Emergency Neurological Life Support® Pharmacotherapy Protocol Version 6.0

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PHARMACOTHERAPY INTRODUCTION

These protocols were created to highlight the use and dosing of common medications used during neurological emergency resuscitation. Many of these medications are relevant to many ENLS protocols and are cross-referenced for ease of access. Adult and pediatric dosing of medications have been discussed but know that some medications may differ in name and availability internationally.

ANTIBIOTICS AND ANTIVIRAL AGENTS

Choosing the appropriate antimicrobial or antiviral agent and dose is essential when treating meningitis and encephalitis. Inflammation of the blood-brain barrier allows antimicrobials to penetrate cerebral tissue. Streptococcus pneumonia meningitis should be treated with dexamethasone (10 mg IV every 6 hours for 4 days) in conjunction with antibiotics to decrease neurological sequelae. (See pediatric considerations.) Selection of an appropriate antimicrobial should be based on the local antibiogram, drug resistance patterns, and age of the patient. See the ENLS protocols *Meningitis and Encephalitis* and *Spinal Cord Compression*, and Pharmacotherapy for more detail on treating CNS infections.

CNS Pathogen	Recommended Therapy
H. influenzae	Third-generation cephalosporin
S. pneumoniae	Vancomycin (Trough goal: 15-20 mcg/mL) PLUS Third-generation cephalosporin
N. meningitidis	Third-generation cephalosporin
L. monocytogenes	Ampicillin
S. agalactiae	Ampicillin
E. coli	Third-generation cephalosporin
Staphylococci	Vancomycin (Trough goal: 15-20 mcg/mL)
HSV, VZV	Acyclovir
CMV	Ganciclovir

Pediatric considerations

Corticosteroids are not recommended in neonates with suspected meningitis due to insufficient data. In infants and children, dexamethasone 0.15 mg/kg/dose (max 10 mg) every 6 hours for 2-4 days has been shown to prevent neurologic sequalae, specifically hearing loss, in the setting of *H. influenzae* type b meningitis when the first dose of dexamethasone is administered immediately prior to or at the same time as the first dose of antibiotics. Avoid steroid therapy when there is a delay in presentation or after antibiotics have been started. For pneumococcal meningitis, studies have shown variable effects in reducing neurologic sequalae; and the use of dexamethasone in pediatric patients for this indication remains controversial. For infants and children older than 6 weeks of age, the use of dexamethasone in pneumococcal meningitis should be evaluated against possible risks of the intervention.

ANTICOAGULANT REVERSAL

Control the bleeding

When rapid reversal of an anticoagulant is necessary, the risk-benefit ratio of continued bleeding to thrombosis is crucial and must be considered on an individual basis. In all cases that include INR elevation or active bleeding, anticoagulation medication should be stopped. If the last dose of an anticoagulant was taken within the 3-5 half-life window, then reversal should be considered in patients with a high bleeding risk. These agents are relevant for the ENLS protocols *Intracerebral Hemorrhage, Subarachnoid Hemorrhage, Traumatic Brain Injury, Traumatic Spine Injury, and Spinal Cord Compression.*

Vitamin K Antagonist Reversal

<table>
<tr><th>INR</th><th>Clinical Setting</th><th>Treatment Options</th></tr>
<tr><td rowspan="2">< 4.5</td><td>No bleeding</td><td>Hold warfarin until INR in therapeutic range</td></tr>
<tr><td>Rapid reversal required (< 24 hrs)</td><td>Hold warfarin
Vitamin K 2.5mg PO
If urgent reversal needed (≤ 12 hrs) for procedure, consider 4PCC 25 IU/kg IV</td></tr>
<tr><td rowspan="2">4.5-10</td><td>No bleeding</td><td>Hold warfarin until INR in therapeutic range
Consider vitamin K 2.5 mg PO if risk factors for bleeding*</td></tr>
<tr><td>Rapid reversal required (< 24 hrs)</td><td>Hold warfarin
Give vitamin K 5 mg PO
If urgent reversal needed (≤ 12 hrs) for procedure, consider 4PCC 35 IU/kg IV</td></tr>
<tr><td rowspan="2">> 10</td><td>No bleeding</td><td>Hold warfarin until INR reaches therapeutic range
Give vitamin K 2.5-5 mg PO or 1-2 mg IV*
Repeat every 24 hours as necessary</td></tr>
<tr><td>Rapid reversal required (< 24 hrs)</td><td>Hold warfarin
Give vitamin K 1-2 mg IV
Repeat every 6-24 hours as necessary
If urgent reversal needed (≤ 12 hrs) for procedure, consider 4PCC 50 IU/kg IV</td></tr>
<tr><td>ANY INR</td><td>Serious or life-threatening bleeding
OR
Invasive procedure required ≤ 12h</td><td>Hold warfarin
Give vitamin K 10mg IV over 30 minutes
Recheck INR 30 minutes after PCC administered

