CARDIAC PHARMACOLOGY

Jason W. Gatling MD
Associate Professor
CardioThoracic Anesthesia

Core Concepts

- **Vasopressor** = drug used to elevate Arterial BP
- ↑ ABP alone is insufficient to treat hypotension / shock
- Goal: re-establish blood flow to vital organs

1. **ABP ≠ Flow**
2. **$DO_2 = CaO_2 \times CO$**
3. **$CO = HR \times SV$**

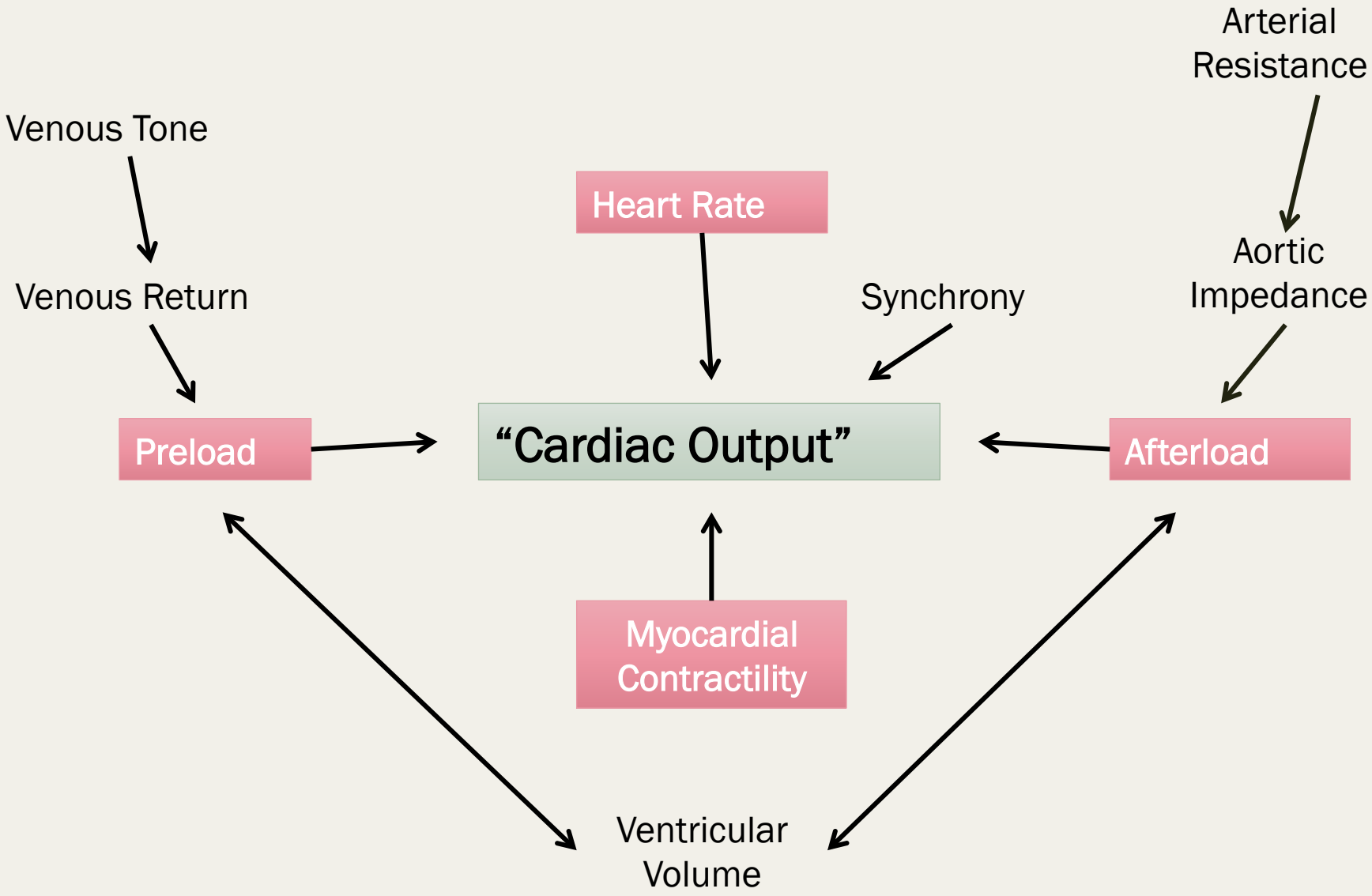
Stroke Volume

- Determinates:

