding onto the surface of the brain. This is usually caused by a “weak spot” in a blood vessel, also known as an aneurysm. Twenty percent of individuals affected have multiple aneurysms. Subarachnoid hemorrhages can also be non-aneurysmal in cause. Examples of this would be a traumatic SAH, rupture of an AVM, or other unidentified causes. The following guidelines address management of aneurysmal subarachnoid hemorrhage

II. RISK FACTORS FOR ANEURYSMAL SAH

- Hypertension
- Cigarette Smoking (greatest risk occurring 3 hours after smoking)
- Binge alcohol drinking
- Drug abuse
- Use of stimulants
- Gender: Incidence is greater in females than in males
- Age (range 20-65; mean age 50; most common between 35-60)
- Disorders associated with weakened blood vessels:⁵⁵
 - Fibromuscular dysplasia (FMD)
 - Aneurysms in other blood vessels
 - Polycystic kidney disease
 - Ehler-Danlos syndrome
 - Marfan’s syndrome
 - Alfa-one antitrypsin deficiency

III. PRIOR TO SECURING THE ANEURYSM (Surgical Clip/Neurovascular Coil):

Admission labs, tests and procedures

- Admit to the NeuroICU
- Assess Hunt and Hess Scale⁵⁷ (Clinical Grade) and Fisher Grade⁵⁵ (CT Grade) (See Appendix A)
- Obtain routine labs, including:
- BMP, Ca²⁺, Mg²⁺, PO₄⁻², CBC, PT, INR, PTT, serial troponins, type and screen
- Obtain the following studies:
 - 12-lead EKG, portable chest X-ray, non-contrast head CT, CT angiogram (CTA; unless contraindicated due to allergy or renal dysfunction)
- Alert research coordinator to determine eligibility for clinical studies

Neurologic

- Place EVD immediately in all patients with hydrocephalus that is symptomatic or have GCS <8.
 - EVD is left open, at 20 cm above the tragus (EAM) as a start and then adjusted as dictated by ventricular size on HCT or clinical status. The level of

the EVD should generally not be lowered prior to securing of the aneurysm as this may predispose to rebleeding.

- Start seizure prophylaxis
 - Leviteracitam load: 1000mg PO/IV on admission
 - Leviteracitam 500 mg PO/IV q12 hrs x 7 days for seizure prophylaxis
 - If evidence of renal dysfunction, dose accordingly
 - It is preferable to administer leviteracitam orally or enterally when able
 - Discontinue AED POD #7 if there have been no clinical or electrographic seizures
- Anti-Fibrinolytics
 - Consider in patients who cannot be secured in < 24 hours

Cardiovascular

- Place Arterial line in all patients
- Maintain SBP within 10% of baseline SBP if known. If baseline SBP cannot be determined, then maintain SBP < 160 mm Hg.
 - If SBP > 160 mmHg, optimize analgesia and treat with IV anti-hypertensives
 - Titratable anti-hypertensives (drips) are favored to control blood pressure to avoid large blood pressure fluctuations.
- Start nimodipine 60 mg PO/NGT q4hrs. If BP drops after administration, then decrease nimodipine dose to 30 mg q2hrs.
- Statins
 - Statins taken as home medications should be continued upon admission for SAH.
- Vascular access
 - Place a triple lumen subclavian or IJ venous catheter in selected patients.
 - Avoid IJ if evidence of severe intracranial hypertension exists or patient is felt to be at high risk for developing intracranial hypertension.
 - Indications for central line placement:
 - High grade patient (HH \geq 3)
 - Hemodynamic instability
 - Need for vesicant medications (sedation or vasopressors)
 - Venous access difficulty
- Obtain a transthoracic echocardiogram when:
 - Unexplained hypotension
 - Ischemia or ST changes are present on EKG
 - Response to vasopressor medications is suboptimal
 - Initial cardiac enzymes are abnormal

Renal (Fluids and Electrolytes)

- Goal is to maintain euvoemia.
 - Hypotonic IVF should be avoided.
- Maintain Na⁺ within normal range.
- Maintain Mg⁺² within normal range.

Endocrine (Glycemic Control)

- Blood glucose monitoring and sliding scale insulin q4 hrs in all patients
- Target glycemic threshold <200mg/dL.
- Start insulin infusion per HUP Insulin Infusion protocol in patients with serum glucose >200mg/dL x 2 on SSI coverage

Prophylaxis

- Stress ulcer prophylaxis with either H2 blocker or PPI
- Venous thromboembolism prophylaxis
 - Pneumatic compression boots upon admission
 - Prophylactic dose anticoagulation should be withheld until after the aneurysm is secured due to risks of re-rupture. After craniotomy, anticoagulants can be started 24h after the procedure.
- Alcohol abuse/withdrawal
 - Thiamine, folate, MVI in patients with alcohol abuse history/concern
 - For patients who exhibit sign/symptoms of withdrawal, or who have a history of alcohol withdrawal, consider starting a taper of long-acting benzodiazepines.

Other issues

- Analgesia
 - Pain should be controlled with lowest effective dose of IV or PO medications that do not limit clinical neurological examination. Overly sedating medications should be avoided.
- Anti-emetics
 - Anti-emetics that are unlikely to cause sedation or have CNS side effects are preferred (ie: ondansetron, trimethobenzamide) if necessary

IV. ANEURYSM OCCLUSION:

There are two main methods for obliterating aneurysms: surgical clipping and endovascular coiling. The feasibility of both methods is assessed and a collaborative decision between neurosurgery and interventional neuroradiology is made to determine optimal treatment based on aneurysm morphology and patient characteristics.⁵⁵ Certain aneurysms are better suited to one technique or another. Endovascular treatment is often the preferred technique for posterior circulation aneurysms and ruptured aneurysms in elderly patients (>70 years of age) given higher surgical risks. Aneurysms in the middle cerebral artery, ruptured aneurysms with large intraparenchymal hematomas are commonly approached surgically. Combined endovascular and surgical techniques may be required for some very large or complex aneurysms. The advent of Guglielmi platinum detachable coils (GDC)³⁰ in the 1990s introduced endovascular therapy for cerebral aneurysms. Alternative methods for obliterating the aneurysmal sac include stent-assisted coiling, balloon-assisted coiling, flow diverters and embolic agents.

The optimal timing of surgery is unclear. The International Cooperative Study on the Timing of Aneurysm Surgery^{31, 32} demonstrated that although pre-operative re-bleeding rates were lower with early surgery, timing of surgery had no effect on overall outcome.

Early surgery (1 – 3 days post SAH) has become common practice, in part because it is associated with lower rates of re-bleeding and allows for more aggressive treatment of vasospasm.

- Attempts are made to obliterate the aneurysm within 3 days of SAH, either by endovascular or open surgical techniques.

V. POST ANEURYSM OCCLUSION MANAGEMENT:

Neurologic

- Intracranial Hypertension
 - Maintain ICP < 20 mmHg, CPP \geq 60 mmHg (see *NeuroICU Protocol*).
- Vasospasm detection
 - Continuous EEG monitoring:
 - Consider monitoring in patients with Fisher Grade III SAH and/or GCS \leq 8 with cEEG.
 - In all other patients, consider cEEG to detect early ischemic changes. In awake patients, changes in alpha variability can be used to trigger a trial of hypertensive therapy (see below) followed by vascular imaging with a CTA or conventional angiogram (see *cEEG Protocol*).
 - TCD monitoring:
 - Obtain daily TCD. This must include MCA velocity/extracranial ICA velocity (Lindgaard ratio). See appendix B for interpretation.
 - Algorithm for approach to TCD and clinical examination data: See appendix C
- Treatment of Vasospasm or DCI
 - Triggers for treatment:
 - TCD elevation (Lindgaard ratio >3)
 - Clinical exam change (DCI)
 - Clinical concern for vasospasm or DCI should be followed by immediate diagnostic testing with imaging. Previous studies on hypervolemic therapy have failed to show any benefit.
 - Minimize risk of volume overload and avoid hypovolemia
 - Prophylactic therapy with hypervolemia, hemodilution is no longer recommended
 - Induced hypertension continues to remain effective in increasing cerebral blood flow; the loss of innate autoregulation during vasospasm makes cerebral perfusion pressure more dependent on systemic blood pressure
 - This strategy is not recommended for prophylaxis but during vasospasm to reduce the risk of ischemia in patients developing vasospasm
 - Use of norepinephrine, dopamine and phenylephrine have all been shown to be beneficial in improving neurological outcome
 - If nimodipine administration results in hypotension, dosing intervals should be changed to more frequent, lower doses.

