Arterial Blood Pressure

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Arterial Blood Pressure (BP)

- The lateral pressure force generated by the pumping action of the heart on the wall of aorta & arterial blood vessels per unit area.
- Pressure inside big arteries (aorta & big vessels).
- Measured in (mmHg), & sometimes in (cmH_2O), where 1 mmHg = 1.36 cmH_2O.
- **Systolic B.P**. :The maximum pressure exerted in the arteries during systole (90-140 mmHg).
- **Diastolic B.P. :**The minimum pressure within the arteries during diastole (60-90 mmHg).

Arterial Blood Pressure (continued)

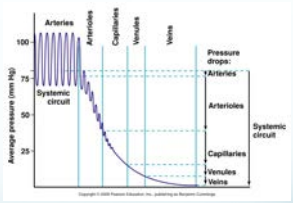
- Diastolic pressure is more important, because diastolic period is longer than the systolic period in the cardiac cycle.
- **Pulse pressure** = Systolic BP – Diastolic BP.
- **Mean arterial pressure** = This is the average arterial pressure throughout the cardiac cycle.

  = Diastolic BP + 1/3 Pulse pressure.

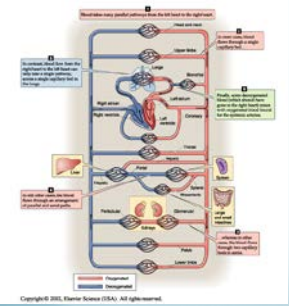
Blood pressure values: what do they mean?

- Pulse pressure:
  PP = SP-DP
- Mean arterial blood pressure = MABP
- MABP = **DP + 1/3 (SP-DP)**

CO = MABP = SV x HR
TPR



Mean Arterial Blood Pressure (MAP)



"average arterial blood pressure during a cardiac cycle"

Perfusion pressure

main driving force for propelling blood to the tissues

MAP = DP + 1/3 (SP-DP)

For a BP of 120/80, MAP is ~ 93.5 mmHg

A MAP of ~ 60 mmHg is sufficient for end organ perfusion.

Hypertension Clinical Manifestation

Dx is made after multiple readings over several weeks

NIH/Joint Committee Definition:

Category	Systolic		Diastolic
Optimal	<110	and	< 80
Normal	<120	and	<80
High Normal	120-139	or	80-89
Stage 1	140-159	or	90-99
Stage 2	160-179	or	100-109
Stage 3	=>180	or	=> 110

Measurement

http://www.nlm.nih.gov/medlineplus/ency/article/003398.htm

3 Ways to Measure Blood Pressure

Aneroid Monitor | Digital Monitor | Finger/Wrist Monitor

http://familydoctor.org/online/famdocen/home/common/heartdisease/treatment/128.html

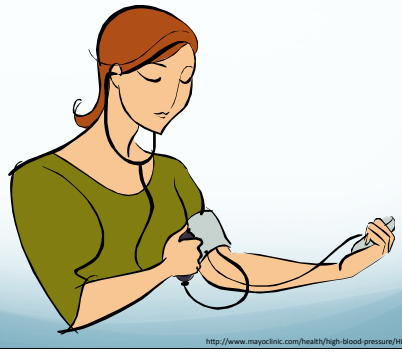
Steps to Follow before Taking Your Blood Pressure

- Don't use 30 minutes prior to taking your blood pressure:
  - Caffeine,
  - Alcohol, or
  - Tobacco.
- Go to the bathroom.
- Rest 3-5 minutes before taking your blood pressure.
- Sit comfortably.
  - Legs and ankles uncrossed
  - Back supported

Tips for Accurate Use

- Same time of day
- Use the same arm
  - Left
- Don't measure
  - immediately upon waking up, or
  - immediately after exercising.
    - Wait an hour.

How to Take Your Blood Pressure



http://www.mayoclinic.com/health/high-blood-pressure/HI00016

- Place your arm, raised to the level of your heart, on a table or a desk, and sit still.
- Wrap the correctly sized cuff smoothly and snugly around the upper part of your bare arm.
- Make sure that if you have rolled up a sleeve to place the cuff on your arm that it does not get too tight around your arm.
- Take a repeat reading two to three minutes after the first one to check accuracy.
- Be certain that the bottom edge of the cuff is 1 inch above the crease of your elbow.

Arterial blood pressure

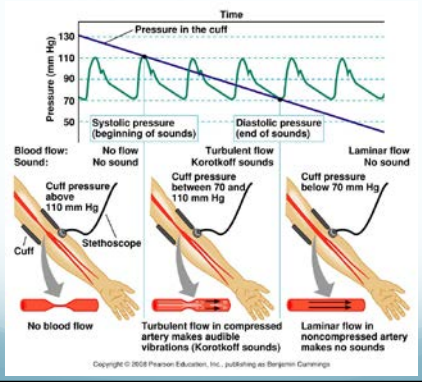


Figure 14.8

Remember Blood Pressure….

- Varies throughout the day
- Is often higher in the morning
- Talk about your personal blood pressure goals with your doctor.