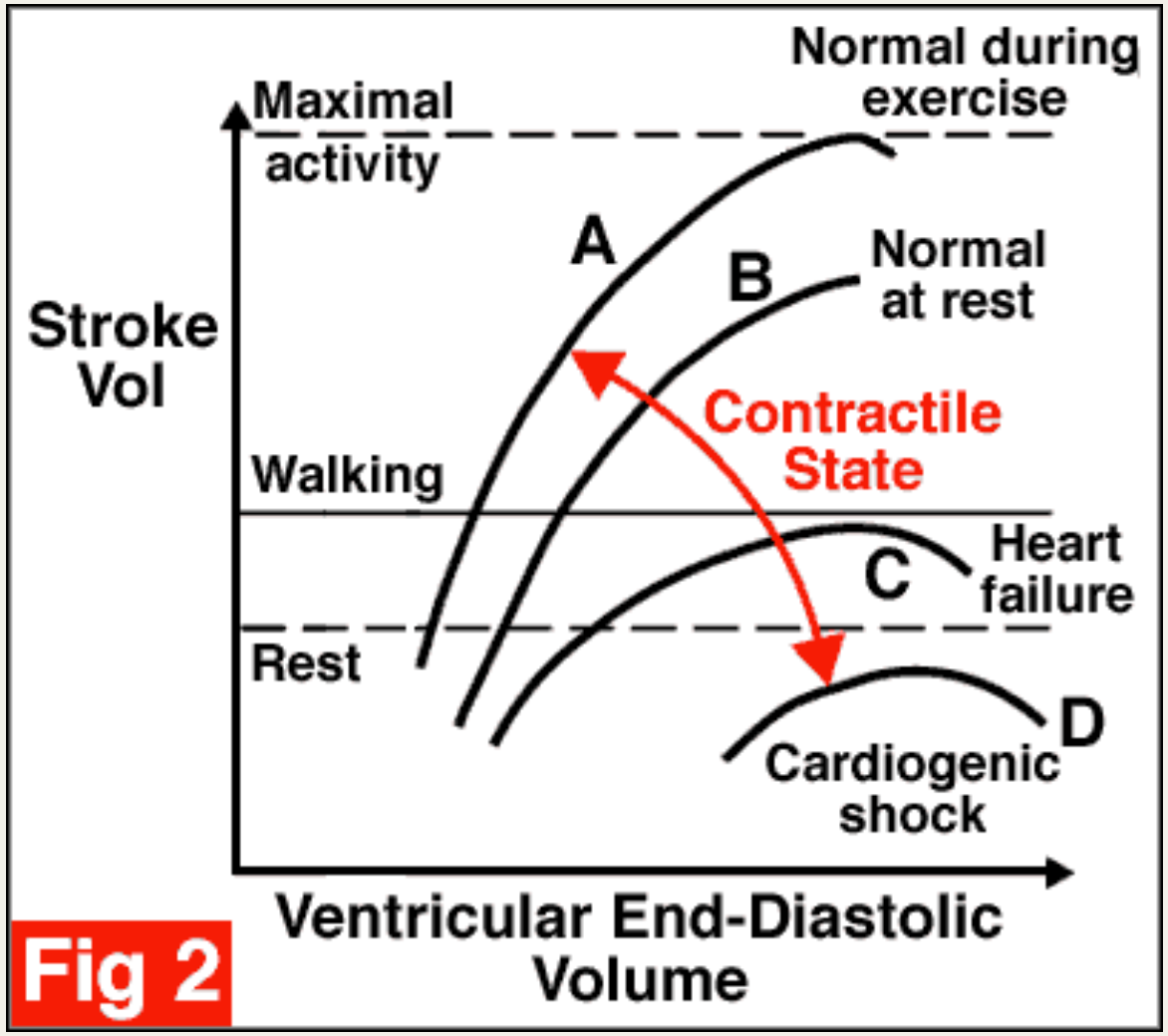
  *1) **Contractility** – inotrophic state of myocardium*

  *2) **Preload** – end-diastolic myocardial length*

  *3) **Afterload** – resistance to volumetric ejection*


Arterial Resistance
Venous Tone
Heart Rate
Aortic Impedance
Venous Return
Synchrony
Preload
“Cardiac Output”
Afterload
Myocardial Contractility
Ventricular Volume

