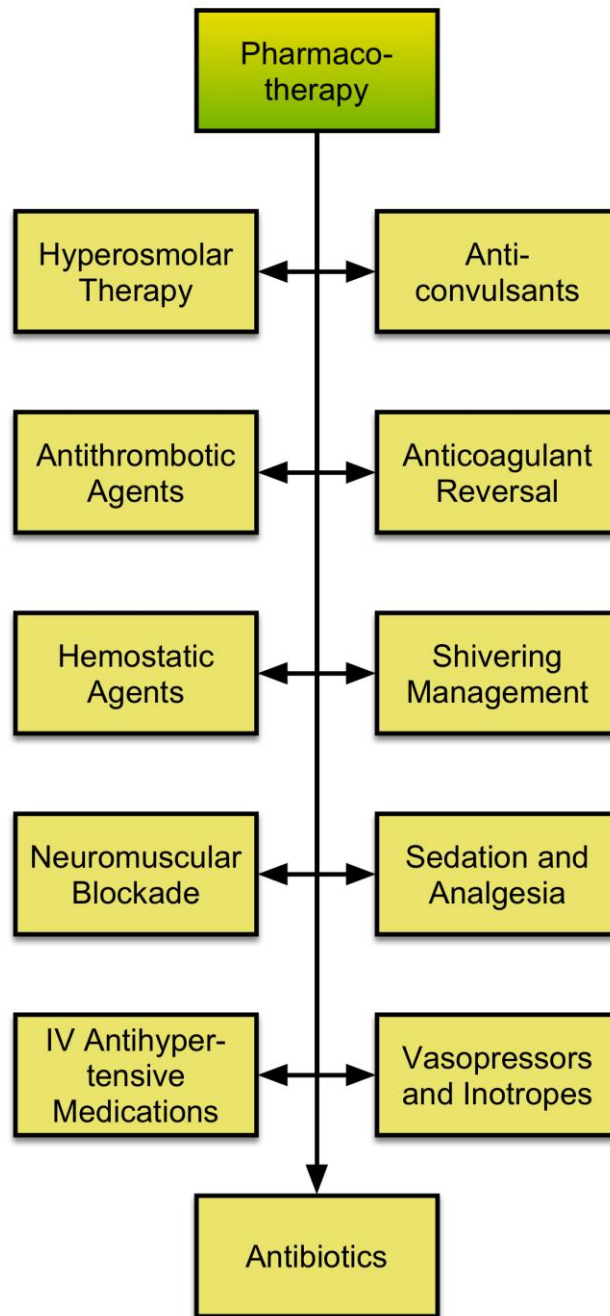


Emergency Neurological Life Support

Pharmacotherapy

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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 into cerebral tissue. Streptococcus pneumonia meningitis should be treated with dexamethasone (10mg IV every 6 hours for 4 days) in conjunction with antibiotics to decrease neurological sequelae. Selection of an appropriate antimicrobial should be based on the local antibiogram, drug resistance patterns, and age of the patient. See the ENLS protocol [Meningitis and Encephalitis](#) and [Spinal Cord Compression](#), and Pharmacotherapy for more detail on treating CNS infections.

CNS Pathogen	Recommended Therapy
<i>H. influenzae</i>	Third-generation cephalosporin
<i>S. pneumoniae</i>	Vancomycin (Trough goal: 15-20 mcg/ml) PLUS Third-generation cephalosporin
<i>N. meningitidis</i>	Third-generation cephalosporin
<i>L. monocytogenes</i>	Ampicillin
<i>S. agalactiae</i>	Ampicillin
<i>E. coli</i>	Third-generation cephalosporin
Staphylococci	Vancomycin (Trough goal: 15-20 mcg/ml)
HSV, VZV, CMV	Acyclovir 10 mg/kg/dose every 8 h based on IBW



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](#). Detailed drug information can be found in the Pharmacotherapy ENLS chapter.

Reversal of Warfarin														
Clinical Setting	INR	Treatment Options												
NO Bleeding Rapid reversal required (<24 hrs)	< 4.5	Vitamin K 2.5mg PO If urgent reversal needed (\leq 12 hrs) for procedure consider 4-factor PCC 25 IU/kg IV												
	4.5-10	Vitamin K 5 mg PO If urgent reversal needed (\leq 12 hrs) for procedure consider 4-factor PCC 35 IU/kg IV												
	> 10	Vitamin K 1-2 mg IV, repeat every 6-24 hours as necessary If urgent reversal needed (\leq 12 hrs) for procedure consider 4-factor PCC 50 IU/kg IV												
Serious or Life threatening bleeding	ANY INR	Give vitamin K 10 mg IV over 30 minutes If patient volume overloaded give PCC Recheck INR 30 minutes after PCC administered												
		<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 33%;">INR</th> <th style="width: 33%;">4-factor PCC dose</th> <th style="width: 33%;">Max dose</th> </tr> </thead> <tbody> <tr> <td>2-3.9</td> <td>25 units/kg</td> <td>2500 units</td> </tr> <tr> <td>4-6</td> <td>35 units/kg</td> <td>3500 units</td> </tr> <tr> <td>>6</td> <td>50 units/kg</td> <td>5000 units</td> </tr> </tbody> </table>	INR	4-factor PCC dose	Max dose	2-3.9	25 units/kg	2500 units	4-6	35 units/kg	3500 units	>6	50 units/kg	5000 units
		INR	4-factor PCC dose	Max dose										
		2-3.9	25 units/kg	2500 units										
		4-6	35 units/kg	3500 units										
>6	50 units/kg	5000 units												
If volume is needed give 15-20 ml/kg FFP Recheck INR after FFP administered														