Hypertension Pathophysiology

- **Primary (Essential) Hypertension:**
  - Elevated BP without an identified cause
  - Accounts for 95% of all cases of hypertension
  - Cause – unknown
    - Contributing Factors: Increased SNS activity, overproduction of Na+ retaining hormones & vasoconstrictors, increased Na+ intake
    - Risk Factors: Modifiable

Primary Hypertension Pathophysiology

- **Heredity** – interaction of genetic, environmental, and demographic factors
- **Water & Sodium Retention** – 20% of pts with high Na+ diet develop HTN
- **Altered Renin-Angiotensin Mechanism** – found in 20% of patients
- **Stress & Increased SNS Activity**
- **Insulin Resistance & Hyperinsulinemia**
- **Endothelial Cell Dysfunction**

Primary Hypertension Risk Factors

- Age
- Alcohol
- Cigarette Smoking
- Diabetes Mellitus
- Elevated serum lipids
- Excess Na+ in diet
- Gender
- Family History
- Obesity
- Ethnicity

Secondary Hypertension Pathophysiology

- Specific cause of hypertension can be identified
- 5+% of adult hypertension
- Causes:
  - Coarctation or congenital narrowing of the aorta
  - Renal disease – renal artery disease / parenchymal
  - Endocrine disorders: Pheochromocytoma, Cushing Syndrome, Hyperaldosteronism, thyroid and parathyroid
  - Neurology disorders – brain tumors / head injury
  - Sleep apnea
  - Medications – sympathetic stimulants
  - Pregnancy-induced hypertension

Physiological variations in arterial B.P.:

- **Age:**

Arterial B.P. increase with age ? due to loss of arterial elasticity.

- **Sex:**

After menopause, arterial B.P. becomes higher in females? due to hormonal changes (↓ of estrogen).

- **Race :** Orientals > Westerns … ? dietry factors, or weather.
- **Diurnal variation:**

Normally Arterial B.P. Is lowest in the early morning and highest in the afternoon.

- **Exercise:**

Arterial B.P. increases during exercise especially systolic arterial B.P.

- **Emotions:**

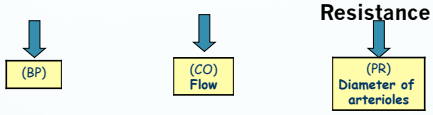
Arterial B.P. increases in Strong emotional stress.

- **Gravity:**

On standing the , the gravity increases arterial B.P. below a reference point (in the right atrium near the tricuspid valve) in the heart and decreases it above that point.

Factors determining ABP:

Blood Pressure = Cardiac Output X Peripheral Resistance



- **BP depends on:**
  1. Cardiac output ⇒ CO = SV X HR.
  2. Peripheral resistance.
  3. Blood volume.

Regulation of Arterial Blood Pressure

Regulation of ABP:

- Maintaining B.P. is important to ensure a steady blood flow (perfusion) to tissues.
- B.P. is **regulated neurally** through centers in medulla oblongata:
  1. Vasomotor Center (V.M.C.), or (pressor area):
     ⇒ **Sympathetic fibers.**
  2. Cardiac Inhibitory Center (C.I.C.), or (depressor area):
     ⇒ **Parasympathetic fibers (vagus)**

Regulation of ABP (continued)

cardiac control centers in medulla oblongata

1. Cardiacaccelerator center (V.M.C)	2. Cardiacinhibitory center (C.I.C)
↓	↓
Sympathetic n. fibers	Parasympathetic n. fibers

✓ **Regulatory mechanisms depend on:**

a. **Fast acting reflexes:**
   Concerned by controlling CO (SV, HR), & PR.
b. **Long-term mechanism:**
   Concerned mainly by regulating the blood volume.

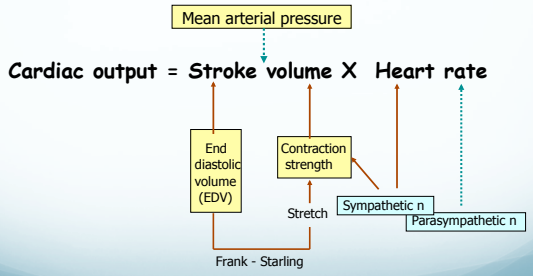
Regulation of Arterial Blood Pressure

A. Regulation of Cardiac Output

Regulation of CO:

- A fast acting mechanism.
- CO regulation depends on the regulation of:
  - **a.** Stroke volume, &
  - **b.** Heart rate

Regulation of the CO:



Neural regulation

- Sympathetic nerves
  - Constrictor nerves – mediator noradrenaline · α1 adrenoreceptors
  - Elevates Ca^{++} through phospholipase C pathway (IP_3)
- Parasympathetic nerves
  - In tissues which need sudden increase in blood flow (salivary gland, external genitalia)
  - Mediator acetylcholine has indirect effect
    - inhibition of noradrenalin release
    - production of NO

Sympathetic input · HEART

ACTIONS
- Nerve fibers release NE
- SA, atria, and ventricles
- ↑ HR and contractility
  - R side SA node
  - L side contractility