Frank-Starling Curve



Hemodynamics

1. Adrenergic agonists:
   - ***Vasopressors*** *(sympathomimetics)*
   - ***Inotropes*** *(catecholamines)*

2. “α” & “β” receptors
   - *dose related*
   - *mixed receptor activation*

Hemodynamics

- Receptor effects:
  1. *HR (chronotropism)*
  2. *Cardiac contractility (inotropism)*
  3. *Conduction velocity (dromotropism)*
  4. *Cardiac rhythm*
  5. *SVR*
- **Venous return** effects as important as inotropic actions and more important than arteriolar effects.

Hemodynamics

- **Low Output Syndrome** – abnormalities of the heart, blood volume, or blood flow distribution
  - *Septic Shock – most common distributive abnormality*
    - R_x with volume repletion & multiple adrenergic agents

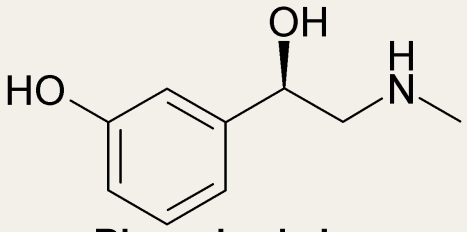
Adrenergic Receptors

- Targets of **Catecholamines**
  - *Epi & Nor-Epi*
- Cause a sympathetic response –> “Fight-or-Flight”
- Class of “G” protein-coupled receptors
- Two main receptor groups: “α” and “β”
  - *“α_1” – G_q coupled receptor*
  - *“α_2” – G_i coupled receptor*
  - *“β_1, β_2” – G_s protein receptors linked to adenylate cyclase*
    - Agonist binding causes ↑ of cAMP leading to cAMP-dependent protein kinase (PKA) mediated intracellular events

Adrenergic Agents

Phenylephrine

- *aka:* ***Neosynephrine***
- *Pure "**α**" agonist*
- ***Venous** > arterial constriction*
- *↑ venous return (↑ pre-load & BP)*
- *Baroreceptor mediated **reflexive bradycardia** and ↓ CO*
- *↑ SVR (↓ CO & ↑ myocardial O_2 requirement)*
- *Dose:*
  - 50-100 mcg IVP
  - 0.1-0.5 mcg/kg/min gtt
    - *10 mg in 250 NS (40 mcg/ml)*
- ***Caution:** may evoke myocardial ischemia*

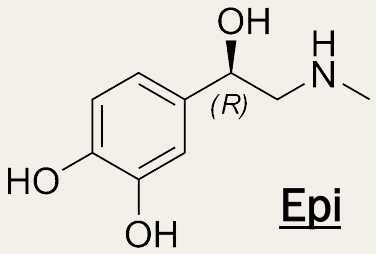


Phenylephrine

Epinephrine

- *Equal "α" & "β" effects*
  - "α" effects predominate renal & cutaneous vasculature to ↓ blood flow
  - "β" effects ↑ blood flow to skeletal muscles
  - Global ↑ **inotropy** (contractility) & ↑ **SVR**
  - Acute stimulation of atrial / ventricular dysrhythmias
- Clinical treatment for:
  1. *Cardiac arrest or life-threatening allergic rxn*
  2. *Prolong regional anesthesia*
  3. *Hemostasis and bloodless arthroscopic field*
  4. *Asthma*

Epinephrine

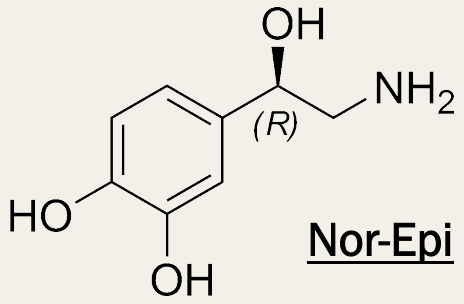


Epi

- Dose:
  - *0.01 – 0.05 mcg/kg/min*
    - 8 mg in 250 NS (32 mcg/ml)
  - *1-100 mcg IVP*
- Actions:
  - *bronchodilation*
  - *low dose "β_2" vasodilation and cardiac inotrophy*
  - *high dose "α" vasoconstriction*
  - ↑ *blood glucose*