Emergent Reversal of Factor Xa Inhibitors	
Apixaban (Eliquis) Rivaroxaban (Xarelto) Edoxaban (Savaysa®)	<ul style="list-style-type: none"> • If ingested within 3 hours, administer activated charcoal 50 g • Administer PCC 25-50 units/kg over 10 min <ul style="list-style-type: none"> ◦ If volume needed consider 15-20 ml/kg FFP <p><u>May consider (weak evidence):</u></p> <ul style="list-style-type: none"> • FFP 15-20 ml/kg • rFVIIa 20 mcg/kg and may repeat x 1 • FEIBA 25-50 units/kg

Emergent Reversal of Direct Thrombin Inhibitors	
Dabigatran (Pradaxa)	<ul style="list-style-type: none"> • If ingested within 3 hours, administer activated charcoal 50g • If aPTT elevated and life-threatening bleed, administer idarucizumab (Praxbind®) 5gm IV • Consider Emergent Hemodialysis if idarucizumab unavailable <p><u>May consider (weak evidence):</u></p> <ul style="list-style-type: none"> • FFP 15-20 ml/kg
Bivalirudin (Angiomax)	<ul style="list-style-type: none"> • Very short half-life (25 minutes), turn off infusion. • Monitor aPTT to confirm clearance • Supportive measures to control bleeding

Reversal of Heparin and Low Molecular Weight Heparin (LMWH)	
Unfractionated heparin	<ul style="list-style-type: none"> • Protamine neutralizes heparin. Dosing is based on time since last dose of heparin. <ul style="list-style-type: none"> ◦ Immediate: 1mg/100 units of heparin given (max = 50 mg) ◦ 30 minutes: 0.5 mg/100 units ◦ > 2 hours: 0.25 mg/100 units
Enoxaprin (Lovenox®) Dalteparin (Fragmin®)	<ul style="list-style-type: none"> • Protamine partially reverses the effect of LMWH (about 60%) • Protamine is not useful if more than 12 hours since last dose • Monitor anti-factor Xa activity
Fondaparinux (Arixtra®)	<ul style="list-style-type: none"> • Protamine is NOT helpful; supportive care <p><u>Weak evidence, but may consider either:</u></p> <ul style="list-style-type: none"> • PCC 50 units/kg • rFVIIa 20 mcg/kg (may repeat x 1)



Anticonvulsants

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 (Cerebryx®)	Load: 20 mg/kg IV Maintenance: 4-6 mg/kg/day divided in 2-3 doses
Valproate sodium (Depacon®)	Load: 20-40 mg/kg IV Maintenance: 10-15 mg/kg/day divided into 2-4 doses
Levetiracetam (Keppra®)	1000-3000 mg/day IV in 2 divided doses
Lacosamide (Vimpat®)	Load: 200-400 mg/day IV Maintenance: 200 mg every 12 hours
Phenobarbital	Load: 20 mg/kg IV 1-3 mg/kg/day divided into 1-3 doses

Refractory Status Epilepticus	
Midazolam (Versed®)	Bolus: 0.2 mg/kg IV Infusion: 0.05 - 2 mg/kg/hour
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/hour

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](#).

Recombinant t-PA 0.9 mg/kg (not to exceed 90 mg total dose) IV is the only 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.

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, 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.

Dosing:

- Tranexamic acid 1 g IV over 10 minutes every 4-6 hours
- Aminocaproic acid (Amicar) 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, and can worsen heart failure and pulmonary edema. For emergent use, HTS concentrations greater than 3.0% should be given through a central line, and 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

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	Initial dose: 2.5 mg/hour Titration: 2.5mg/hour every 15 minutes to goal BP (max = 15 mg/hour) Children: 0.5 mcg/kg/min to start; max 5 mcg/kg/min
Clevidipine	Initial dose: 1-2 mg/hour Titration: increase dose every 90 seconds to goal BP (maximum 32 mg/hour)
Esmolol	250-400 mcg/kg/min
Intermittent dosing	
Hydralazine	10 - 20 mg every 4 - 6 hours
Labetalol	10 - 80 mg every 10 min

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, provide skeletal muscle relaxation during mechanical ventilation, or manage shivering during temperature management. Short acting agents are preferred, and concomitant sedation is necessary. A 'train-of-four' stimulator should be used with a goal of 1-2 responses per 4 stimulations. Preferred agents are:

