Management of Non-Chemo Drug Extravasation

Some non-chemo vesicant drugs may be especially likely to harm soft tissue with infiltration or extravasation.[21,22] **They can be classified as**:[16,17,21,22,25]

- **Hyperosmolar meds** (e.g., hypertonic saline, parenteral nutrition, sodium bicarbonate) cause osmotic shifts leading to inflammation and cell death.
  - Common preventive strategies: Infuse through a central line. In particular, ≥600 mOsm/L may not be as well tolerated by peripheral veins.[21,22] (For reference, the osmolarity of 0.9% sodium chloride is 308 mOsm/L and for 3% saline it's 1,026 mOsm/L.)
- **Drugs with very high or low pH** (e.g., acyclovir, amiodarone, phenytoin, vancomycin), which damage tissue and cause vasoconstriction.
  - Common preventive strategies: Dilute medication and infuse slowly. See detailed recommendations below.
- **Vasopressors** (e.g., norepinephrine, phenylephrine, vasopressin), which cause ischemia and necrosis.
  - Common preventive strategies: Infuse through a central line, especially for longer durations and if a large peripheral vein is not available.[25]

General treatment for non-chemo extravasations includes these steps:[1-3,15,17,18,21,22,24]

- Immediately stop the infusion.
- Aspirate residual drug through the needle or catheter.
- Elevate the affected limb to minimize swelling.
- Apply a **cold** (to reduce swelling and localize the agent) **OR** a **warm** (for vasodilation and to disperse the agent) compress. Apply dry compresses for 20 minutes every 6 to 8 hours for up to 3 days.[2,22,24] The choice of **cold or warm** will depend on the offending agent.
- Administer an analgesic.

Drug treatments depend on the causative agent, and may include the following: (doses below have been cited in the literature):

- To distribute the causative agent away from the site (commonly used for hyperosmolar and pH-related extravasation injury):
  - **Hyaluronidase** (US only) 150 units/mL. Dilute to 15 units/mL with 0.9% sodium chloride. Inject 0.2 mL intradermally, into five sites around the extravasation area.[8,22] Administer within about one hour of extravasation.[18,22] Note that warm compresses may complement the action of hyaluronidase, while cold compresses may theoretically act in opposition.[21]
- To counteract local vasoconstriction (commonly used for vasopressor extravasation):
  - **Phentolamine** 5 to 10 mg, in 10 to 20 mL 0.9% sodium chloride, intradermal or subcutaneously, around the edges of the extravasation area as multiple small injections (e.g., 0.2 to 1 mL at a time [using a new needle for each injection]).[21,22] Administer as soon as possible to prevent tissue necrosis (best outcomes within 12 hours of extravasation).[22,27]
  - **Terbutaline** (US only) 1 mg in 10 mL 0.9% sodium chloride (for larger areas) or 1 mL 0.9% sodium chloride (for localized ischemia). Administer subcutaneously at the edges of the extravasation area.[22,24,25] Can repeat dose after 15 minutes.[22]
  - **Nitroglycerin** topical formulations used include patch or 2% ointment (US only), as a 1-inch strip, every 8 hours as needed.[14,21,22,24]

Silver sulfadiazine cream may help with extravasation of hyperosmolar drugs.[21] Topical or systemic steroids have not been shown to be effective and can slow healing and promote infection.[21] Severe cases may require surgical intervention.[16,17,22] **Note that treatments are often based on case reports and animal data**.

The following chart contains non-chemo drugs that have some evidence for treatment of extravasation. Warm or cold compresses are included if data supporting use of one or the other are available. Some preventive strategies are also included. Additional sources of information for treating extravasations of drugs not listed may include drug manufacturers, poison control centers, or hospital protocols (consider developing protocols, if you don't already have them).