MECHANISM
- ß1 receptors – pacemaker activity
- ß1 myocardium contraction

Parasympathetic input · HEART

ACTIONS
- Vagus nerve releases ACH
- SA and myocardium
- HR and conduction velocity
  - R side SA node (HR)
  - L side contractility (slight)

MECHANISM
- Muscarinic receptors (M2)
  - ß γ subunit (HR)
  - Nitric oxide (weak inotropic effect)

Sympathetic input – Blood vessels

ACTIONS
- Activated ·Vasoconstriction throughout body
  - Skin/kidney BVs most abundant
- De·activated – Vasodilation

MECHANISM
- Norepinephrine
  - α > ß
- Epinephrine
  - ß > α

Vasoconstriction – α 1
Vasodilation – ß2

Parasympathetic input – Blood vessels

ACTIONS	MECHANISM

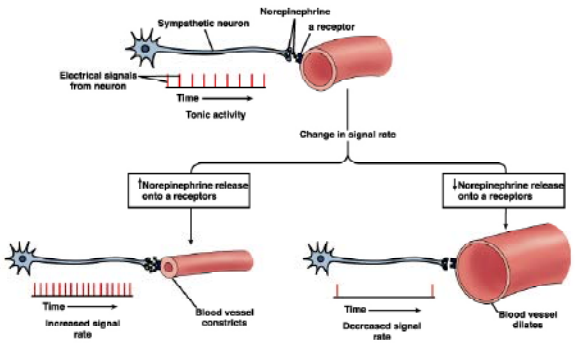
• Vasodilation of BVs
  • Less common than the sympathetic activity
  • Salivary glands, g.i. glands, reproductive tissues
	• ACH increases vasodilation indirectly through other second messengers.

Sympathetic activation of skeletal muscle

- Causes *vasodilation*
  - Release of ACH
  - Action is on pre-capillary sphincters

Vasoconstriction in all vascular beds except skeletal muscle Increased HR and contractility

Control center is not medulla but rather cerebral cortex
-"fight or flight" response
-Anticipatory response to exercise



Adrenal medulla

- Sympathetic release of epinephrine and norepinephrine
  - Global effects on increasing arterial blood pressure.

Regulation of Arterial Blood Pressure

B. Regulation of Peripheral Resistance

Blood pressure regulation

vasodilatation		vasoconstriction	
stimulation of cGMP	stimulation of cAMP	inhibition of cAMP	Stimulation of IP_3
In smooth muscle, cGMP and cAMP stimulates Ca^{2+} pump of the sarcoplasmic reticulum Decrease of Ca^{2+} concentration in smooth muscle cell		Slower decrease of Ca^{2+}	IP_3 releases Ca^{2+} from the sarcoplasmic reticulum
NO ANP	adenosine A_2 histamine H_2 adrenaline β_2 VIP	serotonin adrenaline α_2 angiotensin II	serotonin adrenaline α_1 vasopressin

Regulation of Peripheral Resistance (PR):

- A fast acting mechanism.
- Controlled by 3 mechanisms:
  1. Intrinsic.
  2. Extrinsic.
  3. Paracrine.
- Extrinsic mechanism is controlled through several reflex mechanisms, most important:
  1. Baroreceptors reflex.
  2. Chemoreceptors reflex.

Regulation of blood flow

myogenic	stretch-activated cation channels cause vasoconstriction
metabolic	metabolic products cause vasodilatation
shear dependent	vasodilatation by NO, which is produced in vascular endothelium
neural	•sympathetic constrictor nerves in most tissues •parasympathetic dilator nerves in some secretory and spongiform tissues
humoral	•constriction by angiotensin II, epinephrine, vasopressin, serotonin •dilatation by ANP, histamine, inflammatory mediators

Myogenic autoregulation

- Arterioles contracts when they are distended (brain, kidney, heart)
- Mechanism
  - Stretch-activated Na^+ and Ca^{2+} channels of vascular smooth muscle
  - Depolarization of membrane, which then activates L-type Ca^{2+} channels
  - Muscle contraction

Metabolic regulation

- Adenosine
  - Causes vasodilatation, except of kidney and pulmonary artery
  - Activation of adenosine A_{2A} membrane receptor – elevation of cAMP
- pO_2
  - Reduction in pO_2 increases production of vasodilator agents (PGI_2 and NO)
- pCO_2
  - Elevated pCO_2 leads to elevated H^+ in extracellular fluid – acidosis causes membrane hyperpolarization (K^+) – vasodilatation (except of lung)

Shear-dependent regulation

- Endothelial cell reacts on many physiological stimuli with production of several substances which influence smooth muscle cell
  - Stretching
  - Shear stress induced by blood flow
  - Hormonal levels
  - Substances released from blood elements (trombocytes, macrofages)
- Synthesis of NO and PGI_2 (vasodilators)

