



Clinical Pharmacology & Toxicology Pearl of the Week

~ Drug-Induced Edema ~

Drug-induced edema is caused by many drugs & can coincide with or worsen pre-existing peripheral edema

Tissue edema develops due to one or more of the following:

- Increased vascular permeability
- Increased hydrostatic pressure
- Decreased oncotic pressure in the blood vessels

Drugs that directly or indirectly upset the balance between hydrostatic and oncotic pressures (Figure 1) or that alter vascular permeability have the potential to cause tissue edema.

Drug-related changes to hydrostatic pressure occur via \uparrow blood pressure (BP) &/or \uparrow blood volume (BV; either \uparrow total body volume via Na^+ + H_2O retention or \uparrow blood pooling via vaso/venodilation)

Drug-induced alteration to vascular permeability can occur via numerous mechanisms, some of which include:

- Bradykinin (describe what happens with bradykinin that vascular permeability is affected)
- Histamine release from mast cells
- Increased nitric oxide release
- Activation of the complement cascade

Table 1: Drugs implicated in causing peripheral edema

<u>Common Culprit Drugs</u>	<u>Edema Mechanism</u>	<u>Pharmacologic/Physiologic Mechanism</u>
Non-DHP CCBs: amlodipine, nifedipine	\uparrow hydrostatic pressure	Precapillary vasodilation via L-type calcium channels
Neuropathic pain agents: gabapentin, pregabalin	\uparrow hydrostatic pressure	Precapillary vasodilation via L-type calcium channels
Non-Steroidal Anti-Inflammatories: ibuprofen, ketorolac, naproxen	\uparrow BV & BP	Decreased GFR via inhibition of prostaglandins --> activation of renin angiotensin aldosterone system (RAAS) , sodium & water retention
ACE inhibitors: ramipril, perindopril, enalapril etc.	\uparrow vascular permeability	Decreased degradation of bradykinin
Dopamine agonists: pramipexole, ropinirole	Hypothesis is \uparrow BV	? via activation of RAAS system
Insulin	\uparrow BV	Activation of sodium channels in the distal nephron (mineralocorticoid-like activity)
Nitrates	\uparrow venous hydrostatic P	Potent venodilatation via Nitric Oxide & cGMP --> blood pooling
Steroids: glucocorticoids, mineralocorticoids, estrogen, testosterone	\uparrow BV & BP	RAAS activation, mineralocorticoid receptor activation --> sodium & water retention
Antipsychotics: quetiapine, olanzapine, clozapine	Hypothesis is ?compensatory \uparrow BV	many have alpha-1 antagonist properties --> orthostasis, activation of RAAS --> sodium & water retention

Management involves deciding whether the edema is severe or life-threatening (ie: ACE-inhibitor angioedema), in which case the drug should be discontinued immediately.

If it is not severe/life threatening, then depending on the mechanism of edema, options include stopping/switching the medication, using diuretics (beware of the prescribing cascade if doing so), RAAS-blocking agents (beta blockers, ACEi or ARBs) & compression stockings to control the edema.

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory \(ARD\)](#) by searching “Pharmacology” from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory \(ARD\)](#) by searching “Toxicology” from the ARD home page.

More CPT Pearls of the Week can be found [HERE](#).

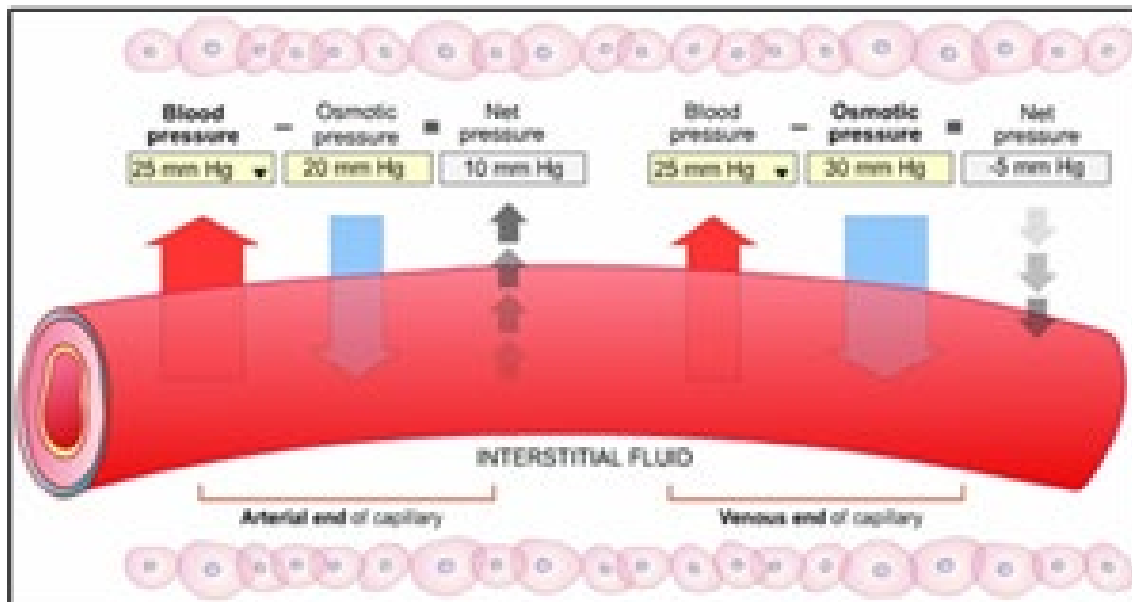


Figure 1 : Arterial & Venous Pressure Gradients

Created: Feb 28, 2019

Reviewed: Feb 19, 2025