Drug	Treatment Options	Comments
Calcium salts	• **Warm** compress • Hyaluronidase[22]	• **Mechanism**: hyperosmolarity[22] • Dilute calcium chloride to 3 mg/mL or less when administering via peripheral line.[20,28]
Contrast media	• **Cold** or **warm** compress to alleviate symptoms[22] • Hyaluronidase (data are conflicting)[22]	• **Mechanism**: hyperosmolarity[3,6] • Tissue damage is most likely with ionic agents.[3,6,7]
Dextrose (≥10%)	• Hyaluronidase[8]	• **Mechanism**: hyperosmolarity[8]
Mannitol	• **Warm** compress[22] • Hyaluronidase[9,22]	• **Mechanism**: hyperosmolarity[9,21]
Methylene blue	• Topical nitroglycerin[22] • Phentolamine[22]	• **Mechanism**: vasocontriction[22]
Nafcillin (US only)	• Hyaluronidase[10]	• **Mechanism**: not clear; possibly hyperosmolarity[22]
Parenteral nutrition	• **Warm** compress[22] • Hyaluronidase[1] • Topical nitroglycerin[1,22]	• **Mechanism**: hyperosmolarity[1] • Formulations with up to 900 mOsm/L are considered safe for peripheral administration.[23]
Phenytoin	• **Warm** compress[11,22] • Hyaluronidase[12] • Topical nitroglycerin[11]	• **Mechanism**: high pH[a,11] (vehicle composition and formation of precipitates may also contribute) • Extravasation may result in "purple glove syndrome."[11]
Potassium salts	• Hyaluronidase[22]	• **Mechanism**: hyperosmolarity[22] • Adult recommended infusion rate is 10 mEq/hour.[20]

Drug	Treatment Options	Comments
		• Concentration limits for peripheral administration may vary by institution. Most allow 0.1 mEq/mL to be infused peripherally, and some may allow 0.2 mEq/mL to be infused via peripheral line.[20]
Promethazine	• No proven treatment.[4] Sympathetic blockade (i.e., nerve block) and systemic heparin therapy have been used to manage inadvertent intra-arterial administration and extravasation of promethazine based on animal data.[4,19,22]	• **Mechanism**: low pH,[a] chemical irritant[19] • Suggested preventive strategies include:[5] o Dilute doses in 0.9% sodium chloride to allow for slower administration. o Start with smaller doses such as 6.25 to 12.5 mg. o Infuse doses through a large vein over 10 to 15 minutes. • ISMP recommends removing promethazine from formulary and all areas of the hospital.[29]
Saline (3%)	• Hyaluronidase[22]	• **Mechanism**: hyperosmolarity[22]
Vasopressors • Dobutamine • Dopamine • Epinephrine • Norepinephrine • Phenylephrine • Vasopressin	• **Warm** compress[21,22,24] • Phentolamine[13] • Terbutaline[24] • Topical nitroglycerin[14,22,24]	• **Mechanism**: vasoconstriction, low pH[a,13,21,22] • Infusing pressors through central lines is usually recommended, but some data suggest the risk of extravasation injuries from infusing vasopressors through peripheral lines may be lower than thought.[26] • Hyaluronidase or cold compresses can extend/worsen vasoconstriction.[21c] • Topical nitroglycerin is preferred over phentolamine for extravasation due to vasopressin.[24]

a. Do not attempt to neutralize acidic or basic extravasations due to the potential for heat and gas formation.[21,22]

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

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B	Inconsistent or limited-quality patient-oriented evidence.*	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69:548-56. https://www.aafp.org/pubs/afp/issues/2004/0201/p548.html.]

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Vasopressors for Shock

Updated February 2025

The first chart below addresses choice of vasopressor for different shock states. For dosing and additional drug information (e.g., pharmacology), see the second chart, below.
Interactive note: Roll over **blue text** to view additional information.