Nitric oxide synthesis

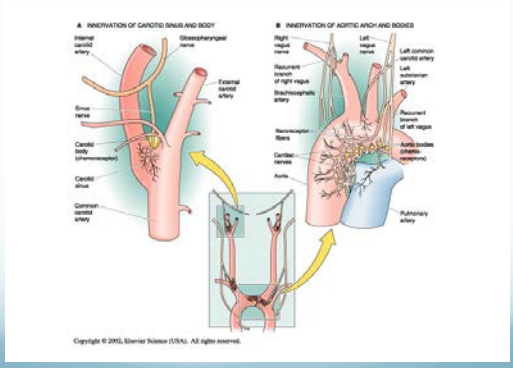
- Shear stress and a variety of receptor-mediated agonists raise vascular endothelial [Ca^{++}] and cause the Ca^{++}-calmodulin complex to activate endothelial nitric oxide synthase (eNOS).
- NO is produced from the amino acid L-arginine.
- NO is a gas and diffuses into adjacent VSM where it activates soluble guanylate cyclase, produces cGMP and causes vasodilatation

Extrinsic mechanism
1. Baroreceptors reflex:

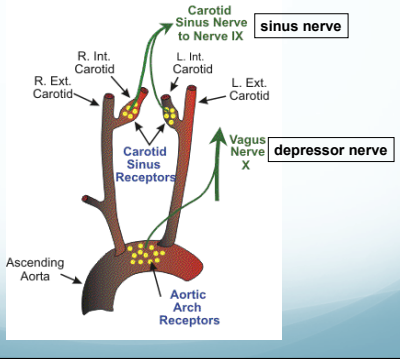
- Baroreceptors are receptors found in carotid sinus & aortic arch.
- Are stimulated by changes in BP.

↑ BP
→ + Baroreceptors
→ = V.M.C → = Sympathetic → Vasodilatation & ↓ TPR
→ ++ C.I.C → + Parasympathetic → Slowing of SA node (↓ HR) & ↓ CO

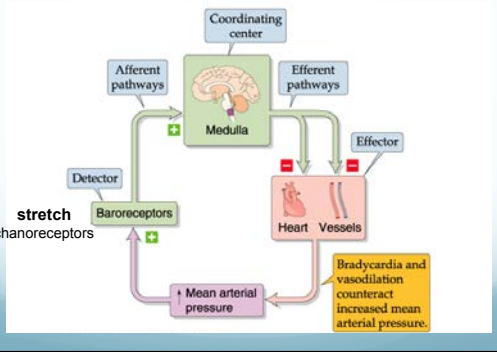
Carotid and Aortic Baroreceptors



<u>High pressure</u> baroreceptors respond to stretch in the aortic arch and carotid sinus.



Baroreceptor Feedback Loop for the Regulation of Mean Arterial Blood Pressure



Carotid nerve fires **above and below** normal pressures.
Aortic nerves are activated **above** normal pressures.

MAP ~ 93.5 mmHg

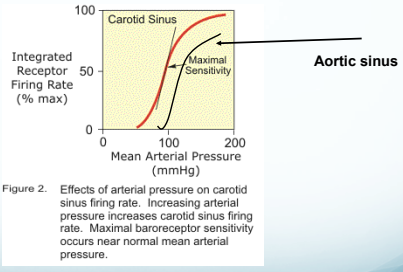


Figure 2. Effects of arterial pressure on carotid sinus firing rate. Increasing arterial pressure increases carotid sinus firing rate. Maximal baroreceptor sensitivity occurs near normal mean arterial pressure.

Aortic sinus

The aortic receptors help reinforce the carotid activation above normal pressures.

Medulla Oblongata

Nucleus of the Tractus Solitarius (NTS)

Vagal/glossopharyngeal **AFFERENTS**

Cardio-inhibitory area
Vasomotor area

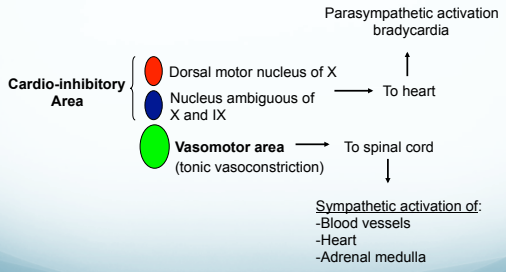
Increased firing of Baroreceptors by stretch

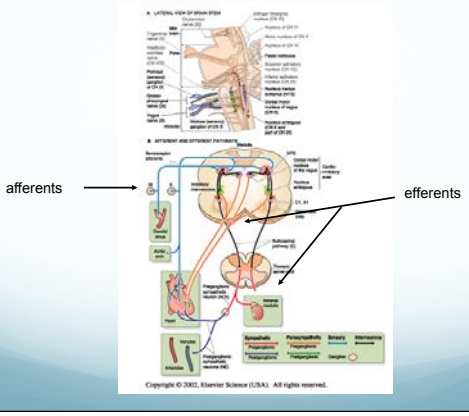
Sympathetic and Parasympathetic **EFFERENTS**