- Vascular imaging with a CTA should be performed when clinically feasible.
 - CTA should be obtained in all patients with suspected vasospasm who do not have contraindications to the procedure.
 - If CTA is indeterminate or shows evidence of vasospasm, proceed to cerebral angiography.
 - Perfusion imaging may be considered in appropriate patients.
- Advanced cerebral monitors (Licox, microdialysis, etc...) may be considered on a case-by-case basis.

Cardiovascular

- For patients undergoing craniotomy for aneurysm coiling, SBP should be maintained ≤ 160 mmHg for 24 hours after surgery to minimize risk of postoperative bleeding. Thereafter, SBP parameters should be liberalized to 100 – 200 mmHg.
- In aneurysms that are endovascularly coiled, blood pressures can be liberalized to 100-200 mmHg immediately post-procedure.
- A higher blood pressure may be needed to achieve adequate regional brain perfusion and these parameters may be adjusted in individual patients (refer to treatment of vasospasm/DCI above).
- The presence of other, unruptured aneurysms should not influence hemodynamic management.
- Target euvolemia with administration of isotonic or hypertonic IVF as needed.

Fluid and Electrolyte Management

- Maintain $\text{Na}^+ \geq 135$ mmol/L (see *CSW Protocol*).
- Treat hyponatremia with IV normal saline and oral salt tabs.
- For refractory cases, consider the use of fludrocortisone 0.3mg/day or hypertonic saline bolus/infusion to raise serum Na to the target range.
- Maintain Mg^{+2} within normal range

Endocrine (Glycemic Control)

- Blood glucose monitoring and sliding scale insulin q4 hrs in all patients
- Target glycemic threshold <200 mg/dL.
- Start insulin infusion per HUP Insulin Infusion protocol in patients with serum glucose >200 mg/dL x 2 on SSI coverage

Temperature Control

- Maintain strict normothermia (see *Normothermia Protocol*).

Nutrition

Early enteral nutrition benefits critically-ill patients.⁵³ In the neurologically injured patients, continuous enteral feeding via small bore tube or NGT/OGT is safe.⁵⁴

- Continuous enteral feeding should begin on POD #1 (see *NeuroICU Feeding Protocol*).
- TPN should only be considered in patients who have contraindications or intolerance to enteral feedings.

Prophylaxis

- See above recommendations for GI and DVT prophylaxis.
- Subcutaneous heparin 5000U TID should be added on POD #1.

VII. TRANSFER/DISCHARGE PLAN:

- Low grade (I-II) patient criteria to transfer out of NeuroICU
 - Day 10 if no evidence of vasospasm for 48hrs
- High grade (III-V) patient criteria to transfer out of NeuroICU
 - Day 14 and no evidence of vasospasm for 48hrs.
- Nimodipine stop after 21 days, not discharged on nimodipine.
- Acute brain injury rehab

Approach to TCD and clinical examination data

EXAM	TCD	ACTION
Normal	Normal	None
Normal	Abnormal	CTA, Perfusion scan
Deteriorating	Normal	Hypertensive rx, CTA, Perfusion scan
Deteriorating	Abnormal	Hypertensive rx, Angiogram
Comatose	Normal	Consider surveillance CTA, cEEG
Comatose	Abnormal	Non-contrast CT, Angiogram Consider cEEG

Risk factors associated with or predictive of vasospasm⁵⁵

Younger age	IVH on admission CT	Dehydration
Cigarette smoking	Hydrocephalus	Hypotension
Poor admission clinical grade	Hyponatremia	Hypoxia
Admission systolic blood pressure	Anti-fibrinolytic agents	Fever
Thick or diffuse SAH on admission CT	Increased ICP	

Intraventricular Nicardipine for SAH associated vasospasm

Cerebral vasospasm remains a major cause of morbidity and mortality after SAH. Several reports suggest that administration of nicardipine intrathecally is both safe and efficacious for this condition.

Indications

- Aneurysmal subarachnoid hemorrhage
- Documented morphologic evidence of severe cerebral vasospasm
 - Computed tomographic angiogram
 - Conventional angiogram
- Patient already undergoing standard vasospasm treatment including nimodipine, seizure prophylaxis, statins, ventriculostomy, and HHH (hypertension, hypervolemia, hemodilution) therapy. Patients may or may not have already undergone intra arterial nimodipine or angioplasty prior to this therapy.
- Agreement by both neurocritical care and neurosurgery attendings that the vasospasm is severe with no disqualifying contraindications with agreement to proceed. Suggested additional functional criteria for “severe” spasm:
 - Cerebral blood flow decrements on computed tomographic perfusion study or stable xenon computed tomographic cerebral blood flow evaluation , OR
 - Bedside signs or symptoms such as altered exam, brain hypoxia

Contraindications

- Absolute
 - Allergy to nicardipine
 - No ventriculostomy
- Relative, ie, the treating physician must weigh potential benefits vs possible harm
 - Unsecured aneurysm thought responsible for the subarachnoid hemorrhage
 - Elevated intracranial pressure
 - Central nervous system infection
 - Immunosuppressed
 - Intraventricular hemorrhage with compromised ventriculostomy function

Administration

- Dose: Twice daily, 4 mg nicardipine in 2 ml preservative free saline followed by 2 ml preservative free saline flush. Withdraw 4 ml of cerebrospinal fluid before injection (send daily for analysis).
- Sterile technique including chlorhexidine skin preparation, mask, hat, sterile gloves. Sterile drape under the chlorhexidine treated stopcock and tubing
- Clamp ventriculostomy for 1 hour after injection
- Administer for five days. Stop for at least one dose. Reevaluate after therapy cessation for recurrence of original indications. If reevaluation results in need to continue then do so

for serial three-day periods, with cessation and evaluation for continuation at the end of each such therapeutic epoch

- Drug can only be administered by neurosurgery or neurocritical care physician or neurocritical care certified registered nurse practitioner in the NeuroIntensive Care Unit and limited to appropriate patients on the Neurosurgical service.

Monitoring

- Intracranial pressure continuously during post injection clamp period
- Intracranial pressure hourly
- Cerebrospinal fluid output hourly
- If in place, PbO₂, with specific attention to changes in PbO₂ trend.
- Daily transcranial Doppler ultrasonography
- Repeat of the studies justifying the therapy (computed tomographic angiogram or conventional angiogram and flow study or clinical signs) on day 2 of therapy, and then, to evaluate for continuation, on day 5 and every three days until therapy stopped.
- Consider computed tomographic perfusion study or stable xenon computed tomographic cerebral blood flow evaluation before, during, and after therapy to document flow effects
- Daily cerebrospinal fluid white blood cell count, glucose, protein from cerebrospinal fluid withdrawn for daily nicardipine injection

Potential Side Effects and Their Management

- Cerebral hyperemia. Manifest as post injection rising intracranial pressure and brain tissue PO₂. Suggested treatment: decrease any pressors, hyperventilate, drain cerebrospinal fluid, intracranial hypertension treatment protocol. Consider cessation of nicardipine therapy, risk vs benefit analysis
- Meningitis: May be chemical vs infectious. Apply standard of care. Consider cessation of nicardipine therapy, risk vs benefit analysis.

Antifibrinolytic Therapy to Prevent Aneurysm Re-bleeding

Recurrence of bleeding after SAH is a major cause of morbidity and mortality, affecting 25 to 40% of patients in the first 3 to 4 days after their initial bleeding event. Two thirds of these recurrent hemorrhages are fatal. Thus, prompt repair and securing of a ruptured aneurysm is a cornerstone of management of aneurysmal SAH. Usually, aneurysm repair (either endovascular or open) is performed within the first 24 hours of rupture; however, there are instances where repair may have to be delayed. In these instances, consider using **antifibrinolytic therapy** (e.g. ϵ -aminocaproic acid or tranexamic acid) as a procoagulant to prevent short term re-bleeding. ***Antifibrinolytic therapy increases the risk of thrombotic complications, however, this risk may be offset by the reduction in rebleeding rates.*** At HUP, ϵ -aminocaproic acid (EACA, AMICAR®) is used most often as an antifibrinolytic agent. The latest review from 2013 Cochrane Database Systemic Review shows no strong evidence for antifibrinolytic drugs in the treatment of people with aneurysmal subarachnoid hemorrhage, even in those who have treatment strategies to prevent cerebral ischemia. Discussion with Neurocritical care and neurosurgical team is warranted prior to considering this line of therapy.