Norepinephrine

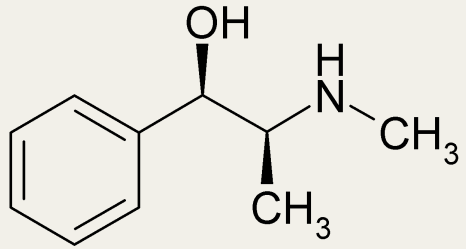
- aka: **Levophed**
- "α" > "β" effects
- ↑ SVR
- ↓ tissue blood flow & ↑ MVO_2
- Require central access for continuous infusion
- Dose:
  - *0.1-0.5 mcg/kg/min gtt*
    - 8 mg in 250 NS (32 mcg/ml)
  - *5-20 mcg IVP*
- R_x for vasodilation when <u>properly</u> volume resuscitated



Nor-Epi

Ephedrine

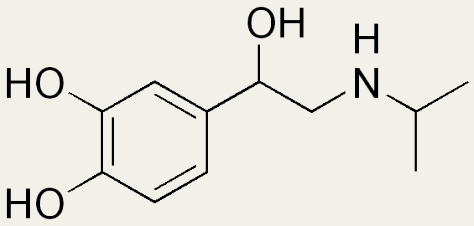
- Similar CV effects of Epi
  - *except greatly ↓ potency & 10x longer duration*
- **Veno** > arterial constriction
- ↑ venous return & CO
- Modest & predictable ↑ BP
- Dose:
  - *5-20 mg IVP*
- OB drug of choice
  - *uterine blood flow directly parallels Ephedrine induced ↑ in BP*



Ephedrine

Isoproterenol

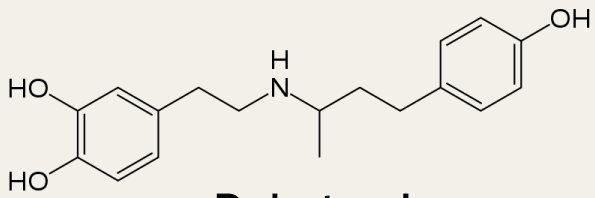
- Nonspecific "β" agonist
- ↑ CO
- Small ↓ SVR
- R_x: CHF with bradycardia, asthma, pulm HTN
- ? May cause myocardial ischemia in vulnerable pts
- **Chemical Pacemaker** in complete heart block
- Continuous IV infusion
- Dose:
  - *1-10 mcg/min*
    - 1 mg in 250 NS (4 mcg/ml)



Isoproterenol

Dobutamine

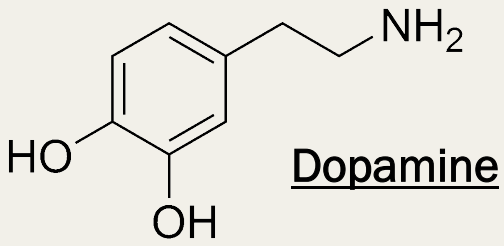
- Synthetic catecholamine derived from Isoproterenol
- Direct "β_1" receptor activation
- No Norepi release / DA receptor stimulation
- Strong inotropic effect (↑ contractility)
- Caution: ↑ SA / AV condution
- Uses: EF < 30%, poor contractility after CPB
- Dose:
  - *2-20 mcg/kg/min*
    - 250 mg in 250 NS (1 mg/ml)



Dobutamine

Dopamine

- "**DA, β, α**" receptor activation in dose related escalation
- "**DA**": 0.5-2 mcg/kg/min
  - *? ☺ Renal dopamine dosage*
  - *Shown in multiple studies*
- "**β**": 2-10 mcg/kg/min
- "**α**": >10 mcg/kg/min
- Caution:
  - *Tachycardia & dysrhythmias*
  - *↑ PA pressure*
  - *Insulin secretion inhibited (hyperglycemia)*
  - *Gangrene upon extravasation*