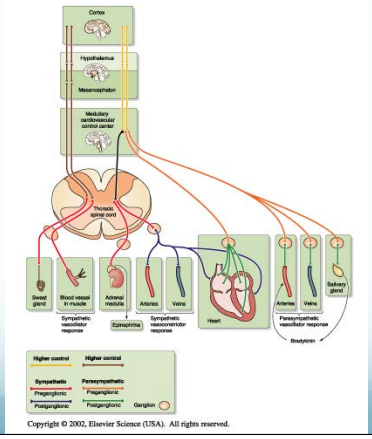
↑ **MAP**

<u>TARGET ORGANS</u>
-heart
-blood vessels
-adrenal medulla
-glands (skin/sweat)

Coordination of Medullary Cardiovascular Inputs

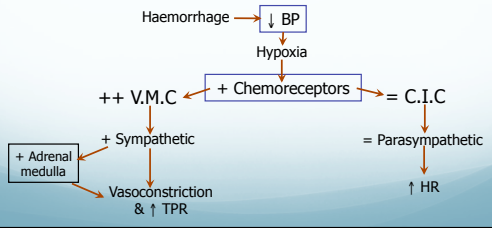






2. Chemoreceptors reflex:

- Chemoreceptors are receptors found in carotid & aortic bodies.
- Are stimulated by chemical changes in blood mainly hypoxia (↓ O_2), hypercapnia (↑ CO_2), & pH changes.



Chemoreceptors

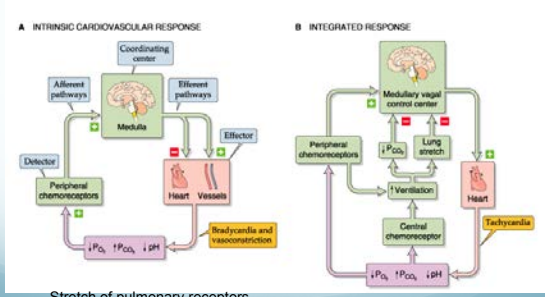
- Peripheral (ventilation)
  - Sense low O_2
  - Carotid and aortic (glomus cell)
  - Synapse with IX and X, respectively
- Central (medulla/CNS)
  - Sense low pH primarily

① Exert a positive drive on **vasomotor** area

② Exert a positive drive on **cardio-inhibitory area**

Vasoconstriction and Bradycardia

Net result of Chemoreceptor stimulus is an integration of central and peripheral chemoreceptors



Stretch of pulmonary receptors
cancel peripheral stimulus on cardio-inhibitory area –causing tachycardia

3. Other Vasomotor Reflexes:

1. **Atrial stretch receptor reflex:**

   ↑ Venous Return ⇒ ++ atrial stretch receptors ⇒ reflex vasodilatation & ↓ BP.

2. **Thermoreceptors:** (in skin/or hypothalamus)
   - Exposure to heat ⇒ vasodilatation.
   - Exposure to cold ⇒ vasoconstriction.

3. **Pulmonary receptors:**

   Lung inflation ⇒ vasoconstriction.

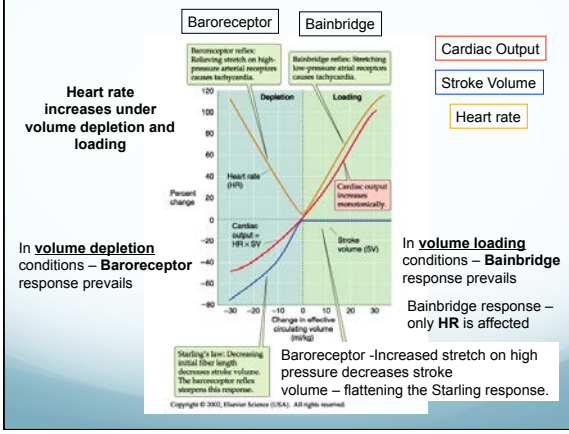
Bainbridge reflex (atrial stretch reflex)

- **Receptors** : baroreceptors type A,B .
- **Location** : in Atrial walls
- *Stimulus for* **type A** :increased atrial **pressure** during atrial **systole**
- *Stimulus for* **type B** : atrial **distension** during atrial **diastole**.
- **Afferent** : **Vagus nerve**
- **Center** :**CVC** in medulla oblongata
- **Response** : **↑ heart rate**
  ↓ B.P.

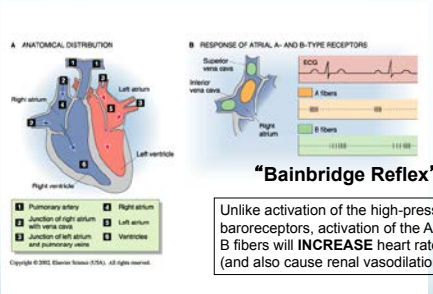
SIGNIFICANT : to equalize **input** with **output** of heart

Atrial (Bainbridge) Reflex.

- A sympathetic reflex initiated by increased blood in the atria
  - Causes stimulation of the **SA node**
  - Stimulates **baroreceptors** in the atria, causing increased SNS stimulation
- Adjusts **heart rate** in response to **venous return**
- **Stretch receptors** in right atrium : trigger increase in heart rate through increased sympathetic activity.



