Blood Pressure and Antihypertensive Medications

Circulation

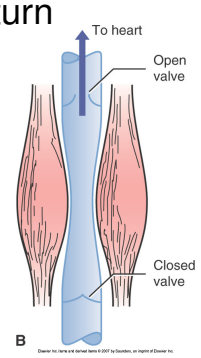
- Two systems
  - Pulmonary (low pressure)
  - Systemic (high pressure)
    - Aorta 120 mmHg
    - Large arteries 110 mmHg
    - Arterioles 40 mmHg
    - Arteriolar capillaries 30 mmHg
    - Venous capillaries 18 mmHg
    - Venules 16 mmHg
    - Muscular Veins 12 mmHg
    - Central Veins 7 mmHg
    - Right atrium -5 mmHg

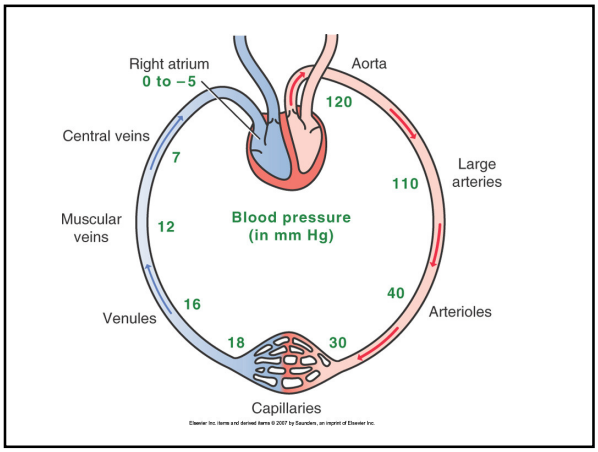
Arterial flow

- Pressure gradient
  - Heart generates pressure
  - Arteries contract or dilate to control flow and pressure
  - Resistance to blood flow
    - Vessel diameter
    - Vessel length
    - Blood viscosity

Venous Return

- Mostly against gravity
  - Follows pressure gradient (small effect)
  - Constriction of venous SMC
  - Constriction of skeletal muscles
  - One way venous valves





Regulation of Cardiac Output

- CO ~ 5liters/min
- CO = HR X SV
- Average HR 70 bpm, average SV 70ml
  - CO = 70 X 70 = 4900 ml/min = 4.9 liters/min

Heart Rate

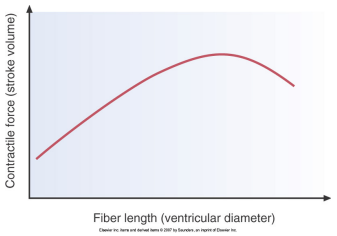
- Autonomic nervous system innervates SA node
  - HR increases
    - Sympathetic stimulation
    - β_1 adrenergic receptors
  - HR decreases
    - Parasympathethic impulses
    - Muscarinic Receptors
    - Vagus nerve

Stroke Volume

- Myocardial contractility
  - Cardiac stretch (Starling's law of the Heart)
  - Sympathetic stimulation (β_1 receptors)
- Cardiac preload
- Cardiac afterload

Starling's Law of the Heart

- More stretch
- More contraction
- Up to a point

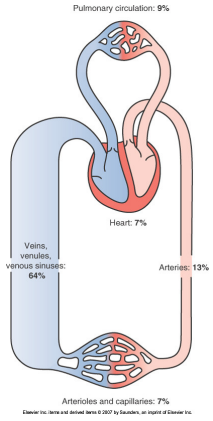


Preload

- Stretch applied to cardiac muscle prior to contraction
- Stretch is determined by amount of blood in ventricle at the end of diastole
  - End-diastolic volume
  - End-diastolic pressure
- How does preload affect Stroke Volume?

Control of Preload

- Affected by drugs
  - Venous tone
  - Blood volume
- Not affected by drugs
  - Skeletal muscle contractions
  - Resistance to flow in veins (e.g. thrombus)
  - Right atrial pressure



Systemic-Pulmonary Balance

- Right and Left heart **MUST** pump same amount of blood
- Very small disturbance can result in death
  - Fun with Math

Afterload

- Load against which a muscle (myocardium) must contract
- Operationally afterload is blood pressure

Arterial Pressure

- MAP = CO X TPR
  - CO = ?
  - TPR regulated by dilation/constriction
- Control mechanisms
  - ANS
  - RAAS
  - Kidneys
  - Local