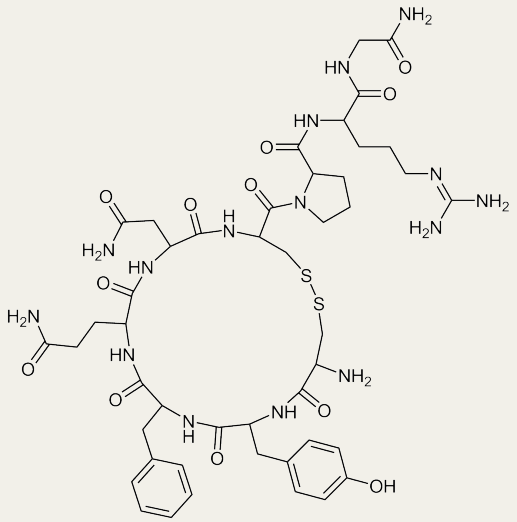


Dopamine

Non-Adrenergic Sympathomimetic Agents

Vasopressin

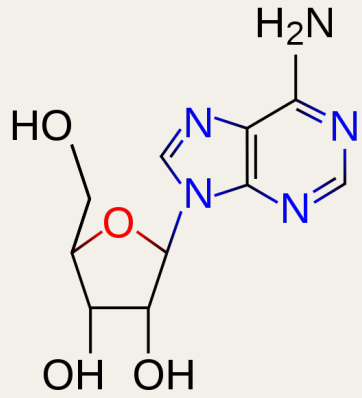
- aka: **Pitressin**
- Exogenous preparation of ADH selective for vascular smooth muscle
- Congener: Desmopressin
- V_1 receptor action (↑ SVR)
- Clinical indication:
  - ***Septic shock*** *(vasodilatory shock)*
  - ***Cardiac arrest*** *2^0 to V-fib / pulseless VT*
- Dose:
  - *0.01 - 0.1 Units / min gtt*
  - *Bolus: 1-4 U IVP*
  - *Standard vial: 20 U / 1 ml*
- **Cautious administration!**



Vasopressin

Adenosine

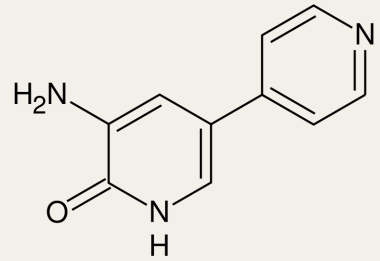
- Endogenous metabolite of ATP
- Negative **chronotropic** effects of SA node
- Negative **dromotropic** effects of AV node
- Causes **ASYSTOLE** for 5-20 sec
- Clinical use:
  - ***Paroxysmal SVT*** *termination*
- Dose:
  - *6 mg IVP (may increase to 12 -> 18 mg)*
  - *100-150 mcg/kg in peds*



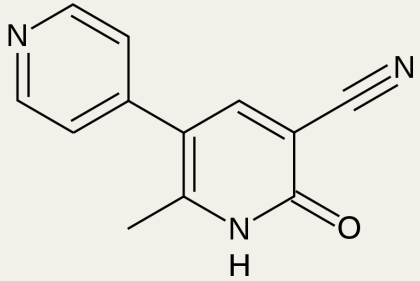
Adenosine

Amrinone / Milrinone

- Phosphodiesterase-3 inhibitor
  - *Potentiates effects of cAMP*
- ↑ CO by positive inotropic effects
- ↓ SVR by vasodilation
- Beware of mild **HYPOtension** with ↑ CO
- Rx: heart failure when conventional diuretics & vasodilators stall
- **Milrinone** (Primacor)
  - *more potent than Amrinone*
  - *NO platelet effects*
- Dose:
  - *loading dose: 50 mcg/kg over 5 min*
  - *0.375 – 0.75 mck/kg/min gtt*



Amrinone



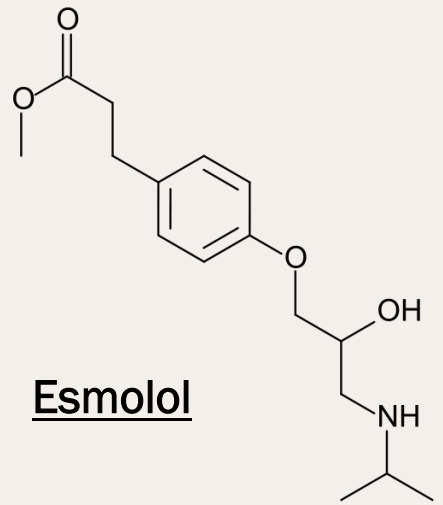
Milrinone

β-Blockers

1. Distinguished by differing pharmacokinetic & pharmacodynamic characteristics
2. Side effects:
   - *Heart block*
   - *Worsening CHF*
   - *Bronchospasm*
   - *Vasoconstriction (of coronary arteries)*
   - *Inhibition of Insulin release*
3. β_1 selectivity – **cardioselective**
   - *Greater safety in pt's with COPD, DM, PVD*