Low Pressure Cardiac Baroreceptors



"Bainbridge Reflex"

Unlike activation of the high-pressure baroreceptors, activation of the A and B fibers will **INCREASE** heart rate. (and also cause renal vasodilation).

Respond to "fullness" or volume
Located in Low pressure sites
Control the effective circulating volume ⟶ ***Indirectly*** regulate MAP

CORONARY STRETCH REFLEX (Lt. vent. Stretch reflex)

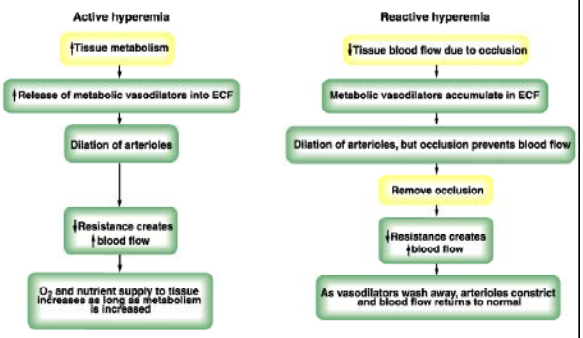
- **Receptors** : **baroreceptors**
- **Location** : in Lt. ventricle near coronary vessels.
- **Stimulus** : Lt. vent. Distension.
- **Afferent** : **Vagus nerve**
- **Center** : **CVC**
- **Response** : **↓ heart rate** **↓ B.P.**

SIGNIFICANT: to maintain Vagal tone that keeps low heart rate at rest.

Coronary chemoreflex (Bezold- Jarisch reflex)

- **Receptors** : **chemoreceptors** (c-nerve fibers).
- **Location** : near coronary vessels of Lt. vent.
- **Stimulus** : chemical changes
- **Center** : **CVC** in medulla
- **Response**: **↓heart rate ↓B.P**

SIGNIFICANT In myocardial infarction, these receptors are stimulated by certain substance released from infarcted tissues and lead to hypotension (as index for severity of case).



REFLEXES FROM EXTRAVASCULAR RECEPTORS

1- Pulmonary stretch reflex.

- **Receptors** : **baroreceptors**
- **Location** : in bronchial wall
- **Stimulus** : lung inflation (inspiration)
- **Afferent** : **Vagus nerve**
- **Response** : **↑ heart rate ↓ B. P**

SIGNIFICANCE: With inspiration, venous return is increased and the input for heart is also increased . So that, by this reflex increased heart rate to equalize input with output *without* increase in B. P (Like Bainbridge reflex)

Pulmonary chemoreflex

- **Receptors** :**chemoreceptors** (C-nerve fiber)
- **Location** : near lung capillaries
- **Stimulus** :**chemical** changes
- **Afferent** : **Vagus nerve**
- **Center** : **CVC**
- **Response** : **↓heart rate ↓ B.P**

SIGNIFICANT : unknown

4. Hormonal Agents:

- NA ⇒ vasoconstriction.
- A ⇒ vasoconstriction (except in sk. ms.).
- Angiotensin II ⇒ vasoconstriction.
- Vasopressin ⇒ vasoconstriction.

Regulation of Arterial Blood Pressure

C. Regulation of Blood Volume

Regulation of Blood Volume:

- A long-term regulatory mechanism.
- Mainly renal:
  1. **Renin-Angiotensin System.**
  2. **Anti-diuretic hormone (ADH), or vasopressin.**
  3. **Low-pressure volume receptors.**

Hormonal regulation

- Renin-angiotensin, vasopressin, ANP
- Adrenaline (epinephrine)
  - Higher affinity for β-adrenoreceptors (heart, splanchnic area, skeletal muscle) – vasodilatation
  - Lesser affinity for α-adrenoreceptors (vasoconstriction)
- Serotonin
  - released from platelets during clotting reaction, elevated Ca^{2+} leads to vasoconstriction
- Histamine
  - Vasodilatation by means of NO production

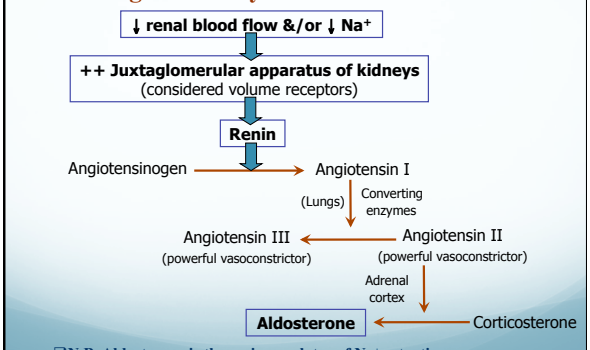
Renin-angiotensin II-aldosteron system

- Regulates ABP by regulating blood volume
- Most important mechanism for Na^+ retention in order to maintain the blood volume.
- A decrease in ABP – decrease in renal perfusion pressure
  - Mechanoreceptors in afferent arterioles
  - Juxtaglomerular cells secret renin (proteolytic enzyme)
  - In plazma, renin catalyzes the conversion of angiotensinogen to angiotensin I (a decapeptide)
  - In lungs, angiotensin I is converted to angiotensin II (catalyzed by angiotensin converting enzyme (ACE) (an octapeptide)

Role of angiotensin II

- In the zona glomerulosa cells of adrenal cortex stimulates production of aldosterone
  - In renal distal tubule and collecting duct increases Na^+ reabsorption – increases ECF volume and blood volume
- In arterioles angiotensin II causes vasoconstriction – increase in TPR
- In the renal proximal tubule stimulates Na^+-H^+ exchange – increase in ECF volume
- In the CNS stimulates thirst an drinking behavior

Renin-Angiotensin System:



❑N.B. Aldosterone is the main regulator of Na^+ retention.