Weight-based dose
<table>
<tr><th>INR</th><th>4-factor PCC dose</th><th>Max dose</th></tr>
<tr><td>1.3-3.9</td><td>25 units/kg</td><td>2,500 units</td></tr>
<tr><td>4-6</td><td>35 units/kg</td><td>3,500 units</td></tr>
<tr><td>>6</td><td>50 units/kg</td><td>5,000 units</td></tr>
</table>
Fixed dose: 1,500 to 2,000 units
If volume resuscitation is necessary, consider FFP 15-20 mL/kg.
Recheck INR after FFP administered.</td></tr>
<tr><td colspan="3">*Consider a supplemental dose of PCC if INR is still elevated and the patient is still bleeding.</td></tr>
</table>

Vitamin K (phytonadione)		
	Onset of action	**Peak Effect**
Oral	6-12 hrs	24-48 hrs
IV	1-2 hrs	12-14 hrs
SQ	Not recommended due to unpredictable or delayed response.	

Pediatric considerations

Consider holding warfarin at any INR in children on warfarin where reversal is needed. Low-dose subcutaneous vitamin K (0.03 mg/kg/DOSE) can be considered for warfarin reversal. In the presence of significant bleeding, immediate reversal with FFP, PCC, or factor VII may be needed. There is limited data for the use of PCC in pediatric patients for emergent reversal of VKA; data for anticoagulation reversal in pediatric patients is limited to case series and case reports. While emergent use may be reasonable, no dosing recommendations are currently available. A phase III study investigating the effects of idarucizumab for dabigatran reversal in children had limited enrollment. There is also limited data for andexanet alfa in children. A case report in an 8-year-old patient showed use of andexanet alfa using a 20% dose reduction of adult dosing.

Factor Xa Inhibitors Reversal

Apixaban (Eliquis®)
Rivaroxaban (Xarelto®)

- If ingested within 2 hours, administer activated charcoal 50 g
- Consider time of last dose and $t_{1/2}$ of agent when deciding to reverse agent. Recommend reversal if last dose given within 3-5 elimination $t_{1/2}$ of the drug to ensure hemostasis
- Andexanet-alfa (see dosing)

Step 1: Determine previous factor Xa agent and dose history
Only indicated for reversal of rivaroxaban and apixaban

Factor Xa Inhibitor	Factor Xa Inhibitor Last Dose	Timing of Last Dose	
		< 8h or unknown	≥ 8h
Rivaroxaban	≤ 10 mg	Low dose	Low dose
	> 10 mg or unknown	High dose	
Apixaban	≤ 5 mg	Low dose	
	> 5 mg or unknown	High dose	

Step 2: Determine Andexanet-alfa dose

Dose	Initial bolus	Maintenance infusion
Low	400 mg IV over 15 min	4 mg/min for 100 min
High	800 mg IV over 15 min	8 mg/min for 112 min

Alternative Option:

- Administer PCC 50 units/kg over 10 min
- If volume needed, consider 15-20 ml/kg FFP

Direct Thrombin Inhibitors Reversal	

Dabigatran (Pradaxa®)	• If ingested within 2 hours, administer activated charcoal 50g PO/NG
	• Drug of choice: idarucizumab 5 gm IV push (two 2.5 gm vials given back to back)
	• Consider the following if idarucizumab not available:
	  • Emergent hemodialysis OR
	  • aPCC 50 units/kg

Bivalirudin (Angiomax®)	• Turn off infusion • Monitor aPTT to confirm clearance • Supportive measures to control bleeding
Argatroban	• Turn off infusion • Monitor aPTT to confirm clearance • Supportive measures to control bleeding

<table>
<tr><th colspan="2">Unfractionated Heparin and Low Molecular Weight Heparin (LMWH) Reversal</th></tr>
<tr><td>Unfractionated heparin</td><td>

Protamine neutralizes heparin. Dosing is based on time since last dose of heparin.