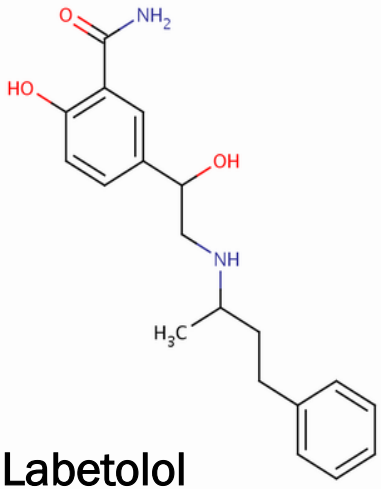
Esmolol

- aka: Brevibloc
- Cardioselective "β_1" blocker
- Dose:
  - *0.25 – 0.5 mg/kg*
  - *50 – 200 mcg/kg/min gtt*
- $t_{1/2}$: 8 – 10 min
- Eliminated very quickly via RBC plasma esterases



Esmolol

Labetolol



Labetolol

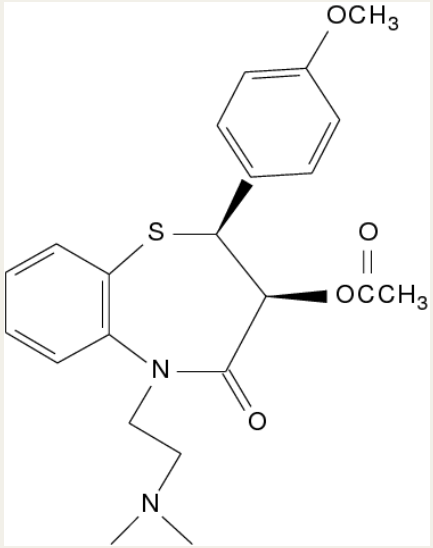
- aka: Trandate
- Selective "α_1" & non-selective "β" blocker
  - *"α" > "β" blocker properties*
- Dose:
  - *0.05 – 0.15 mg/kg IVP (normal dose 5-10 mg)*
- Drug useful in controlling HTN & tachycardia associated with GA

Ca^{2+} Entry Blockers

- Class of drugs that interact with cell membranes to interfere with **movement of Ca^{2+}** into cells through ion-specific **slow** channels
- Heterogeneous group
- Rx:
  - *Supraventricular tachydysrhythmias*
  - *coronary artery vasospasm*
- May exhibit additive myocardial depressant effects with volatile anesthetics
- Augment effect of both DMR & NDMR

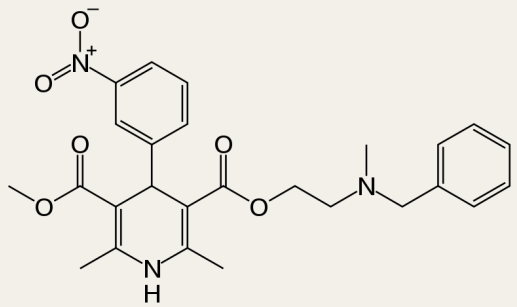
Diltiazem

- Potent **coronary artery vasodilator**
- Poor peripheral vasodilator
- May produce bradycardia
- Dose: 75 – 150 mcg/kg



Diltiazem

Nicardipine

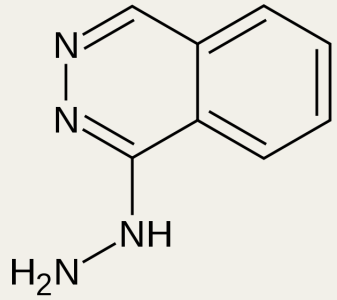


Nicardipine

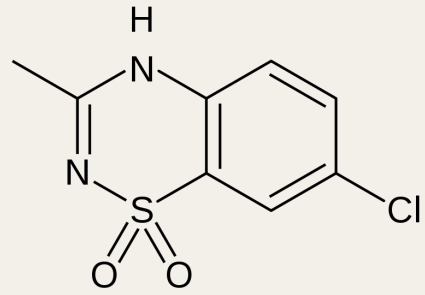
- aka: Cardene
- **Vasodilation** of coronary arteries
- Does NOT alter conduction of SA / AV nodes
- Dose:
  - *Initiate at 5 mg/hr*
  - ↑ *by 2.5 mg/hr (max dose 15 mg/hr)*
  - *Ampule: 25 mg/10 ml*
    - Mix in 240 NS to get final concentration of 0.1 mg/ml

