### Name: Mannitol

Class: Diuretic (Non-Metabolized Osmotic Diuretic)

**Mech**.: Filtered into tubule space  $\rightarrow \uparrow \uparrow$  tubular fluid osmolality  $\rightarrow \downarrow$  fluid reabsorption  $\rightarrow \uparrow$  excretion of water and some Na<sup>+</sup>.

**Absorption**: IV only (oral  $\rightarrow$  osmotic diarrhea). Takes effect in 10 min. Dist.:

# Metab.:

Excretion, t : 1.2 hr.

**Toxicity/S.E.s**: ↑ plasma osmolality. If GFR is reduced (e.g., renal failure or CHF), mannitol stays in ECF  $\rightarrow$  water movement from cells to ECF  $\rightarrow$  potential production/exacerbation of heart failure and hyponatremia. C/i-CHF, renal failure.

Utility: Prophylaxis against renal dysfunction (e.g., in major surgical procedures). Special Features:

#### Name: Furosemide (Lasix)

Class: Diuretic (Loop Diuretic)

**Mech.**: Blocks the Na<sup>+</sup>/ $K^+$ /Cl<sup>-</sup> co-transporter in the apical membrane of the thick ascending limb of Henle's loop  $\rightarrow \uparrow$  excretion of urinary water, Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, & Mg<sup>2+</sup>. Also causes venous and renal vasodilation.

Absorption: Oral, IV. Takes effect in 20 min. Metab.:

Dist.:

**Excretion**, t: 1-1.5 hr. Shorter duration than thiazides.

Toxicity/S.E.s: Hypokalemia (esp. dangerous if pt. is on digitalis), Ca<sup>2+</sup> & Mg<sup>2+</sup> depletion, metabolic alkalosis, volume contraction, mild hyperglycemia, thiazide-like lipid changes, sulfonamide allergy cross-rxn, ototoxicity. C/i-pts. susceptible to volume contraction from excessive diuresis (e.g., elderly), and pts. susceptible to problems w/hypokalemia (e.g., cirrhosis, digitalis). Adverse rxn w/lithium, aminoglycosides. Altered doses of anti-diabetic agents required.

Utility: Diuresis for hypertension when a short-acting diuretic is indicated. Treat HTN refractory to thiazides. Very useful in conditions refractory to less potent diuretics (e.g., CHF, renal insufficiency, nephrotic synd.). Treat hypercalcemia.

Special Features: Most potent diuretics available. Can cause excretion of up to 20% of filtered Na<sup>+</sup>

Name: Acetazolamide (Diamox)		
Class: Diuretic (Carbonic Anhydrase Inhibitor)		
Mech.: Inhib. of CA → ↓ reabsorption of NaHCO <sub>3</sub> in prox. tubule. K+ is exchanged for Na+ in distal tubule. Net = ↑ in urinary HCO <sub>3</sub> , K <sup>+</sup> , and water excretion.		
Absorption: Oral. Takes effect in 30 min.		
Dist.:		
Metab.:		
Excretion, t_: 13 hr.		
Toxicity/S.E.s: Metabolic acidosis, hypokalemia. C/i—cirrhosis.		
Utility: Treat glaucoma and ↑ CNS pressure. Alkalinize urine. Prevent altitude sickness. Diuresis.		
<b>Special Features</b> : Relatively weak diuretic. Generally prescribed for non- diuretic purposes. Effectiveness reduced w/continued therapy because plasma [HCO <sub>3</sub> <sup>-</sup> ] falls.		

# Name: Bumetanide (Bumex)

**Class**: Diuretic (Loop Diuretic)

**Mech**.: Blocks the Na<sup>+</sup>/K<sup>+</sup>/Cl<sup>-</sup> co-transporter in the apical membrane of the thick ascending limb of Henle's loop  $\rightarrow \uparrow$  excretion of urinary water. Na<sup>+</sup>. K<sup>+</sup>. Ca<sup>2+</sup>, & Mq<sup>2+</sup>. Also causes venous and renal vasodilation.

Absorption: Oral. IV. Takes effect in 20 min.

Metab.:

**Excretion**, **t** : 1-1.5 hr.

Dist.:

**Toxicity/S.E.s**: Hypokalemia (esp. dangerous if pt. is on digitalis). Ca<sup>2+</sup> & Mg<sup>2+</sup> depletion, metabolic alkalosis, volume contraction, mild hyperglycemia, sulfonamide allergy cross-rxn, ototoxicity. C/i-pts. susceptible to volume contraction from excessive diuresis (e.g., elderly), and pts. susceptible to problems w/hypokalemia (e.g., cirrhosis, pts. taking digitalis).