Immediate: 1 mg/100 units of heparin given (max = 50 mg)
30 minutes: 0.5 mg/100 units
> 2 hours: 0.25 mg/100 units

</td></tr>
<tr><td>Enoxaparin
(Lovenox®)

Dalteparin
(Fragmin®)</td><td>

Protamine partially reverses the effect of LMWH (about 60%)
<table>
<tr><th>Time since last dose of LMWH</th><th>Dose of protamine</th></tr>
<tr><td>< 8 hrs</td><td>1 mg per for each 1 mg enoxaparin/100 units dalteparin administered (max 50 mg)</td></tr>
<tr><td>8-12 hrs</td><td>0.5 mg for each 1 mg enoxaparin/100 units dalteparin administered (max 25 mg)</td></tr>
<tr><td>> 12 hrs</td><td>Not likely to be useful (max 25 mg)</td></tr>
</table>
Consider reversal beyond 12 hrs in patients with renal insufficiency
Monitor anti-factor Xa activity to confirm reversal

</td></tr>
<tr><td>Fondaparinux
(Arixtra®)</td><td>

Protamine is NOT helpful; supportive care
<u>Weak evidence, but may consider either:</u>

PCC 50 units/kg
rFVIIa 20 mcg/kg (may repeat x 1)

</td></tr>
</table>

ANTISEIZURE MEDICATIONS

Seizures and Status Epilepticus

Status epilepticus is a neurological emergency and warrants rapid treatment using intravenous medications at appropriate doses. See the ENLS protocol *Status Epilepticus* for timing and choice of medication used in treating unremitting seizures. Choice of agent depends on etiology, patient stability, organ function, adverse drug effects, and consideration of drug interactions. Benzodiazepines should be the first agent, followed quickly by administration of a longer duration agent. Goal therapeutic levels should be established and monitored.

First-Line/Emergent	Dosing
Lorazepam (Ativan®)	0.1 mg/kg IV up to 4 mg per dose
Midazolam (Versed®)	0.2 mg/kg IM up to 10 mg per dose
Diazepam (Valium®)	0.15 mg/kg IV up to 10 mg per dose
Maintenance/Urgent	
Phenytoin (Dilantin®) OR Fosphenytoin (Cerebyx®)	Load: 20 mg/kg IV (max adult dose: 2,000 mg, max pediatric dose: 1,500 mg) Maintenance: 4-6 mg/kg/day divided in 2-3 doses (dosing for fosphenytoin is the same, only in phenytoin equivalents)
Valproate sodium (Depacon®)	Load: 40 mg/kg IV (max: 3,000 mg) Maintenance: 10-15 mg/kg/day divided into 2-4 doses
Levetiracetam (Keppra®)	Load: 60 mg/kg IV (max: 4,500 mg) Maintenance: Adults: 1,000-3,000 mg/day IV in 2 divided doses Children: 20-55 mg/kg/day divided q12h
Lacosamide (Vimpat®)	Adult Load: 200-400 mg/day IV Adult Maintenance: 200 mg every 12 hours Children: Initial dose: 2 mg/kg/day divided q12h Usual max dose: < 30 kg: 8-12 mg/kg/day 30-50 kg: 6-8 mg/kg/day

First-Line/Emergent	Dosing
Phenobarbital	Load: 20 mg/kg IV Maintenance: Adults: 1-3 mg/kg/day divided into 1-3 doses Infants and Children ≤ 5 years: 3-5 mg/kg/day in 1-2 divided doses Children > 5 years and adolescents: 2-3 mg/kg/day divided in 1-2 doses

Refractory Status Epilepticus	
Midazolam (Versed®)	Bolus: 0.2 mg/kg IV Infusion: 0.05-2 mg/kg/hr
Propofol (Diprivan®)	Bolus: 1-2 mg/kg IV Infusion: 30-250 mcg/kg/min
Pentobarbital (Nembutal®)	Bolus: 10-15 mg/kg IV Infusion: 0.5-5 mg/kg/hr
Ketamine (Ketalar®)	Bolus: 0.5-4.5 mg/kg IV Infusion: 0.5-10 mg/kg/hr

Pediatric considerations

Routine use of propofol is not recommended due to risk for propofol-related infusion syndrome (PRIS) in children.

Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

ANTITHROMBOTIC AGENTS

Breaking up clots

Antithrombotic agents are used in management of acute ischemic stroke, and the focus of urgent management should be on clot disruption; see ENLS protocol *Acute Ischemic Stroke*.

Alteplase 0.9 mg/kg (not to exceed 90 mg total dose) IV is the only FDA-approved pharmacologic agent available for acute clot disruption in acute ischemic stroke. Drug re-constitution requires special expertise; do not shake the reconstituted infusate, simply swirl the container when reconstituted. Administer 10% of the total dose as an initial IV bolus over 1 minute and infuse the remainder over 60 minutes.

Tenecteplase has also been used as a thrombolytic in acute ischemic stroke (not FDA-approved) at a dose of 0.25 mg/kg IV push (max dose 25 mg).

Pediatric considerations

Use of thrombolytics for AIS in children is extremely limited. Early identification of pediatric stroke and rapid transfer to a regional primary pediatric stroke center is of the upmost importance. For institutions with a previously established pediatric stroke protocol, refer to institutional protocols.

Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

HEMOSTATIC AGENTS

Prevent aneurysm re-bleeding

Antifibrinolytics may play a role in preventing re-bleeding of brain aneurysms after subarachnoid hemorrhage prior to definitive treatment to secure the aneurysm. In order to avoid thrombotic complications, these medications should only be used if surgical intervention must be delayed. Doses should be held 4-6 hours prior to any endovascular procedures, and treatment duration should be less than 72 hours. Precipitous drops in blood pressure can be seen if used in conjunction with nimodipine.

Adult Dosing:

- Tranexamic acid 1 g IV over 10 minutes every 4-6 hours
- Aminocaproic acid 5 gram IV over 1 hour followed by 1 gram/hour infusion

These agents are relevant for the ENLS protocol *Subarachnoid Hemorrhage*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

HYPEROSMOLAR THERAPY

Mannitol vs. hypertonic saline

Mannitol (0.5-1 gm/kg) is an osmotic diuretic, and close monitoring is necessary to avoid hypotension and hypovolemia. Hypertonic saline (HTS) is a volume expander that can worsen heart failure and pulmonary edema. For emergent use, HTS concentrations greater than 3.0% should be given through a central line; dosing varies based on concentration:

Concentration	Dose	Infusion duration
3%	5 ml/kg	5-20 min
5%	3 ml/kg	5-20 min
7.5%	2 ml/kg	5-20 min
23.4%	30 ml	10-20 min

Pediatric considerations

- Hypertonic saline 3%: 2-5 mL/kg over 10-20 min
- Hypertonic saline 23.4%: 0.5 mL/kg (max dose: 30 mL)

These agents are relevant for the ENLS protocols *Intracranial Hypertension and Herniation and Traumatic Brain Injury*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

IV ANTIHYPERTENSIVE MEDICATIONS

Keep blood pressure under control

Blood pressure goals are controversial and vary dramatically between disease states. When blood pressure reduction is required, selection of an agent should be based on rapidity of control, hemodynamic parameters, volume status, organ function, and drug interactions.

Agent	Dose
Continuous Infusions	
Nicardipine (Cardene®)	Adults: Initial dose: 2.5 mg/h Titration: 2.5 mg/h every 15 minutes to goal BP (max = 15 mg/hour) Children: Initial: 0.5 mcg/kg/min Titration: 0.5-1 mcg/kg/min every 15 minutes to goal BP (max 5 mcg/kg/min, do not exceed adult max)
Clevidipine (Cleviprex®)	Adult Initial dose: 1-2 mg/h Adult Titration: increase dose every 90 sec to a max of 21 mg/h (32 mg/h max reported for short-term use) Children, initial dose: 1 mcg/kg/min Children, titration: increase by 0.5 to 1 mcg/kg/min every 2-3 min until goal BP achieved or max 7 mcg/kg/min, not to exceed adult max dose
Esmolol (Brevibloc®)	Adults: 50-300 mcg/kg/min Children: 25-100 mcg/kg/min
Intermittent dosing	
Hydralazine	Adults: 10-20 mg IV every 4-6 hours Children: 0.1-0.2 mg/kg/dose (max = 25 mg/dose) every 4-6 hours
Labetalol	Adults: 10-80 mg IV every 10 min up to 300 mg Children: 0.2-1 mg/kg/dose IV bolus (up to 40 mg/dose); use with caution in children