Vasodilators

- ↓ BP by dose-related direct effects on vascular smooth muscle
- Independent of “α” or “β” receptors
- May evoke baroceptor-mediated ↑ HR
- Hydralazine – contol of peri-op HTN
  - *resistance > capacitance vessels*
    - ↓ Afterload & little effect on preload
  - *Dose: 5 – 10 mg IVP q15 min*
- Diazoxide – treat HTN emergencies
  - *resistance > capacitance vessels*
    - ↓ Afterload & little effect on preload
  - *Dose: 3 – 5 mg/kg IV q 5 min*



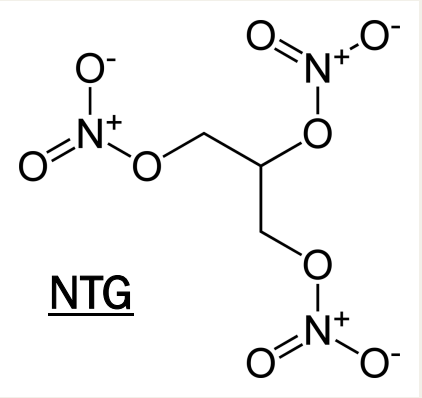
Hydralazine



Diazoxide

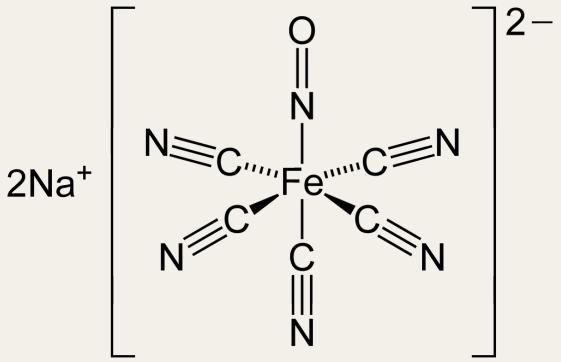
Nitroglycerine

- aka: NTG
- Used to treat Acute Myocardial Ischemia
- Venule site of action
- ⬇ **Preload**
- ⬆ Venous Capacitance
- Less exact control of HTN (vs SNP)
- No risk of cyanide toxicity
- Dose:
  - *0.1 – 0.5 mg IVP*
  - *0.25 – 3 mcg/kg/min gtt*
    - 50 mg in 250 NS (200 mcg/ml)



Nitroprusside

- aka: SNP
- Used to treat ACUTE HTN responses
  - *Aneurysm clipping*
  - *Pheochromocytoma*
  - *Ao repair*
- Acurately titratable (vs. NTG)
- Arterial & Venule smooth muscle relaxation
  - *release of nitric oxide (**NO**) in blood stream*



SNP

Nitroprusside

- ↓ Preload & Afterload
- Hypotension effects potentiated by volative anesthetics
- Dose:
  - *0.25 – 0.75 mcg/kg/min gtt (rarely > 3 mcg/kg/min)*
  - *Acute Treatment: 50 – 100 mcg IVP*
    - 50 mg in 250 NS (200 mcg/ml)

Nitroprusside

- Side effect:
  - *Ferous iron of SNP reacts with sulfhydryl groups in RBC's ➔ cyanide formation*
  - *Cyanide reduced to thiocyanate in liver*
  - *High doses (>10 mcg/kg/min) result in cyanide toxicity*
- Dx:
  - *Tachyphylaxis*
  - *↑ venous oxygen tension*
  - *Metabolic acidosis*
    - Cyanide binds to cytochrome oxidase causing cellular hypoxia
- R_x: Sodium Thiosulfate (150 mg/kg IV in 50 ml H_2O)
  - *Speeds conversion of cyanide ➔ thiocyanate*
  - *Eliminated via renal excretion*