**Utility:** Diuresis for hypertension when a short-acting diuretic is indicated. Very useful in conditions refractory to less potent diuretics, including CHF, renal insufficiency, and nephrotic synd. Also used to treat hypercalcemia.

Special Features: Most potent diuretics available. Far more potent than furosemide. Can cause excretion of up to 20% of filtered Na<sup>+</sup>.

### Name: Ethacrynic Acid (Edecrin)

Class: Diuretic (Loop Diuretic)

Mech.: Blocks the Na<sup>+</sup>/K<sup>+</sup>/Cl<sup>-</sup> co-transporter in the apical membrane of the thick ascending limb of Henle's loop → ↑ excretion of urinary water, Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, & Mg<sup>2+</sup>. Also causes venous and renal vasodilation.

Metab.:

**Absorption**: Oral, IV. Takes effect in 20 min.

Dist.:

#### **Excretion**, **t**\_: 1-1.5 hr.

- **Toxicity/S.E.s**: Hypokalemia (esp. dangerous if pt. is on digitalis), Ca<sup>2+</sup> & Mg<sup>2+</sup> depletion, metabolic alkalosis, volume contraction, mild hyperglycemia, ototoxicity. C/i—pts. susceptible to volume contraction from excessive diuresis (e.g., elderly), and pts. susceptible to problems w/hypokalemia (e.g., cirrhosis, pts. taking digitalis).
- **Utility**: Diuresis for hypertension when a short-acting diuretic is indicated. Very useful in conditions refractory to less potent diuretics, including CHF, renal insufficiency, and nephrotic synd. Also used to treat hypercalcemia.
- **Special Features**: More ototoxic than other loop diuretics. Most potent diuretics available. Can cause excretion of up to 20% of filtered Na<sup>+</sup>.

## Name: Chlorthalidone (Hygroton)

**Class**: Diuretic (Thiazide)

Mech.: Inhib. Na<sup>+</sup> & Cl<sup>-</sup> transport in the cortical thick ascending limb and the early distal tubule → ↑ NaCl and water excretion, & ↓ excretion of Ca<sup>2+</sup> and uric acid.

**Absorption**: Oral  $\rightarrow$  good absorption. Takes effect in 1 hr.

# Dist.:

Metab.:

Excretion, t\_:

- **Toxicity/S.E.s**: Hypokalemia, hyponatremia, hyperuricemia, hypercalcemia, metabolic alkalosis, postural hypotension, hyperglycemia (in patients w/DM), and rare hypersensitivity rxns. C/i—pts susceptible to problems with hypokalemia (cirrhosis, pts on digitalis), hyperuricemia (gout), or hypercalcemia.
- **Utility**: Treat hypertension, CHF, nephrotic synd., other Na<sup>+</sup>-retaining states. Reduce Ca<sup>2+</sup> excretion (e.g., prevention of kidney stones).
- **Special Features**: Most commonly prescribed class of diuretics. Milder diuretic action than loop diuretics. Rel. ineffective in renal insuff.

## Name: Hydrochlorothiazide (Hydrodiuril)

Class: Diuretic (Thiazide)

Mech.: Inhib. Na<sup>+</sup> & Cl<sup>-</sup> transport in the cortical thick ascending limb and the early distal tubule → ↑ NaCl and water excretion, & ↓ excretion of Ca<sup>2+</sup> and uric acid.

**Absorption**: Oral  $\rightarrow$  good absorption. Takes effect in 1 hr.

Dist.: Metab.: Excretion, t\_: Short duration of action. Toxicity/S.E.s: Hypokalemia, hyponatremia, hyperuricemia, weakness, hypercalcemia, metabolic alkalosis, postural hypotension, hypercholesterolemia, hypertriglyceridemia, hyperglycemia (in patients w/DM), and rare hypersensitivity rxns. C/i—pts susceptible to problems with hypokalemia (cirrhosis, pts on digitalis), hyperuricemia (gout), or hypercalcemia. Adverse rxns w/digitalis, lithium. Altered doses of anti-diabetic agents required. Long-term NSAID use may decrease anti-HTN effects.

- **Utility**: Treat hypertension, CHF, nephrotic synd., other Na<sup>+</sup>-retaining states. Reduce Ca<sup>2+</sup> excretion (e.g., prevention of kidney stones).
- **Special Features**: Most commonly prescribed class of diuretics. Most frequently used anti-HTN class of agents. Milder diuretic action than loop diuretics. Rel. ineffective in renal insuff.

### Name: Spironolactone (Aldactone)

Class: Diuretic (Potassium Sparing Diuretic) (Aldosterone Antagonist)

Mech.: Competitive inhib. of aldosterone → block of aldost.-stim. Na<sup>+</sup> reabsorption and K<sup>+</sup>/H<sup>+</sup> excretion in late distal tubule and collecting duct. Also reduces aldost.-stim. ammoniagenesis throughout the nephron.