Antidiuretic hormone

- Secreted by the posterior lobe of the pitiutary gland after
  - increased osmolarity
  - decreased ABP (e.g. hemorrhage), atrial volume receptors are stimulated
- Regulates body fluid osmolarity
- 2 types of receptors:
  - V1: in vascular smooth muscles – cause vasoconstriction of arterioles, increase TRP
  - V2: in renal collecting ducts are involved in water reabsorption, maintain osmolarity

Anti-diuretic hormone (ADH), or vasopressin:

- Hypovolemia & dehydration will stimulate the osmoreceptors in the hypothalamus, which will lead to release of ADH from posterior pituitary gland.
- ADH will cause water reabsorption at kidney tubules.

Atrial natriuretic peptide

- ANP is secreted by the atria in response to increase in ECF volume and atrial pressure
- Mechanism of action:
  - Relaxation of vascular smooth muscle – vasodilatation, decrease TPR
  - In the kidney – increased Na^+ and water excretion = decrease ECFV and ABP

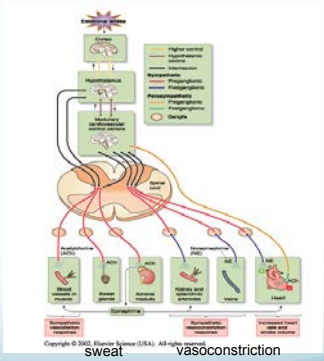
Changes in posture from supine position to standing

- Mechanism of orthostatic hypotension
  - Blood pools in the veins of lower extremities
  - Venous return to the heart decreases, cardiac output decreases (Frank-Starling law)
  - Mean arterial pressure decreases
  - Decreased activation of baroreceptors
  - Increased sympathetic outflow to the heart and blood vessels and decreased parasympathetic outflow

Fight or Flight Reaction (Sudden Sympathetic Drive)

1. Skeletal muscle blood flow – sympathetic cholinergic stimulation - vasodilation.
2. Cutaneous blood flow – sympathetic cholinergic response – sweat glands.
3. Adrenal medulla – sympathetic stimulation release epinephrine – causes **vasodilation in muscle** and **vasoconstriction in kidney/splanchnic** Vessels.
4. Veins – vasoconstriction (sympathetic)
5. Heart – Increased sympathetic stimulus – increased HR and contractility
6. MAP – Overall output is an increase in blood pressure.

Fight or Flight Response



sweat vasoconstriction

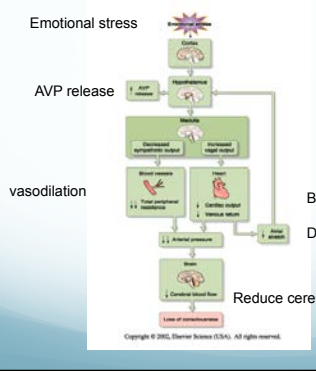
vasodilation epinephrine Heart rate contractility

FAINTING (Massive Parasympathetic Response)

"vasovagal syncope"

1. **Massive vasodilation occurs** – removal of sympathetic tone causes a rapid fall in blood pressure.
2. **Decreased Cardiac output** – Increased vagal output to heart causes bradycardia and decreased stroke volume
3. **Decreased arterial blood pressure** – secondary to vasodilation and CO.
4. **Cerebral blood flow** – reduced (> 10 seconds) – fainting occurs

FAINTING
(Massive Parasympathetic Response)



Integrated Response to Massive Hemorrhage

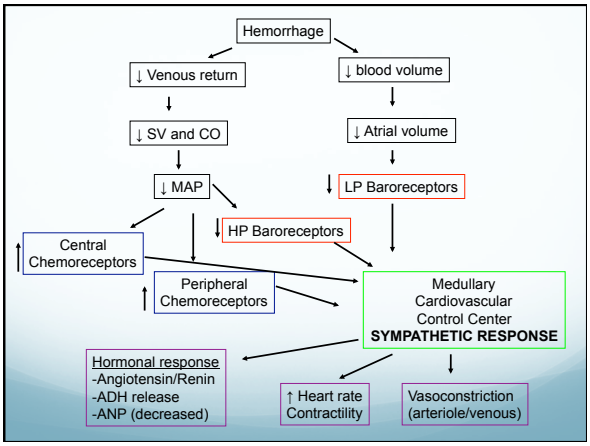
1. **Baroreceptors – high pressure** – **decreased firing** – result is enhanced Sympathetic output and less vagal output
   ↑ **tachycardia, contractility, vasoconstriction** – re-establish MAP