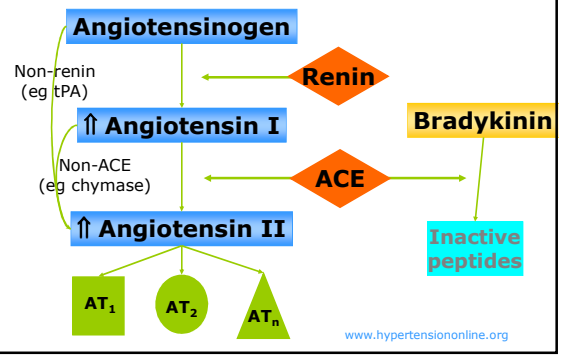
ANS control of MAP

- Adjusts CO and peripheral resistance
- CO = ?
- Arteries
  - Sympathetic stimulation causes constriction
    - α-1 receptors in arteries
  - No parasympathetic innervation
  - Complete removal of sympathetic tone reduces MAP by half

Control of ANS

- Baroceptor reflex
  - Carotid sinus
  - Aortic arch
- When drop in MAP is sensed
  - Constriction of arterioles
  - Constriction of veins
  - Acceleration of heart rate
- Baroceptor resetting

Renin-Angiotensin Cascade



RAAS

- Angiotensin II
  - Constriction of arterioles
    - Hours
- Aldosterone
  - Retention of sodium and water
    - Days
  - Remodeling of heart and muscle
    - Weeks – Months

Renal Retention of Water

- Ultimate control of blood pressure!!!
  - Goal is to maintain renal perfusion
- Under influence
  - GFR
  - RAAS
  - ADH
  - Natriuretic peptides

Natriuretic Peptides

- Peptides that reduce vascular volume and
  - ANP (atrial) – produced by atrial myocytes
  - BNP (brain) – ventricular myocytes and brain
    - Both cause
      - Natriuresis
      - Diuresis
      - Increase vascular membrane permeability
      - Promote vasodilation (inhibition of sympathetic impulses)
  - CNP (endothelium)
    - vasodilation

Hypertension Etiology

- Primary (essential) hypertension
- Secondary - caused by something else
  - Accuracy of Diagnosis
  - Apnea (obstructive sleep)
  - Aldosteronism
  - Bruit (renal)
  - Bad kidneys
  - Catecholamines
  - Coarctation of Aorta

Hypertension Etiology

- Secondary Hypertension – continued
  - Cushing's Syndrome
  - Drugs
  - Diet
  - Erythropoietin (excess)
  - Endocrine disorders

Hypertension Pathogenesis

- Disease of degree
- Hypertension begets hypertension
- End organ damage
  - Heart
  - Brain
  - Kidneys
  - Arteries
  - Eye

Hypertension Pathogenesis

- Arteries
  - Higher pressure causes physical damage
  - Scars elastic arteries
  - Increased risk for atherosclerosis
    - Turbulent blood flow – decreases endothelial function
    - Pressure causes more blood particles to enter intimal space
  - Resetting of baroceptors – causes body to think hypertension is normal

Hypertension Pathogenesis

- Heart
  - Ventricular hypertrophy
    - Vicious cycle
      - Results in smaller chambers→less Cardiac output
      - Less output → has to work harder
      - Works harder → hypertrophies more
    - More at risk for ischemia
    - More vulnerable to coronary artery disease

Hypertension Pathogenesis

- Brain
  - Increased risk of atherosclerotic stroke
  - Increased risk of hemorrhagic stroke
- Kidney
  - Glomerulus is artery, not capillary
  - Increased pressure causes increased GFR
- Eye
  - Retinal arteries sensitive to pressure damage

Hypertension Clinical Manifestations

- The Silent Killer
  - DUN DUN DUN DUN
  - Headache
  - Double vision
  - Lightheadedness
  - Nose bleeds
  - Anxiety
  - Palpitations
  - Sweating
  - Increased urine output
  - Weakness
  - Hematuria
  - Retinal changes
  - Hyperemic ears and mucous membranes
  - Hyperemic conjunctiva
  - Subconjunctival bleed

Approaches to Hypertension Treatment

- Inhibit Sympathetic impulses
  - Inhibit Cardiac contractility and heart rate
  - Inhibit vasoconstriction
- Inhibit RAAS
- Inhibit vasoconstriction
- Inhibit Renal retention of water

Antihypertensive Classes

- Diuretics – Inhibit Renal Retention
- Beta blockers – inhibit heart sympathetic
- Alpha-1 blockers – inhibit artery sympathet
- Alpha-2 agonist – inhibit both sympathetic
- Calcium channel blockers – inhibit cardiac and/or arterial muscle constriction
- ACE inhibitors – inhibit RAAS
- ARBs – inhibit RAAS
- Direct vasodilators – self explanatory