Agent	Dosing	Precautions / Comments
Succinylcholine	<ul style="list-style-type: none"> • Adults: 0.5-1.1 mg/kg IV <ul style="list-style-type: none"> • 2-4 mg/kg IM • Adolescents: 1 mg/kg IV • Children: 2 mg/kg IV 	Severe hyperkalemia may occur in muscle trauma, burns, neuromuscular disease, spinal cord injury, and stroke
Cisatracurium	Adults 0.15 mg/kg IV (up to 0.2 mg/kg) Children: 0.1 mg/kg IV	Longer half-life in elderly Can be used as continuous infusion Eliminated via enzymatic pathway
Rocuronium	Adults: 0.6 mg/kg IV (up to 1.2 mg/kg) Children: 0.45-0.6 mg/kg IV	Prolonged duration in renal failure

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, so lower doses of both agents can be used to achieve the desired effect.

Propofol is often avoided in children because of risk of Propofol Infusion Syndrome. 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®)	<ul style="list-style-type: none"> Maintenance infusion: 5-100 mcg/kg/min
Dexmedetomidine (Precedex®)	<ul style="list-style-type: none"> Loading dose is NOT recommended Maintenance infusion: 0.2-0.7 mcg/kg/hour, max 1.4 mcg/kg/hour
Lorazepam (Ativan®)	<ul style="list-style-type: none"> Loading: 0.02-0.04 mg/kg Intermittent: 0.02-0.06 mg/kg every 2-6 hour Maintenance infusion: 0.01-0.1 mg/kg/hour
Midazolam (Versed®)	<ul style="list-style-type: none"> Loading: 0.01-0.05 mg/kg Maintenance infusion: 0.01-0.1 mg/kg/hour
Analgesics	Dose
Fentanyl (Duragesic®)	<ul style="list-style-type: none"> Bolus: 12.5-100 mcg or 1-2 mcg/kg IVP Maintenance infusion: 0.7-10 mcg/kg/hour or 25-700 mcg/hour
Morphine (Duramorph®, MS Contin®)	<ul style="list-style-type: none"> Bolus: 2-10 mg IVP Intermittent dose: 2-8 mg every 3-4 hour Maintenance infusion: 0.8-30 mg/hour

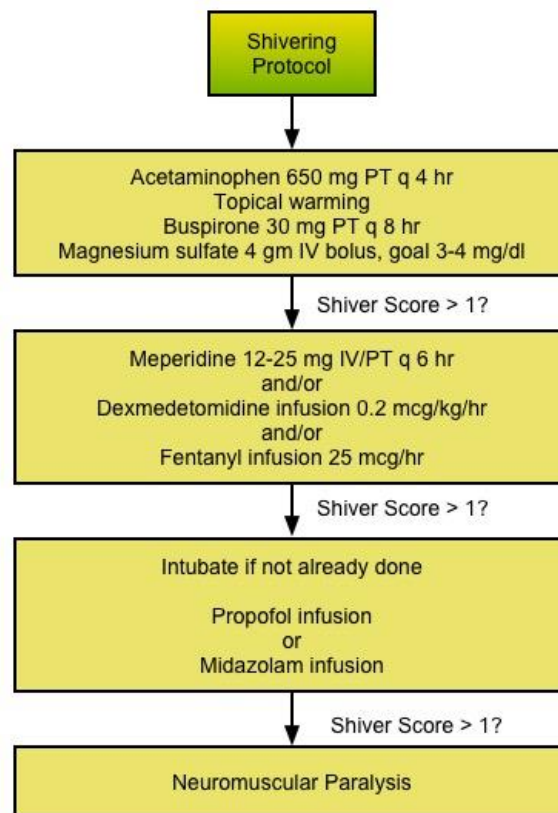


Shivering Management

Follow a protocol

During temperature management and induced hypothermia, 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



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.



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. We have done our best to indicate adult and pediatric dosing of medications but know that these are Western medications primarily so may differ in name from drugs internationally.

Topic Co-Chairs:

Gretchen Brophy, PharmD, BCPS, FCCP, FCCM, FNCS

Theresa Human, PharmD, BCPS, FNCS

Lori Shutter, MD, FCCM, FNCS



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	Dose	Comments
Mixed α / β receptor agonists		
Norepinephrine	2-5 mcg/min, or 0.02-0.06 mcg/kg/min	First line agent for septic shock
Epinephrine	2-5 mcg/kg/min	First line agent for septic shock
Dopamine	Dopa- 1-3 mcg/kg/min β : 3-10 mcg/kg/min α : 10-20 mcg/kg/min	Effective at multiple receptors
Ephedrine	5 to 25 mg slow IVP, may repeat in 5 to 10 minutes	Oral formulation, dose at 25 - 50 mg every 8 - 12 hours
Pure α receptor agonist		
Phenylephrine	10-300 mcg/min, or 0.1-1 mcg/kg/min	May cause reflex bradycardia
Non-adrenergic		
Vasopressin	0.04 units/min	May demonstrate synergistic effect with other vasopressors
Inotropes		
Dobutamine (mixed α / β)	2.5-10 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.