Clinical Scenario	Preferred Vasopressors
Cardiogenic shock	• Initial vasopressor choice depends on whether patient is hypotensive or normotensive.[1] • If hypotensive (e.g., MAP ≤65 mmHg, SBP <90 mmHg, evidence of hypoperfusion):[1] » Start with **norepinephrine**.[1] » Add **doB**utamine or **milrinone** to address low CO.[1] • If blood pressure is preserved, but CO is low:[1] » Start with **doB**utamine or **milrinone**.[1] » Add **norepinephrine** if hypotension develops.[1] • For persistent hypotension, consider vasopressin.[1] • **Special situations**: aortic regurgitation (norepinephrine or epinephrine), aortic stenosis (norepinephrine [phenylephrine if systolic function is preserved]), mitral stenosis (phenylephrine +/- vasopressin).[29]
Septic shock	• **Norepinephrine** (first-line).[4] » If norepinephrine is not available, consider **epinephrine** or **doP**amine.[4] • Consider adding **vasopressin** if MAP target (65 mmHg) not achieved with norepinephrine 0.25 to 0.5 mcg/kg/min.[4] • Consider adding epinephrine for refractory hypotension.[4] • **Angiotensin II** could be used as an adjunct in refractory shock or to limit norepinephrine dose.[4,5] » Based on study population, consider for patients who are hypotensive despite fluid and pressors (e.g., NE, vasopressin, EPI) at a median "NE equivalent" dose of 0.33 mcg/kg/min.[6] • For cardiac dysfunction and hypoperfusion after optimization of volume and MAP, consider **adding doB**utamine to norepinephrine, or **switching to epinephrine alone**.[4] • See our chart, *Sepsis Management in Adults: Pharmacotherapy Focus*, for more information.
Anaphylactic shock	• Epinephrine[3] • Angiotensin II (adjunct[7,8]) » FDA-approved for distributive shock, but most patients in the major clinical trial had septic shock.[6,7]

Drug	Dosing (also see footnotes a and b)	Comments/Pharmacology
Angiotensin II (*Giapreza*)	• Note that dosing is in **NANO**grams/kg/min. • See product information for dosing.	• Causes vasoconstriction and aldosterone release.[7] • May reduce mortality in certain patient subsets (e.g., patients with acute kidney injury requiring kidney replacement therapy or higher renin concentrations).[5] • Has not been studied first-line or compared to other add-on pressors. • Consider for distributive shock refractory to vasopressin or epinephrine.[20]
DoButamine	• Initial 2.5 to 5 mcg/kg/min.[13] • Titration 2.5 to 5 mcg/kg/min every 5 to 15 min.[13] • Max 20 mcg/kg/min.[9]	• Clinical effects depend on dose and baseline physiologic state.[4,13] • Less arrhythmogenic than dopamine.[11] • Tolerance may develop, necessitating dosage increase to get the same effect.[12]
DoPamine	• Initial 2 to 5 mcg/kg/min.[2] • Titration 2 to 5 mcg/kg/min every 5 to 15 minutes.[13] • Max 20 mcg/kg/min.[13] • Septic shock (range) 2 mcg/kg/min to 20 mcg/kg/min)	• Associated with higher risk of arrhythmia and death in septic and cardiogenic shock vs. NE.[1,4,9] • Higher risk of tachycardia and arrhythmias compared to doButamine, milrinone, or EPI.[13] • Beta-1 activity may be useful to increase CO, but arrhythmia risk limits use.[4] • Pharmacologic effects are dose-dependent.
Epinephrine	• Initial 0.02 to 0.05 mcg/kg/min.[13] • Titration 0.02 to 0.05 mcg/kg/min every 5 to 15 min.[13] • **Septic shock** (usual dose) 0.1 to 0.3 mcg/kg/min.[28] • **Cardiogenic shock** (usual dose) 0.01 to 0.5 mcg/kg/min.[9] • **Anaphylactic shock** 5 to 15 mcg/min.[14]	• A continuous infusion is recommended for anaphylaxis refractory to two intermittent EPI doses (IM or IV) and fluid resuscitation.[3,10] • Has more beta-agonist activity than norepinephrine.[20] • Pharmacologic effects are dose-dependent. • EPI impairs splanchnic perfusion compared to NE or dopamine.[13] • Increases glucose.[15] • EPI can increase lactate levels.[15] Due to downregulation of beta-1 receptors, EPI effect on lactate diminishes after 12 hours.[15]