PROTOCOL

(from Starke et al., Stroke, 39:2617, 2008)

- Order 4 g IV loading dose of EACA, followed by 1g/hr continuous IV infusion
- Can continue EACA infusion for 72 hours
- Stop EACA infusion 4 hours prior to angiography or surgical intervention
- Do not use in patients with evidence of active coronary ischemia, EKG changes, troponin elevations or evidence for thromboembolic disease

- In study cited, there was a 76% reduction in rebleeding rate
- DVT incidence increases 8-fold when using EACA, however, rate of PE does not seem to increase appreciably

PERIMESENCEPHALIC SUBARACHNOID HEMORRHAGE

Introduction

Spontaneous, non-traumatic subarachnoid hemorrhage (SAH) most commonly results from rupture of saccular aneurysms (**aneurysmal SAH; aSAH**). Less commonly, it results from rupture of arteriovenous malformations, arterial dissections, tumors, or other vascular abnormalities. In 10% to 20% of cases, no structural cause for the hemorrhage can be identified on radiographic imaging even after digital subtraction angiography (DSA), the gold standard for the detection of a cerebral aneurysm or other vascular source of the hemorrhage. These non-aneurysmal hemorrhages are termed idiopathic SAH or angiogram-negative SAH. Angiogram-negative SAH have been divided into 2 major groups:

Perimesencephalic hemorrhage (PM-SAH), which is strictly defined according to published criteria (see below); and

Non-perimesencephalic hemorrhage (nPM-SAH). The category of nPMH includes those SAH not fitting PMH criteria such as diffuse SAH, cortical SAH, CT negative SAH confirmed by lumbar puncture.

Definition of PM-SAH

The diagnosis of PM-SAH is a diagnosis of exclusion. The bleeding pattern defining PMH is identified on unenhanced CT performed within 24 hours of hemorrhage onset. The PM-SAH pattern is commonly defined using guidelines set out by Rinkel et al. and confirmed by others^{1,2}:

- 1) center of the hemorrhage located immediately anterior to the midbrain, with or without extension of blood to the anterior part of the ambient cistern or to the basal part of the Sylvian fissures;
- 2) no complete filling of the anterior interhemispheric fissure and no extension to the lateral Sylvian fissures, except for minute amounts of blood; and
- 3) absence of frank intraventricular hemorrhage

Thirty-eight percent of angiogram-negative SAH (range 21%-77%) have a PM-SAH pattern on their admission CT scan.

Management

- ****Manage as if they have aneurysmal SAH until definitive vascular imaging (DSA) is obtained**
 - Obtain routine labs
 - EKG, CXR, CT angiogram
 - EVD – if has hydrocephalus that is symptomatic or GCS < 8
 - EVD is left open at 20cm above tragus. Adjust as dictated by ventricular size. Generally not lowered until evaluation for aneurysm has been completed, as it can re-rupture the aneurysm
 - DSM – obtained within 24 hrs of admission
 - DSM must rule out aneurysm in order to diagnose as PM-SAH
- Neurologic
 - MRI brain/spine or MRA neck – consider in atypical clinical presentation and younger patients
 - Vasospasm detection – daily TCD monitoring
 - CT angiogram if has high concerns
 - Nimodipine – 60mg q4h or 30mg q2h
 - Not strong indication as aneurysmal SAH
 - Stop at discharge or at 14 days (whichever is sooner)
 - Seizure prophylaxis – discontinue after negative DSA testing
- Cardiovascular
 - SBP < 140 mmHg until negative DSA testing
 - If meets criteria for PM-SAH, can liberalize SBP goals to maintain normotension

- Fluid and electrolyte management
 - Maintain euvolemia
 - Goal Na > 135 mmol/L, Mg > 2
- Endocrine
 - Goal glucose 140 – 180 mg/dL
- Prophylaxis
 - Subcutaneous heparin 5000 unit TID added 24 hrs after presumed bleeding time
 - GI ppx not required if eating and drinking normally

- Patients should be monitored in the ICU until vascular imaging studies are completed and do not show evidence of an aneurysm.
- Once vascular studies are negative, patients may be discharged to the floor or INCU based on their nursing and monitoring requirements.
- All patients should be considered for evaluation by PT/OT.
- Patients require monitoring for hydrocephalus. The risk of hydrocephalus is highest in the first few days after bleeding; generally, most patients are stable for discharge by post-bleed day #7.
- When deemed stable by the treating team, patients may be discharged to home or other appropriate facility.

SEIZURES/STATUS EPILEPTICUS

CONVULSIVE STATUS EPILEPTICUS MANAGEMENT		
0-5 min	Airway management: O2 via nasal cannula or mask Assess oxygenation (o2 sats or ABG) Consider intubation at any point in protocol	
	Vital signs, EKG monitoring	
	Physical and neuro exams	
	IV access, normal saline drip	
	Blood for glucose, lytes, EtOH, AEDs, ABG, tox screen, CBC	
6-9 min	If hypoglycemic or no blood glucose available, administer glucose	
	Adults: 100 mg thiamine 50 ml of 50% glucose	
10 – 20 min	Administer benzodiazepine (if seizure continues)	
	Lorazepam 0.5 -0.2 mg/kg (rate 2 mg/min IV)	Diazepam 0.2 mg/kg (rate 5mg/min IV)
	May repeat if convulsion does not stop after 5-10 minutes- may need to intubate	
20 – 40 min	Levetiracetam (Keppra) 3 gram load x 1	
	Also refer to Penn's status epilepticus guidelines	
	If seizures continue, give Phenytoin 5-10 mg/kg	
40 – 60 min	Intubate patient or call anesthesiology to intubate	
	Midazolam 0.1 – 0.4 mg/kg IV bolus (0.05-1 mg/kg/hr maintenance)	Phenobarbital 20 mg/kg IV (Adults: rate >50 mg/min)
	Monitor BP	
	Consider EEG	
60 – 80 min	Propofol 1-2 mg/kg IV bolus Maintenance 1-15 mg/kg/hr NOT in children	Pentobarbital 5-20 mg/kg load (rate<25mg/min) Maintenance 0.5 – 1- mg/kg/hr
	Transfer to ICU	
	EEG	
	Neuro exam, CT/LP, repeat labs, make decision on chronic Rx	
80+ min	General Anesthesia	
After Status	Head CT	
	LP	
	Consider EEG if patient not returning to baseline mental status	

Seizure Evaluation

Initial questions

1) Is patient stable?

- Protecting airway (anticipate need for intubation), no longer seizing (anticipate risk for status epilepticus), vitals stable? Disposition (ICU vs Step Down vs Floor)

2) Is the person in status epilepticus? Treat immediately

- Follow protocol for generalized SE (emergent and proceed through steps quickly).
- If focal or NCSE, urgent treatment but not as emergent. Avoid anesthetic if possible, attempt control with IV benzodiazepines and AEDs.

3) What caused this?

- Infectious- recent illnesses, order CBC, UA, CXR, +/- LP
- Drugs- Illicit (UDS), Meds: i.e. antibiotics, tramadol, bupropion, medication non-compliance (AED levels)
- Electrolyte/metabolic abnormality: hyponatremia, hyper/hypoglycemia, hyperammonemia, uremia
- CNS- Stroke, Trauma- stat Non-contrast HCT

Initial Diagnostic Work Up for Status Epilepticus	
Labs	Fingerstick glucose: If glucose is low, administer thiamine 100 mg IV followed by 50 ml of D50. Complete blood count with differential, comprehensive metabolic panel (to include Mg, Ca, PO ₄ , hepatic panel), anti-seizure drug levels (if appropriate), blood gas, troponin, urinalysis, comprehensive toxicology screen (urine or blood), HCG (female of reproductive age), lactate
Imaging	STAT Head CT without contrast: as soon as patient is stabilized without clinical seizures. May not be indicated in patients with a history of epilepsy with a clear precipitant for seizure exacerbation (i.e. missed AED, systemic infection). MRI brain with and without contrast: in patients without a clear etiology or in whom EEG patterns are lie on the ictal-interictal continuum.
Lumbar Puncture	If there is any concern for infectious or inflammatory process, LP should be done following head imaging. Obtain for New-Onset refractory status epilepticus.

4) Does patient NEED cvEEG?