Absorption: Oral. Takes up to 2 days to be effective.

Dist.:

Metab.: Hepatic.

Excretion, t\_: 20 hr.

**Toxicity/S.E.s**: Hyperkalemia, gynecomastia, amenorrhea. Absolutely contraindicated w/hyperkalemia.

Utility: Most efficacious in pts. w/high plasma levels of aldosterone (e.g., 1°

hyperaldosteronism due to an adrenal tumor or hyperplasia;  $2^\circ$  hyperaldost. due to cirrhosis, etc.).

**Special Features**: Only diuretic that acts through the blood side of the tubule. Rel. weak diuretic.

<ul> <li>Name: Metolazone (Mykrox)</li> <li>Class: Diuretic (Thiazide-Like)</li> <li>Mech.: Inhib. Na<sup>+</sup> &amp; Cl<sup>-</sup> transport in the cortical thick ascending limb and the early distal tubule → ↑ NaCl and water excretion, &amp; ↓ excretion of Ca<sup>2+</sup> and uric acid.</li> <li>Absorption: Oral → good absorption. Takes effect in 1 hr.</li> <li>Dist.: Metab.: Excretion, t_:</li> <li>Toxicity/S.E.s: Hypokalemia, hyponatremia, hyperuricemia, hypercalcemia, metabolic alkalosis, postural hypotension, hyperglycemia (in patients w/DM), and rare hypersensitivity rxns. C/i—pts susceptible to problems w/hypokalemia (cirrhosis, pts on digitalis), hyperuricemia (gout), or hypercalcemia.</li> <li>Utility: The only distal nephron diuretic efficacious in patients w/severe renal insufficiency. Treat hypertension, CHF, nephrotic synd., other Na<sup>+</sup>- retaining states. Reduce Ca<sup>2+</sup> excretion (e.g., prevention of kidney stones).</li> <li>Special Features: Strongest inhib. of Na<sup>+</sup> &amp; water reabsorption of the thiazide and thiazide-like diuretics. Often given in comb. w/a loop diuretic. Milder</li> </ul>	<ul> <li>Name: Triamterene (Dyrenium)</li> <li>Class: Diuretic (Potassium Sparing Diuretic)</li> <li>Mech.: Inhib. Na<sup>+</sup> channel in the apical membrane of the late distal tubule and collecting duct → block of electrochemical gradient that drives K<sup>+</sup> &amp; H<sup>+</sup> secretion → diuresis &amp; ↓ excretion of K<sup>+</sup> &amp; H<sup>+</sup>. Weak anti-HTN activity.</li> <li>Absorption: Oral Dist.:</li> <li>Metab.:</li> <li>Excretion, t_: 1° = kidney. 3 hr.</li> <li>Toxicity/S.E.s: Hyperkalemia (most severe), n/v (most common), metabolic acidosis. Hyponatremia may occur in old folks. Absolutely contraindicated with hyperkalemia. Adverse rxns w/lithium, ACE inhibitors. Rare renal failure w/NSAIDs.</li> <li>Utility: Usu. given w/another diuretic (often thiazide or loop). Combination usu. → normal K<sup>+</sup> excretion. Used to prevent or correct hypokalemia, and to avoid K<sup>+</sup> depletion in pts. on digitalis.</li> <li>Special Features: Rel. weak diuretic.</li> </ul>
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# Name: Amiloride (Midamor)

Class: Diuretic (Potassium Sparing Diuretic)

**Mech**.: Inhib. Na<sup>+</sup> channel in the apical membrane of the late distal tubule and collecting duct  $\rightarrow$  block of electrochemical gradient that drives K<sup>+</sup> & H<sup>+</sup> secretion  $\rightarrow$  diuresis &  $\downarrow$  excretion of K<sup>+</sup> & H<sup>+</sup>.

Absorption: Oral

# Dist.:

Metab.:

**Excretion**,  $t_{:} 1^{\circ} = kidney$ . 6 hr.

- **Toxicity/S.E.s**: Hyperkalemia (most severe), n/v (most common), metabolic acidosis. Hyponatremia may occur in old folks. Absolutely contraindicated with hyperkalemia.
- **Utility**: Usu. given w/another diuretic (often thiazide or loop). Combination usu.  $\rightarrow$  normal K<sup>+</sup> excretion.

Special Features: Rel. weak diuretic.

*Type of my disciples.* - To those human beings who are of any concern to me I wish suffering, desolation, sickness, ill-treatment, indignities - I wish that they should not remain unfamiliar with profound selfcontempt, the torture of self-mistrust, the wretchedness of the vanquished: I have no pity for them, because I wish them the only thing that can prove today whether one is worth anything or not - that one endures.

- Nietzsche