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Drug	Dosing (also see footnotes a and b)	Comments/Pharmacology
Midodrine	• Initial 10 mg every 8 hours.[24] • Titration 10 mg/dose.[26] • Max 40 mg every 8 hours.[26] • Decrease by 5 to 10 mg/day if BP stays at goal off vasopressor for 24 hours.[26]	• Alpha-1 agonist.[27] Increases BP.[27] May cause reflex bradycardia.[27] • Used to help discontinue IV vasopressors.
Milrinone	• Usual dose 0.125 to 0.75mcg/kg/min.[9] • Sometimes a 50 mg/kg bolus is given, but may cause hypotension.[9,13]	• Phosphodiesterase-3 inhibitor.[13] Increases CO, decreases SVR.[9] • Reduces SVR, PVR, and PCWP more than doButamine.[9,13] » More likely to cause hypotension than doButamine.[13] • Lower risk of tachycardia and arrythmias than doButamine.[13] • Consider over dobutamine in patients who have recently received a beta-blocker.[13] • Longer half-life than dobutamine, so harder to titrate.[13] • Requires renal dose reduction in kidney impairment.[13]
Norepinephrine	• Initial 0.01 to 0.04 mcg/kg/min.[13] • Titration 0.02 to 0.04 mcg/kg/min every 5 to 15 min.[13] • **Septic shock** (range) 0.02 to 0.19 mcg/kg/min.[16] • **Cardiogenic shock** (usual dose) 0.05 to 0.4 mcg/kg/min.[9]	• **For septic shock**: » Consider adding another pressor when dose nears 0.3 mcg/kg/min.[4,17] » Doses ≥1 mcg/kg/min are associated with higher mortality.[30] • Predominately an alpha agonist.[13] Increases SVR and MAP.[1,4] • Some beta-1 agonist effect, which increases CO.[13] Little effect on HR except at high doses.[4,13] • Lower risk of tachyarrhythmias than doPamine or EPI.[13] • Associated with lower risk of arrhythmia and death in septic and cardiogenic shock compared to **doP**amine.[1,4,9]
Phenylephrine	• Initial 0.1 to 0.3 mcg/kg/min.[13] • Titration 0.1 to 0.4 mcg/kg/min every 5 to 15 min.[13] • Cardiogenic shock (usual dose), 0.1 to 10 mcg/kg/min.[9]	• Alpha-1 agonist.[13] Increases SVR and MAP.[13] • Can reduce CO and HR (due to increased afterload and reflex bradycardia).[1,13,18] • In septic shock, associated with higher mortality than NE.[20] • Consider a max of 1.5 to 2 mcg/kg/min to limit tissue ischemia.[13] • No survival advantage vs NE for septic shock.[19] • Consider for distributive shock refractory to NE, vasopressin, or EPI.[20]
Vasopressin	• **Septic shock**, 0.03 units/min (fixed dose).[4] • **Cardiogenic shock** (usual dose), 0.02 to 0.04 units/min.[9]	• A vasoconstrictor.[20] • In **septic shock**, dose can be increased to 0.06 units/min., but ischemic risk may be > benefit.[4,13,21] • For **septic shock**, consider starting when NE dose reaches 0.25 to 0.5 mcg/kg/min for NE-sparing effect to reduce tachycardia and arrhythmias [Evidence Level A-1].[4,20,21] • Limited data suggest vasopressin use may be associated with lower mortality in septic shock at 90 days.[20] • Reduces risk of atrial fibrillation when used with a catecholamine vasopressor (e.g., NE) in **distributive shock**.[22] • No outcomes data in cardiogenic shock. • Consider the patient's dose and use an appropriate bag size to minimize waste.

Abbreviations: BP = blood pressure; CO = cardiac output; EPI = epinephrine; HR = heart rate; MAP = mean arterial pressure; NE = norepinephrine; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; SBP = systolic blood pressure; SVR = systemic vascular resistance

Footnotes:

a. **Goals** of therapy for shock: achieve and maintain adequate tissue perfusion.[9] Consider a MAP target of 65 mmHg in adults based on data from other populations (recommended in septic shock).[4,9] Balance MAP target with vasopressor side effects (e.g., arrhythmias, myocardial ischemia).[9] Some markers to consider include lactate, mixed or central venous oxygen saturation, urine output, serum creatinine, liver function tests, cognitive function, and temperature.[4,9,20] Individualize targets.[9]

b. **Dosing**. Doses are variable and not well-defined for most indications. Assess and correct volume status before using IV vasopressors.[20] To minimize side effects (e.g., myocardial or other organ ischemia, arrhythmias), use vasopressors for the shortest time at the lowest dose necessary to maintain organ function.[13,25]

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