Indications for Continuous EEG	
Indication/Setting	Rationale
Recent Clinical Seizure without return to baseline <ul style="list-style-type: none"> Not purposeful on exam (i.e. not withdrawing or localizing to pain) Subtle motor findings (look for nystagmus, mild facial/extremity twitching) 	Convulsive seizures/SE can transition to non-convulsive seizures/NCSE after treatment in 20-50%.
Screening for Non-Convulsive Seizures (NCSz) or NCSE in at-risk patients <ul style="list-style-type: none"> History of epilepsy, acute brain injury (SAH, TBI, ICH), brain tumor, recent convulsive status epilepticus (CSE), fluctuating mental status, and paroxysmal events that are concerning for seizures, comatose patient, anoxic, intensive care unit (ICU) patient 	NCSz/NCSE are prevalent in the critically ill and need EEG to detect.
Monitoring and treatment of known non-convulsive seizures	Characterization and quantification of events to adjust treatment
Abnormal routine EEG <ul style="list-style-type: none"> Epileptiform discharges or Periodic discharges 	Higher risk of seizures
Loss of reliable exam in setting of clinical concerns above (i.e. comatose, anoxic) <ul style="list-style-type: none"> Patient on continuous anesthetic infusion (i.e for refractory SE) Paralytic 	Electro-clinical Dissociation, EEG will be the primary mean to detect seizures.

If Stable, obtain a good Seizure/Spells History

- Initial onset, type of epilepsy if known (generalized vs localized vs multifocal- prior MRI and EEG for localization), typical semiology of spell (aura/warning, description of event with specific body parts involved with duration, post-ictal confusion with duration, tongue biting and urinary incontinence, weakness)
- Frequency of events and last event.
- Current anti-epileptic medications and doses, ensure accuracy and compliance
- Heighten index of suspicion for alternate etiology than simply breakthrough if significant change in usual seizure character or frequency. (i.e. infectious, neoplastic/paraneoplastic, autoimmune)

CONTINUOUS EEG (LTM) GUIDELINES

1. LTM EEG requests only placed by the NICU fellow/attending or Neurology SAR/attending. Non-neurology or NICU services must contact Neurology consult team to request LTM (except for hypothermia hook-ups, which can only be requested from 7 am – 11 pm during the week and 7 am – 7 pm on weekends).
2. LTM reads via email at noon and 5 PM: EEG fellow will contact team with urgent reads, limit calls to EEG fellow
3. Process to obtain LTM:
 - a. Place order in EPIC (type in LTM or EEG, select continuous)
 - b. Send an email to EEGReaders@uphs.upenn.edu, with initials and MRN of the patient, and brief clinical history
4. AFTER HOURS LTM READING:
 - a. New hook up screened by tech (20 min) and fellow will contact team ONLY if there is a concerning finding.
 - b. TECH WILL EMAIL THE EEGREADERS email after every LTM hook-up.
 - c. ALL TECHNICAL ISSUES: should contact tech directly (not fellow)
 - d. Only patients in active STATUS EPILEPTICUS read after 5 pm (once at 9 pm, once 3 am if deemed necessary by the EEG fellow)
 - e. BURST SUPPRESSION: must be monitored by in-house team
 - f. Calls to the fellow:
 - i. Only from Neurology, NICU fellow or an attending (JAR must d/w SAR prior to call)
 - ii. No non-urgent calls (see criteria below regarding when to hook up a patient to LTM) LTM guidelines:
 - g. Criteria for requesting LTM after 5 PM
 - i. Transfer from an OSH for LTM and patient is comatose
 - ii. Convulsions cease but patient has no exam (concerning for nonconvulsive status epilepticus)
 - iii. multiple clinical events highly concerning for seizure (patient obtunded/comatose)
 - h. LTM requests INAPPROPRIATE after 5 PM:
 - i. hypothermia (goal: hook up patient within 12 hours)
 - ii. subarachnoid hemorrhage
 - iii. patients not in coma (e.g. neurological exam able to rule out status epilepticus)

GUIDELINE FOR USE OF KETAMINE FOR THE TREATMENT OF REFRACTORY STATUS EPILEPTICUS

UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM

BACKGROUND

Ketamine is a noncompetitive NMDA receptor antagonist with a unique mechanism of action that has shown to be effective in the treatment of status epilepticus (SE) when traditional GABAergic agents have failed.

Models of prolonged status epilepticus demonstrate a downregulation of functional GABA_A receptors, with simultaneous upregulated expression of NMDA receptors promoting the excitatory action of glutamate. This suggests that ketamine is a rational antiepileptic agent to be considered for use in later stages of SE, and explains the nature of development of pharmacoresistance to agents targeting the GABA receptor in refractory status epilepticus.

DEFINITIONS

1. Status epilepticus (SE)
 - a) Generalized convulsive seizure lasting > 5 minutes or 2 convulsive seizures without interim return to baseline mental status
 - b) For the purposes of this guideline, SE refers to the spectrum of this disease state as a whole, including refractory and super-refractory SE
2. Refractory status epilepticus (RSE)
 - a) Ongoing generalized seizures despite administration of a benzodiazepine (first-line therapy) and an additional IV AED (second-line therapy) at adequate doses
3. Super-refractory status epilepticus (SRSE)
 - a) Failure of one or more first-line continuous anesthetic agents (midazolam, propofol) to achieve seizure- or burst-suppression within 24 hours of initiation of the initial anesthetic agent
 - b) Alternatively, recurrence of seizures upon weaning of first-line anesthetic agents

INDICATIONS FOR USE

- Adjunctive therapy in patients with super-refractory status epilepticus (SRSE)*
- Ketamine may also be considered earlier (adjunctive therapy) in patients with dose-limiting side effects during treatment with midazolam or propofol (e.g., refractory hypotension requiring high dose vasopressor therapy)*

*CONCOMITANT USE WITH OTHER CONTINUOUS ANESTHETIC AGENTS

- Little data exists on the use of ketamine alone as a first-line or sole agent for the treatment of RSE/SRSE
 - No prospective data exists for use in adults (case reports/series only)
 - In most reports, ketamine was added adjunctively to other continuous anesthetic (GABAergic) agents (midazolam, propofol, pentobarbital)
- In the context of above indications for use of ketamine, it should be initiated for adjunctive use with other anesthetic agents already in place in order to achieve the goal of seizure- or burst-suppression

RESTRICTIONS

Use is restricted to patients undergoing continuous EEG monitoring in the Neuro ICU or other ICU with Neurology consultation

CONTRAINDICATIONS

Absolute:

- Absence of an established airway (e.g., mechanically ventilated)
- Patients with active or unstable cardiac or coronary disease (i.e., acute atrial or ventricular arrhythmias, STEMI/NSTEMI)

Relative:

- Severe or uncontrolled hypertension (SBP >200) or tachycardia (HR>120)
- History of tachyarrhythmias, distant, well controlled coronary artery disease (CAD, including: stable angina, prior myocardial infarction), or known severe right heart failure
 - Recommended to omit or use smaller loading doses in these patients
- Known or suspected schizophrenia, psychosis, bipolar disorder or generalized anxiety disorder

PHARMACOKINETICS

1. Onset of effect: 30-60 seconds after bolus administration
2. Volume of distribution: highly lipophilic with Vd of 2.4 L/kg

3. Metabolism: hepatic, to several inactive and active metabolites
 - a) Active metabolite, norketamine – 33% potency of parent compound
 - b) Major substrate of CYP 2B6, 2C9, and 3A4
 - c) Possible drug interactions: phenytoin and phenobarbital (strong CYP3A4 inducers)
 - i. Concomitant use of either of these agents may lower ketamine concentrations
 - ii. Patients who have been maintained on either of these therapies are likely to require higher doses of ketamine to achieve therapeutic effect
4. Half-life elimination: 2-3 hours
5. Excretion: primarily urine (inactive drug)