These agents are relevant for the ENLS protocols *Acute Ischemic Stroke, Intracerebral Hemorrhage and Subarachnoid Hemorrhage*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

NEUROMUSCULAR BLOCKADE

Rapid sequence intubation, refractory ICP elevations, shivering

Neuromuscular blocking agents are used primarily to facilitate tracheal intubation or provide skeletal muscle relaxation during surgery, to facilitate mechanical ventilation, or assist in treatment of malignant ICP or refractory shivering during targeted temperature management. Short-acting agents are preferred, and concomitant sedation is necessary. Monitoring the train-of-four (TOF) with a peripheral nerve stimulator (PNS) in conjunction with the clinical assessment (vital signs, synchrony with the mechanical ventilator) should always be used to evaluate the extent of paralysis. The TOF goal is generally 1-2 responses per 4 stimulations. Caution should be used when using a PNS in hypothermic patients, as the TOF may be unreliable and misleading. Therefore, caution should be exercised when using PNS in the setting of hypothermia. Preferred agents are:

Agent	Dosing	Precautions / Comments
Succinylcholine (Anectine®)	Adults: 0.5-1.1 mg/kg IV • 2-4 mg/kg IM Adolescents: 1-1.5 mg/kg IV • 3-4 mg/kg IM Children: 1-2 mg/kg IV • 3-4 mg/kg IM Infants: 2-3 mg/kg IV • 4-5 mg/kg IM	Severe hyperkalemia may occur in muscle trauma, burns, neuromuscular disease, spinal cord injury, and stroke
Cisatracurium (Nimbex®)	Adults 0.15 mg/kg IV (up to 0.2 mg/kg) Children: 0.1-0.15 mg/kg IV	Longer half-life in elderly Can be used as continuous infusion Eliminated via enzymatic pathway
Rocuronium (Zemuron®)	Adults and children: 0.6 mg/kg IV (up to 1.2 mg/kg)	Prolonged duration in renal failure
Vecuronium	Adults and children: 0.1 mg/kg/dose (up to 0.2 mg/kg)	

These agents are relevant for the ENLS protocols *Intracranial Hypertension and Herniation, Resuscitation Following Cardiac Arrest, and Traumatic Brain Injury*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

SEDATION AND ANALGESIA

Treat pain and agitation

Sedation and analgesia treatment goals must be identified and communicated clearly. These agents are affected by end-organ dysfunction and drug interactions, so choices must be individualized. The minimum effective dose should be used, and many of these agents are synergistic when used together; therefore, lower doses of both agents can be used to achieve the desired effect.

Benzodiazepines are well tolerated as are opiates. These agents are relevant for the ENLS protocols *Intracranial Hypertension and Herniation, Resuscitation after Cardiac Arrest, and Traumatic Brain Injury*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

Sedatives	Dose
Propofol (Diprivan®)	• Maintenance infusion: 50-100 mcg/kg/min

Dexmedetomidine (Precedex®)	• Loading dose is NOT recommended
	• Maintenance infusion:
	  • Adults: 0.2-1.4 mcg/kg/h
	  • Children: 0.2-0.7 mcg/kg/hr. Doses up 2.5 mcg/kg/h have been reported

Lorazepam (Ativan®)	• Loading: 0.02-0.04 mg/kg
	• Intermittent: 0.02-0.06 mg/kg every 2-6 h
	• Maintenance infusion:
	  • Adults: 0.01-0.1 mg/kg/h
	  • Children: 0.05 mg/kg/h, rarely used due to concern for propylene glycol toxicity