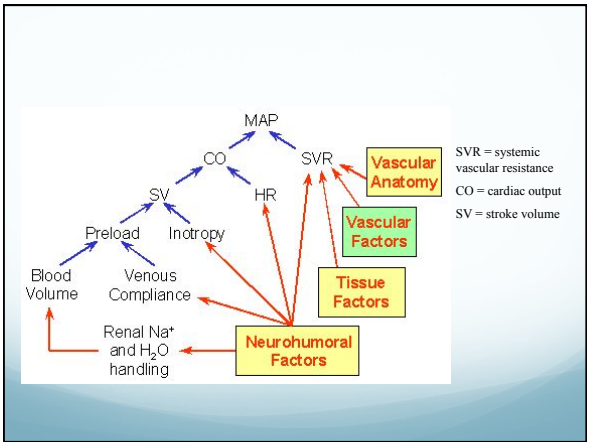
2. Baroreceptors – low pressure – reduced VOLUME – less activity of LPBs. Increased sympathetic output – vasoconstriction particularly of kidney BVs Increased release of **Anti-diuretic hormone**

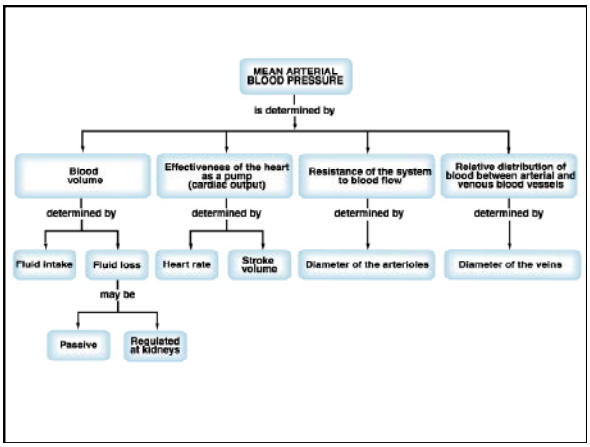
3. Peripheral Chemoreceptors – low MAP reduces perfusion of carotid/aortic bodies Local hypoxia – **increased firing of chemoreceptors – vasoconstriction** and changes in ventilation.

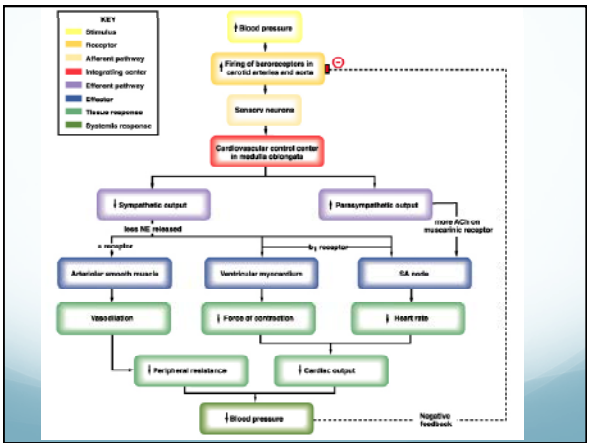
4. Central Chemoreceptors – fall in blood pH (acidosis) – increased sympathetic Output – **vasoconstriction**

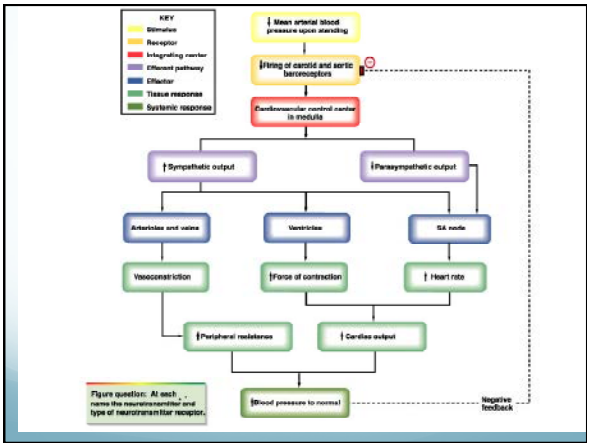
5. Adrenal medulla – as a result of sympathetic stimulation – increased Medullary **secretion of epinephrine** (a BP drop to 40 mmHg - 50 fold increase in Epi)










KEY
Stimulus
Receptor
Integrating center
Efferent pathway
Effector
Tissue response
Systemic response
↓ Mean arterial blood pressure upon standing
↓ Firing of carotid and aortic baroreceptors
Cardiovascular control center in medulla
↑ Sympathetic output
↓ Parasympathetic output
Arterioles and veins
Ventricles
SA node
Vasoconstriction
↑ Force of contraction
↑ Heart rate
↑ Peripheral resistance
↑ Cardiac output
↑ Blood pressure to normal
Negative feedback
Figure question: At each ___ name the neurotransmitter and type of neurotransmitter receptor.