DOSING AND ADMINISTRATION

1. Loading dose:
 - a) Initial dose: 1-2 mg/kg IV x 1
 - b) May repeat additional bolus doses of 0.5-2 mg/kg every 5-10 minutes, if continued seizures after initial bolus
 - c) Maximum total loading dose: 5 mg/kg
 - d) NOTE: loading doses are based on actual body weight, capped at a patient weight of 100 kg
 - e) Administer bolus doses at a rate of 0.5 mg/kg/min
2. Continuous infusion:
 - a) Starting dose: 0.5-1 mg/kg/hr (“dosing” (admission) body weight)
 - b) Titrate infusion by 0.5 mg/kg/hr every 5-10 minutes until goal of seizure- or burst-suppression achieved on EEG
 - i. Infusion up-titration may be done in conjunction with administration of supplemental bolus doses, per above, until maximum loading dose of 5 mg/kg is achieved
 - c) Maintain infusion at rate where seizure- or burst- suppression is achieved
 - i. If breakthrough seizures occur, titrate infusion up by 0.5-1 mg/kg/hr every 4-6 hours
 - d) Maximum infusion rate: 10 mg/kg/hr
 - i. Note: Typical continuous infusion rates range from approximately 0.5-5 mg/kg/hr in published studies

DURATION OF THERAPY AND WEANING OF INFUSION

- Duration of therapy and rate of tapering are at the discretion of the Neuro ICU team or Neurology Consult
- Therapeutic doses to achieve seizure- or burst-suppression are typically maintained for 24-48 hours
 - Consider a longer duration of therapy if recurrence of seizures upon weaning of infusion
- The infusion is typically weaned to off over a period of 12-24 hours
 - As a guide, this may be accomplished by titrating the infusion dose down by 10-20% of the steady-state infusion dose every 2-4 hours
- Recurrence of seizures upon tapering may require halting of dose down-titration, and up-titration back to previous step for an additional 24-48 hours while additional AEDs are added/maximized

PROCEDURE

1. Provider and RN restrictions/credentialing:
 - a) Ketamine bolus and infusion may be administered by an ACLS-certified nurse if the following conditions are met:
 - i. Provider places the order for ketamine in PennChart
 - ii. Loading and subsequent bolus doses must be administered via Alaris pump as “bolus from bag”
 - iii. ICU provider (including critical care attending, critical care fellow, advanced practice provider (APP), or anesthesiologist) must be physically present for at least 15 minutes if bolus doses are administered
 - iv. A new order must be placed for all bolus doses and infusion rate changes (non-nursing-titratable infusion)
 - b) Subsequent monitoring and assessment, including for infusion titrations, may be done by the critical care nurse
2. Check expiration dates for the infusion - ketamine bag expires 24 hours after being hung

ADVERSE EFFECTS

- Hypertension
- Tachycardia; new or worsening tachyarrhythmias
- Hypersalivation (increased production of oral secretions)

- Emergence reactions (in patients quickly regaining consciousness after ketamine discontinuation) – manifestations may include agitation, confusion, delirium, and psychosis

MONITORING

- As outlined in Procedure section above: ACLS-certified RN and initial supervision by ICU provider (critical care attending/fellow/APP, or anesthesiologist) for bolus dose administration. Subsequent monitoring and assessment, as outlined in this guideline, may be done by the critical care nurse.
- HR and BP should be assessed and documented every 15 minutes for 1 hour after bolus administration and/or increases in infusion rate
- Subsequent assessments should be documented every 1 hour while on continuous infusion
- Continuous telemetry is required for the entire course of therapy
- Continuous EEG monitoring should be used to guide adequacy of therapy

DOCUMENTATION

- Ketamine is classified as a schedule III controlled substance in the US and in the state of PA. All associated policies for nursing documentation in the EMR and procedures for documenting waste should be observed.
- Nurse must document the initiation of therapy and any dose changes in the electronic medical record. An independent double check is required at initiation, change of shift, when hanging a new bag, and with a change of the order/infusion rate.

ABBREVIATIONS

- AED: antiepileptic drug
- EEG: electroencephalogram
- LTM: long-term monitoring (implementation of continuous EEG)

APPROVALS/REVIEWS

Critical Care Pharmacy (10/22/18)
 Neurocritical Care Faculty (HUP/PPMC, 11/27/18)
 Epilepsy (10/30/18)
 UPHS Critical Care Committee (12/11/18)
 UPHS & Entity P&T (Jan-Feb 2019)

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NEUROMUSCULAR EMERGENCIES

GUILLAIN-BARRE SYNDROME

- Pathophysiology / epidemiology
 - Acute autoimmune polyradiculoneuropathy
 - Generally demyelinating but can be axonal or mixed
 - affects 1-4/100,000 annually
- Presentation:
 - ascending motor/sensory loss, areflexia (in early stage, can be normal), neuropathic pain, dysautonomia, neuromuscular respiratory distress
- Risk factors / triggers
 - Preceding GI or URI symptoms
 - Campylobacter, CMV, EBV, influenza A, mycoplasma pneumonia, Zika, immunization (influenza A, rabies), surgery, trauma, organ transplant, cancer
- Workup
 - Assess respiratory status
 - vital capacity (VC) and negative inspiratory force (NIF), follow q2 hour
 - can be misleading due to poor seal and effort
 - Intubate if VC < 15cc/kg, NIF < -30 cm H₂O & trending downward
 - NO role for BiPAP unlike MG crisis
 - Consider early elective intubation
 - Avoid succinylcholine (risk of hyperkalemia)
 - Pulse ox and ABG changes will lag hypoventilation!
 - Estimated VC = counting aloud in one breath x 100 cc (ex. counts to 25 = 2.5 liters). If facial weakness, VC may be lower due to poor seal on apparatus.
 - If patient vented for >7 days, consider trach and PEG
 - CSF:
 - albumin-cytologic dissociation (high protein with normal/low cells)
 - May be normal in first 48 hours
 - Serum: ganglioside abs (GM1, GM1b, GD1a, GQ1b)
 - EMG/NCV: confirmatory study
 - MRI of spine: consider to rule out cord compression or transverse myelitis
 - HIV, HSV, CMV, Hep titers, Lyme (consider urine porphyrin, heavy metal screen)
- Treatment
 - PLEX/IVIg: similar efficacy
 - PLEX: administer every other day for total 5 treatment (need HD catheter)
 - IVIg: 0.4g/kg daily x 5 days (need consent)
 - Premeds: Tylenol 650mg, Benadryl 25 – 50 mg
 - No role for steroids
 - Dysautonomia:
 - Labile blood pressure, pulse
 - Careful not to over-treat as vital signs can be labile (attempt non-pharmacologic intervention first if stable) and use short acting agents
 - May need pacemaker
 - Pain management: can have severe radicular pain
 - NSAIDS +/- opiates early, Gabapentin, TCAs
 - GI and DVT prophylaxis
 - Order PT/OT/Rehab consults – may need SNF

MYASTHENIA GRAVIS EXACERBATION (or “myasthenic crisis”)

- Pathophysiology / Epidemiology:
 - Autoimmune condition caused by production of autoantibodies targeting post-synaptic AchR or receptor associated proteins of the neuromuscular junction
 - 2:3 M:F, bimodal peaks – female 20s, males 50s, 20% bulbar only, 2/100,000 annual
- Presentation:
 - Fatigable weakness improving with rest, facial diparesis, ptosis, neck extensor weak, nasal voice, hypotonic/weak, neuromuscular respiratory failure (restlessness, diaphoresis, accessory muscle use, tachypnea, tachycardia, weak neck flexor/extensor, nasal/staccato speech, paradoxical breathing)
 - * classically need to differentiate from “cholinergic crisis” from overdose of mestinon – weakness, fasciculations, inc sweating/salivation, and miosis
- Risk factors / triggers: med non-compliance, excessive activity, infection, stress, or drugs
- Workup
 - Assess respiratory status
 - vital capacity (VC) and negative inspiratory force (NIF), follow q2 hour
 - can be misleading due to poor seal and effort
 - Intubate or consider BiPAP if VC < 15cc/kg, NIF < -30 cm H2O & trending downward.
 - Avoid succinylcholine (risk of hyperkalemia)
 - Pulse ox and ABG changes will lag hypoventilation!
 - Estimated VC = counting aloud in one breath x 100 cc (ex. counts to 25 = 2.5 liters). If facial weakness, VC may be lower due to poor seal on apparatus.
 - If patient vented for >7 days, consider trach and PEG
 - Check CXR and cultures
 - Eliminate any medications that can exacerbate myasthenic symptoms
 - Vincent et. al. Myasthenia gravis. The Lancet, 2001; 357: 2122:28.
 - If new diagnosis:
 - check acetylcholine receptor antibodies
 - order EMG/NCV with repetitive stim, consider single fiber
 - check thyroid function tests, infection, other causes of respiratory failure
 - consider chest CT to rule out thymoma
- Acute treatment
 - Mestinon
 - 30 PO TID, increase to 60-120 mg q4-6 hrs (maintenance), can increase to 120 mg q3 hrs (maximum)
 - Long acting Mestinon (timespan) can be given qhs for pts with nocturnal or early morning weakness.
 - IV mestinon dose is 1/30th of oral dose
 - Use robinul for excessive GI cholinergic effects but watch for ileus
 - existing anticholinesterase medications should be stopped while patient’s on vent, due to increased secretions affecting weaning. Restart at ½ dose 1 day prior to extubation.
 - PLEX/IVIg – similar efficacy
 - If initial therapy has minimal response, it is reasonable to administer the other therapy
 - PLEX: administer every other day for total 5 treatment (need HD catheter)
 - IVIg: 0.4g/kg daily x 5 days (need consent)
 - Premeds: Tylenol 650mg, Benadryl 25 – 50 mg
 - High dose steroids (> prednisone 1mg/kg IBW)
 - Benefits seen in 2-6 weeks, but can acutely worsen symptoms
- Long-term treatment
 - Prednisone, Imuran, other immune suppressants
 - thymectomy (less effective for late-onset patients or ocular myasthenia).
- GI and DVT prophylaxis
- Order PT/OT/Rehab consults – may need SNF