Midazolam (Versed®)	Adults • Loading: 0.01-0.05 mg/kg • Maintenance infusion: 0.01-0.1 mg/kg/h Children • Loading: 0.05-0.1mg/kg • Maintenance infusion • Initial: 0.03-0.12 mg/kg/h. • Usual range: 0.024 to 0.36 mg/kg/h • Whenever possible, use preservative free product for continuous infusions

Analgesics	Dose
Fentanyl (Duragesic®)	Adults • Bolus: 12.5-100 mcg or 1-2 mcg/kg IVP • Maintenance infusion: 0.7-10 mcg/kg/h or 25-700 mcg/h Children • Bolus: 1-2 mcg/kg • Maintenance infusion: Initial, 1 mcg/kg/h
Hydromorphone (Dilaudid®)	Adults • Oral: 2-4 mg every 4-6 hours • Intermittent dose: 0.2-1 mg every 4-6 hours Children: • Oral: 0.03-0.08 mg/kg/dose every 3-4 hours • IV: 0.01-0.015 mg/kg every 3-8 hours • Maintenance infusion: 0.003-0.005 mg/kg/h
Morphine (Duramorph®)	Adults • Bolus: 2-10 mg IVP • Intermittent dose: 2-8 mg every 3-4 hours • Maintenance infusion: 0.8-30 mg/h Children • Bolus 0.1-0.2 mg/kg IV over 5min • Intermittent dose: 0.05-0.1 mg/kg every 3-4 hours • Maintenance infusion: Initial, 0.01 mg/kg/h Titrate up as required (usual range: 0.01-0.04 mg/kg/h)

Pediatric considerations

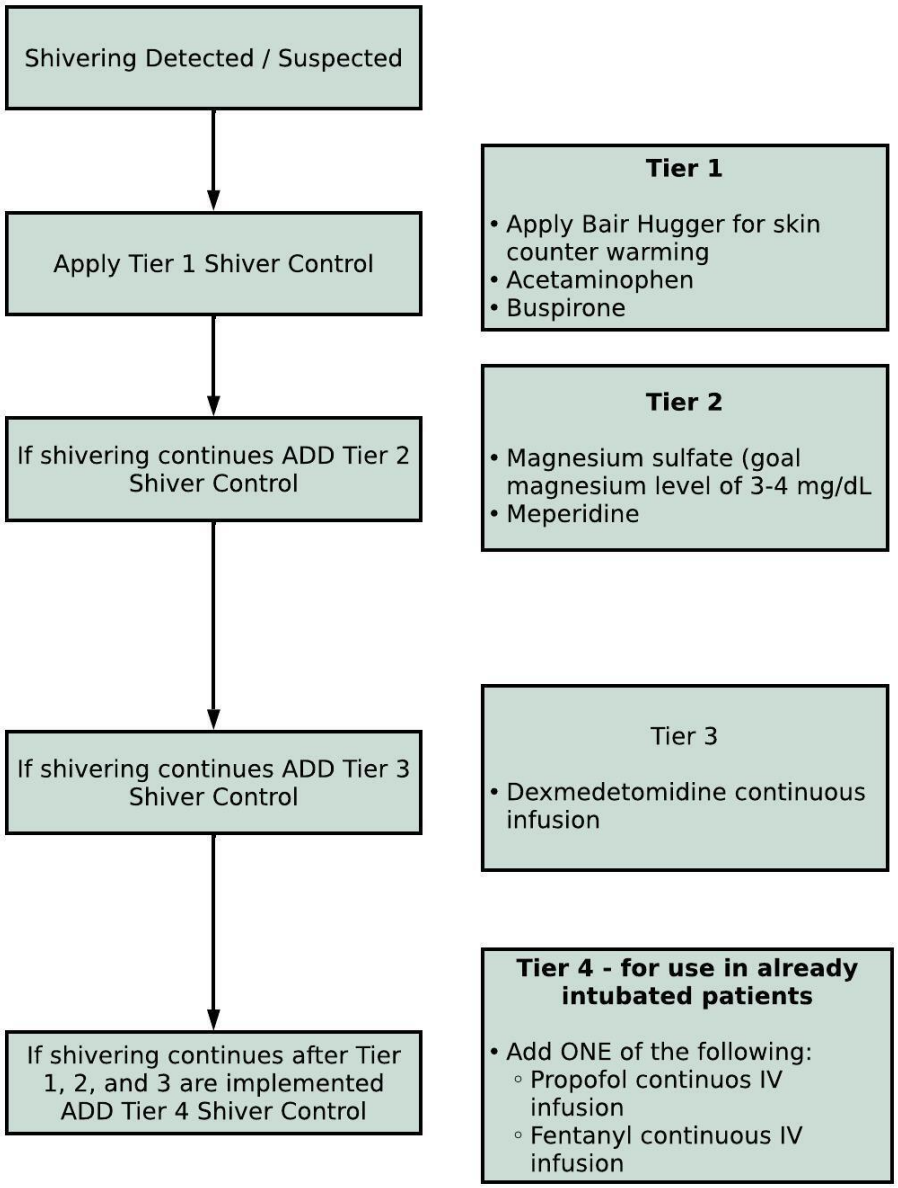
In general, pediatric doses should not exceed adult doses. Routine use of propofol is not recommended due to risk for propofol-related infusion syndrome (PRIS) in children.