ACUTE SPINAL CORD COMPRESSION

Unlike the brain, the cord rarely recovers function. Initiate treatment as soon as possible.

Presentation:

- 1) Assume cord compression in any cancer patient with back pain
- 2) Consider if the patient has progressive neurological symptoms, including weakness/numbness (especially symmetric and without facial involvement) and bladder/bowel symptoms.
- 3) Note general condition, vitals (ie, respiratory distress), back pain, history of trauma, known cancer or infection, duration of symptoms, recreational drug use, history of chronic steroid use (which can mimic cord compression).

Exam points:

- ❖ Note vital signs (especially for respiratory distress, autonomic instability).
- ❖ Check for a sensory level.
- ❖ Check rectal exam (for saddle anesthesia, diminished rectal tone).
- ❖ DTRs may be diminished (ie. spinal shock) or hyperreflexic.
- ❖ Percuss the spine for tenderness.
- ❖ Note signs of rheumatoid arthritis which is associated with atlanto-occipital dislocation.

Workup + Treatment

- 1) *If trauma suspected, immobilize the neck* (usually already done in the ED)
- 2) STAT MRI spine. Consider starting with plain films if there is a delay in getting an MRI, but the on-call Neurorads fellow should be made aware of the emergent need.
- 4) Possibly hematology-oncology consult and XRT within 12 hrs if appropriate

SPINAL CORD LESIONS

<u>Localization</u>	<u>Symptoms and signs</u>
Craniocervical Junction	Neck pain, head tilt, down-beat nystagmus, UMN weakness x 4
Cervical Spinal Cord	Neck pain, LMN in UE at level of lesion & b/l UMN below, sensory level, bowel/bladder
Thoracic Spinal Cord	Back pain, radicular signs, spastic paraparesis, sensory level, bowel/bladder
Cauda Equina Syndrome	Low back & perineal pain, flaccid paraparesis, areflexic bowel/bladder
Conus Medullaris	Areflexic bowel/bladder, minimal LE weakness, perineal sense loss
Anterior Cord Syndrome	Motor & spinothalamic tract (pain/temp) with spared position sense, bowel/bladder
Central Cord Syndrome	Suspended sensory level (pain/temp), UMN weakness below, intact position sense
Brown – Sequard Syndrome	Ipsilateral UMN weakness and position sense below lesion, contralateral pain/sense loss below lesion

Acute Traumatic Spinal Cord Injury

- The pathophysiology of acute spinal cord injury is complex and multifaceted. It involves a primary mechanical injury
- The primary injury appears to initiate a host of secondary injury mechanisms including:
 - i. vascular compromise leading to reduced blood flow,
 - ii. electrolyte shifts, permeability changes, loss of cellular membrane integrity, edema, and loss of energy metabolism,
 - iii. biochemical changes including neurotransmitter accumulation, arachidonic acid release, free-radical and prostaglandin production and lipid peroxidation
- Ischemia of the spinal cord underlies much of the mechanism of posttraumatic SCI
- Ischemia appears to be related to both local and systemic vascular alterations
- Local vascular alterations are due to the direct spinal cord injury and focal, post-injury vasospasm
- Systemic vascular alterations include reduced heart rate, cardiac arrhythmia, reduced mean arterial blood pressure, reduced peripheral vascular resistance and compromised cardiac output
- Respiratory insufficiency and pulmonary dysfunction is common after traumatic spinal cord injury, particularly when the injury occurs at cervical spinal cord level
- Spinal immobilization of all trauma patients with SCI is recommended except;
 - i. when patient is awake, alert, and not intoxicated
 - ii. without neck pain or tenderness
 - iii. who do not have an abnormal motor or sensory examination
 - iv. who do not have any significant associated injury
- The ASIA international standards are recommended as the preferred neurological examination tool.
- Maintaining a mean arterial blood pressure of 85-90 mm Hg after SCI is recommended.
- Administration of methylprednisolone for the treatment of acute SCI is not recommended.
- Early administration of venous thromboembolism prophylaxis (within 48-72 h) is recommended

LUMBAR PUNCTURE/CSF ANALYSIS

- ❖ Contraindications: skin infection over puncture site, $plt < 50K$, $inR > 1.5$, increased ICP (get prior head CT in age > 60 , immunocompromised, h/o CNS disease, abnormal neuro exam including poor mental status),
- ❖ Equipment checklist (before you put on sterile gloves): consent, kit, 22gu 5" needle ' the harpoon'. Gauze, extra sample containers, gloves, mask, chlorhexidine swabs, IV meds if needed, assistance holding the patient if needed.
- ❖ Sample destinations: all can be dropped off to the main lab on Founders 7, but if you don't trust transport.....
 - Micro: Gates 4, send a lot and ask them to hold extra so you can add on tests later
 - Immunology (Cytometry, flow cytometry – separate container for each): Founders 6, closes at 5pm, not open on weekends, useless on an old sample unless you add special reagent (rumor has it 1: 1 mix with alcohol) immediately after collecting.
 - Paraneoplastic (1-2cc CSF in a red top, SST of blood): Dr. Dalmau's lab, Johnson Pavilion 408. This can be refrigerated over night. It is part of a research protocol, call 746-4707 to have consent faxed over to you.
 - 14-3-3: Dr. Grossman's secretary will help you or send out for you M-Th in the morning.
- ❖ Opening pressure: measured in the lateral decubitus position w/legs straightened (bent legs can falsely elevate it)
 - Normal: 110mm H₂O in infants, 150 mmH₂O in children, 180 mm H₂O in adults and 250 mm H₂O in obese adults
 - Low values usually due to prior LP and can be seen in spontaneous dural tears
 - High values due to hydrocephalus, idiopathic intracranial hypertension (i.e. pseudotumor), cryptococcal meningitis.
 - Protein: increased by 1mg/dl for every 1000 RBCs
 - Isolated increase is a nonspecific abnormality seen in any process that disrupts the blood-brain barrier 9e.g. diabetes complicated by cerebrovascular disease, and aging itself)
 - Increased without a corresponding elevation in cell count is Albumino-cytologic dissociation. This is the classic picture of Guillain-Barre.
 - Super high protein (in the 2-3 gram range) occurs in states of very low CSF flow with partial obstruction, often due to tumor
- ❖ Glucose: should be about 2/3 of that in blood
 - Low values (Hypoglycorrhachia) are never good. Possibilities include tumor, bacterial meningitis, some fungal meningitis and sarcoidosis.
- ❖ Cell count: Send the first and last tubes. RBCs will decrease between the two in traumatic taps, but remain high if there are really RBCs in the CSF. Determine the true number of CSF WBCs by subtracting 1 RBC for every 700 RBCs (assuming normal serum WBCs). Cells disintegrate in CSF that sits around for more than 4 hours before laboratory analysis, resulting in '*pseudo normalization*' of CSF.
- ❖ Micro: each test takes about 1cc of CSF. Many tests require approval. A good technique is to send a large sample to the lab and add on tests as necessary/approved.
 - Beware of possible false positive VDRL and EBV PCR and false negative HSV PCR if tap is traumatic
 - HSV and VZV antibody encephalitis testing needs to be compared with serum. Serum: CSF ratio of less than 20 suggests intrathecal synthesis of antibodies
 - PCR testing should be done for suspected HSV1 and HSV2 DNA. (HSV2 can reactivate with fever and may be detected by PCR in the CSF of patients with other etiologies for encephalitis), also useful for VZV, enteroviruses, HIV-1 RNA,

- EBV DNA (seen in primary CNS lymphoma in HIV patients), West Nile virus DNA, CMV DNA, JC virus, and HHV6 DNA. PCR is not useful for Lyme.
- Intrathecal anti-borrelial antibody is currently the best test for CNS Lyme testing.
 - Latex particle agglutination tests are available for many bacterial antigens: Neisseria, Streptococcus pneumoniae, H. influenzae type B, group B streptococci and E. coli – this useful for rapid diagnosis in patients who have been pretreated and whose Gram stain and cultures are negative. These tests are highly specific and can be done within one hour, but they are not highly sensitive. A negative test does not exclude infection
 - No rapidly available PCR exists for bacterial DNA
 - Cryptococcal antigen testing is highly specific, sensitive and fast.
- ❖ Other Studies
 - 14-3-3 immunoassay for Creutzfeldt-Jakob disease can be falsely positive in HSV encephalitis, tuberculous meningitis and degenerative disorders. It should be interpreted in light of clinical symptoms and EEG abnormalities
 - CSF protein electrophoresis (includes oligoclonal bands): done for suspected MS. Requires same-day serum protein electrophoresis or lab will not run the CSF test. Bands are not specific for MS.
 - ❖ Guidelines to avoid panic
 - Don't panic when you see grossly bloody CSF – you haven't penetrated the aorta (unless the blood is spurting our Monty Python style – then it's probably okay to panic). Send tubes 1 and 4 for cell count.

LAB PANELS

- ❖ Ischemic stroke: ESR, RPR, fasting lipids for all. TSH if atrial fibrillation
- ❖ Hypercoagulability venous
 - Acute: antiphospholipid (anticardiolipin in sunrise), dilute viper venom time, tissue thromboplastin time (automatic if prior tests ordered), Beta 2 microglobulin, prothrombin gene mutation, urinalysis, age appropriate malignancy screen.
 - When acute clot resolved, off coumadin (heparin OK): protein C, protein S, antithrombin levels
- ❖ Hypercoagulability arterial: above acute tests plus HIT ab in appropriate clinical setting
- ❖ CSF inflammation and its mimics = inflammogram
 - CSF: electrophoresis (bands, myelin basic protein), VDRL, JC virus PCR (if immunosuppressed)
 - Serum: SPEP, ANA, ANCA, SSA/B, ACE, RPR, Lyme ab, HIV, B12, ESR, TSH
- ❖ Peripheral neuropathies: EMG/NCS may help guide you
 - Sensory- Motor polyneuropathy: HbA1c, TSH, BUN/Cr, RPR, B12, ANA, ANCAs, Lyme, LFTs, SPEP, UPEP, SSA/B, RF, ESR, HIV, consider heavy metal screen (needs special navy blue top tube)
 - Sensory neuropathy: SSA/B, anti-Hu
 - Mononeuritis multiplex: HbA1c, Lyme ab, SPEP/UPEP, ANA, ANCA, ESR, RPR, HIV, hepatitis serologies, consider cryoglobulins
- ❖ Paraneoplastic: see under lumbar puncture section above

NEURORADIOLOGY

Relative Imaging Densities

Tissue	MRI			CT
	T1	T2	Gad/other	
Bone	Dark	Dark		Bright
Air	Dark	Dark		Dark
Fat	Bright	Bright		Light Gray
Water	Dark	Bright	+flair except CSF	
Brain	Anatomic	Reverse Anatomic		Reverse Anatomic
Infarct	Dark	Bright	Subacute +gad	Darker w/time
Tumor	Dark	Bright	+ gad	Dark
Demyelinating	Dark	Bright	+ flair, acute + gad	Dark
Blood 0-24h	Isodense	Bright	+ susceptibility	Bright
Blood 24h to 3-5d	Isodense	Dark	+ susceptibility	Bright
Blood 3-7d	Bright	Dark	+ susceptibility	Less bright
Blood 1wk -month	Bright	Bright	+ susceptibility	Darker
Blood 2wk-yr	Dark	Dark	+ susceptibility	Dark

- ❖ Blood volume on CT scan (in cc) = 0.5 x max length x max width x number of slices x thickness of cuts
- ❖ Hounsfield units for CT scans
 - Bone 1000 Gray matter 35-40
 - Calcium 100 White matter 25-30
 - Acute Blood 85 CSF 0
 - Tumor 30-60 Adipose -100
 - Air -1000
- ❖ An approach to reading head CTs
 - Collections (extraaxial, intraaxial, cisternal, epidural, subdural, parenchymal, intraventricular etc)
 - Midline shift (look at pineal gland and septum) & patency of cisterns
 - Degree & pattern of hypoattenuation, sulcal effacement, hyperdense vessels, lentiform nucleus obscuration, insular ribbon obscuration (signs of stroke)
 - Fractures, pneumocephalus, hydrocephalus, edema pattern
- ❖ TCD criteria for > 50% intracranial stenosis (speeds are mean velocities)
 - MCA >100 cm/s, or >1:2 comparing L vs. R
 - ACA/ICA (siphon) >90cm/s
 - PCA >60cm/s
 - Verts, basilar >80cm/s

Criteria for Portable CT Scans

It is crucial that Portable CT scanning orders outline the rationale for scan in the comment section. When a patient requires a portable HCT, the comment section should clearly define the rationale and everyone should be aware (bedside nurse, NCC-NSG team) IE: Leaking ventric with risk of infection in neuro compromised non- intubated patient. We continue our efforts to secure 24/7 availability for CT scanning for our ICU patients.

There is an on-call system for CT tech response within an hour's timeline of a portable HCT request. For portable CT, 2 techs are now in house Monday thru Friday from 0700-2300, on-call after those hours and 1500-0700 on weekends. Any portable need after hours should be requested STAT with comment section highlighting details and a phone call to CT to call in the tech.

Appropriate patient populations for Portable CT Scan: Scan Criteria

- Post-operative Craniotomy
- Acute TBI
- Acute Neurological change in any ICU patient – NeuroICU/CT/Rhoads 5
- Gravely ill with high transport risk

For best project cooperative and results please note the following:

- NP/Resident/MD ordering Portable CT: Use comments section to direct request:
 1. Portable CT
 2. Specify time if time is a factor (ventric clamp trial, etc)
 3. Reason for portable CT: acute change in MS, new CN deficit, motor decline etc.

Steroid Preperation of Patients with Contrast Dye Allergy

Slow steroid prep:

50 mg prednisone 12 h before CT followed by 50 mg prednisone 2 h before CT followed by 25-50 mg IV Benadryl 1 h before CT scan

Rapid steroid prep:

40 mg IV solumedrol 4 h before CT followed by 50 mg IV Benadryl 1 H before CT scan

Emergent steroid prep:

200 mg IV hydrocortisone and 50 mg IV Benadryl 1 h before CT scan

SCALES AND FORMULAE

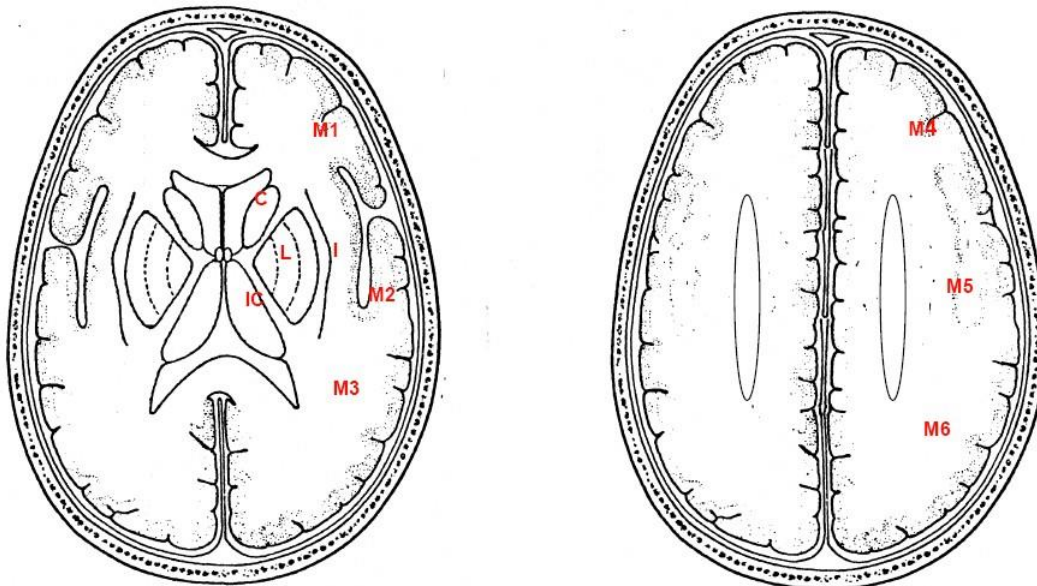
Glasgow Coma Scale

(add up all components to get score, if patient intubated give 1 for verbal score)