SHIVERING MANAGEMENT

Follow a protocol

During therapeutic temperature management, shivering counteracts attempts to set body temperature. Sustained shivering should be avoided as it counteracts cooling induction, increases metabolic rate, and may contribute to ICP elevations and increased brain oxygen consumption. The Adult ENLS anti-shivering protocol is shown in the figure below.

Sample Shivering Protocol for Adult Patients



The Bedside Shivering Assessment Scale

0	No shivering
1	Shivering localized to the neck and/or thorax only
2	Shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	Shivering involves gross movements of the trunk, upper and lower extremities

These agents are relevant for the ENLS protocols *Intracranial Hypertension and Herniation and Resuscitation after Cardiac Arrest*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.

VASOPRESSORS AND INOTROPES

Augment blood pressure and provide cardiac support

Vasopressor agents are used in a variety of situations when blood pressure augmentation is desired to treat shock, vasospasm, or improve cerebral or spinal perfusion pressure. Their effects are produced through actions at adrenergic (alpha and beta), dopamine, and vasopressin receptors. Vasopressin is a nonadrenergic vasopressor used in diabetes insipidus and as a second-line agent in refractory shock. Dobutamine and milrinone function primarily as inotropes. The selection of a vasopressor or inotrope should be based on goals of care and desired physiologic effects.

Category/Drug	Initial Dose	Comments
Mixed α/β receptor agonists		
Norepinephrine	2-5 mcg/min, or 0.02-3 mcg/kg/min Children: initial 0.1 mcg/kg/min (range: 0.05-2 mcg/kg/min)	First-line agent for septic shock
Epinephrine	0.02-1 mcg/kg/min Children: 0.1-1 mcg/kg/min	First-line agent for septic shock
Dopamine	Dopa: 1-5 mcg/kg/min β: 5-10 mcg/kg/min α: 10-20 mcg/kg/min	Effective at multiple receptors
Ephedrine	5-25 mg slow IVP, may repeat in 5-10 min Children: 0.1-0.3 mg/kg/dose (max 25 mg); not routinely used	Oral formulation, dose at 25-50 mg every 8-12 hours
Pure α receptor agonist		
Phenylephrine	10-200 mcg/min, or 0.1-1 mcg/kg/min Children: 0.1 to 0.5 mcg/kg/min	May cause reflex bradycardia

Category/Drug	Initial Dose	Comments
Non-adrenergic		
Vasopressin	0.04-0.08 units/min Children: 0.03-0.12 units/kg/h	May demonstrate synergistic effect with other vasopressors
Inotropes		
Dobutamine (mixed α/β)	2.5-10 mcg/kg/min Children: 1-20 mcg/kg/min	Good in decompensated heart failure
Milrinone (non-adrenergic)	0.25-0.75 mcg/kg/min	Reduce dose in renal dysfunction

These agents are relevant for the ENLS *protocols Intracranial Hypertension and Herniation, Resuscitation after Cardiac Arrest, Subarachnoid Hemorrhage and Traumatic Brain Injury*. Detailed drug information can be found in the *Pharmacotherapy* ENLS chapter.