Response	Score
Eye opening	
Opens eyes spontaneously	4
Opens eyes in response to speech	3
Open eyes in response to painful stimulation (eg, endotracheal suctioning)	2
Does not open eyes in response to any stimulation	1
Motor response	
Follows commands	6
Makes localized movement in response to painful stimulation	5
Makes nonpurposeful movement in response to noxious stimulation	4
Flexes upper extremities/extends lower extremities in response to pain	3
Extends all extremities in response to pain	2
Makes no response to noxious stimuli	1
Verbal response	
Is oriented to person, place, and time	5
Converses, may be confused	4
Replies with inappropriate words	3
Makes incomprehensible sounds	2
Makes no response	1

ASPECTS Score

10 = normal; subtract one point for hypodensity in each of the 10 regions noted below. See also-
www.aspectsinstroke.com



NIH Stroke Scale Score**1a. Level of consciousness**

- 0 alert
- 1 drowsy
- 2 stuporous
- 3 coma

1b. LOC questions (month, age)

- 0 both correct
- 1 one correct
- 2 incorrect

1c. LOC commands (close eyes, make a fist)

- 0 both correct
- 1 one correct
- 2 incorrect

2. Best gaze

- 0 normal
- 1 partial gaze palsy
- 2 forced deviation

3. Visual fields

- 0 no visual loss
- 1 partial hemi
- 2 complete hemi
- 3 bilateral hemi

4. Facial palsy

- 0 normal
- 1 minor
- 2 partial
- 3 complete

5ab-6ab. Motor (L/R arm, L/R leg)

- 0 no drift
- 1 drift
- 2 can't resist gravity
- 3 no effort against gravity
- 4 no movement
- 9 amputation/joint fusion

7. Limb ataxia (FNF, HKS)

- 0 absent
- 1 present in one limb
- 2 present in 2 limbs

8. Sensation (pin)

- 0 normal
- 1 partial loss
- 2 severe loss

9. Best language

- 0 no aphasia
- 1 mild-mod aphasia
- 2 severe aphasia
- 3 mute

10. Dysarthria

- 0 none
- 1 mild-mod
- 2 near to unintelligible or worse/mute
- 9 intubated/barrier

11. Extinction and inattention

- 0 no neglect
- 1 partial neglect
- 2 complete neglect

Note: 9's are not added in the final score

Thrombolysis in Cerebral Infarction (TICI) Scoring for Post-Treatment Reperfusion

- Grade 0 = No perfusion
- Grade 1 = Perfusion past the initial obstruction, but limited distal branch filling with little or slow distal perfusion
- Grade 2a = Perfusion of <67% of the vascular distribution of the occluded artery (e.g., filling and perfusion through 1 M2 division)
- Grade 2b = Perfusion of ≥67% of the vascular distribution of the occluded artery (e.g., filling and perfusion through 2 or more M2 divisions).
- Grade 3 = Full perfusion with filling of all distal branches

ICH Score

ICH Score (Hemphill, 2001)	Points
A. Glasgow comas score	
3 – 4	2
5 – 12	1
13 – 15	0
B. ICH volume (in cc)	
> 30 cc	1
< 30 cc	0
C. Intraventricular hemorrhage	
Yes	1
No	0
D. Age	
> 80	1
< 80	0

30 day percentage mortality for ICH based on points:

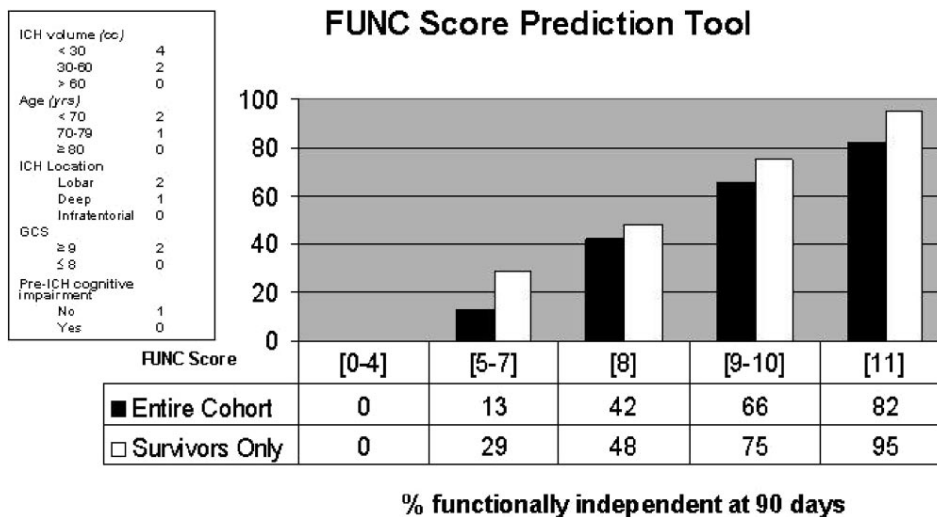
0: 0% 1: 13% 2: 26% 3: 72% 4: 97% 5: 100%

Modified ICH Score

Components	ICH score points
GCS score	
15-13	0
12-5	1
4-3	2
ICH volume (ml)	
< 20	0
21-50	1
> 51	2
IVH or Hydrocephalus	
No	0
Yes	1
Total MICH score	0-5

mICH 2, 3 and 4 surgical option better than conservative treatment

mICH 0, 1 and 5 conservative option better than surgical option



SUBARACHNOID HEMORRHAGE GRADING SCALES

Hunt and Hess Scale

Grade	Clinical findings
0	No SAH
1	Asymptomatic or mild headache, mild nuchal rigidity
2	Moderate to severe headache, nuchal rigidity, no neurologic deficit, except cranial nerve palsy
3	Drowsiness, confusion, or mild focal deficit
4	Stupor or mild to moderate hemiparesis; possible early decerebrate rigidity
5	Deep coma, decerebrate posturing, moribund

WFNS

Grade	Clinical findings
I	GCS=15, no motor deficit
II	GCS 13-14, no motor deficit
III	GCS 13-14, yes motor deficit
IV	GCS 7-12, yes or no – motor deficit
V	GCS 3-6, yes or no – motor deficit

Fisher Scale (risk of vasospasm increases with grade until grade 4 which has lower risk)

Grade	CT scan findings
1	No blood detected
2	Diffuse, thin layer of subarachnoid blood (vertical layers < 1 mm thickness)
3	Localized clot or thick layer of subarachnoid clot (vertical layers > 1mm thickness)
4	Intracerebral or intraventricular blood with diffuse or no subarachnoid blood

Modified Fisher Scale (risk of vasospasm increases linearly with grade)

Grade	CT scan findings
0	No blood detected
1	Diffuse or focal thin subarachnoid blood

- (no intraventricular blood)
- 2 Diffuse or focal thin subarachnoid blood
(with intraventricular blood)
- 3 Diffuse or focal thick subarachnoid blood
(no intraventricular blood)
- 4 Diffuse or focal thick subarachnoid blood
(with intraventricular blood)

Transcranial Doppler (TCD) Normal Values

Vessel	Mean Velocity (cm/sec)
MCA (M1)	40 – 80
ACA (A1)	35 – 60
PCA (P1)	30 – 55
ICA	61 ± 16
OA	21 ± 5
Carotid Siphon	55 ± 15
VA	25 – 50
BA	25 – 60

Transcranial Doppler (TCD) interpretation

Mean MCA velocity (cm/sec)	Lindgaard ratio (MCA velocity/ICA velocity)	Interpretation
< 120	<3	Normal
120-150	3 – 4	Mild Vasospasm
150 – 200	5 – 6	Moderate Vasospasm
>200	>6	Severe Vasospasm