Regulation of blood pressure

\[ \text{MAP} = \text{CO} \times \text{TPR} \]

\[ \text{HR} \quad \text{SV} \]

↑Sympathetic activity
↓Capacitance of large veins

Figure 11-1. Anatomic sites of blood pressure control.

Katzung
Cardiac Output (CO) is influenced by:

**Preload** = venous return
(Starling's law of the heart!)

**Afterload** = resistance to CO
(TPR + pulmonary/aortic resistance)
Regulation of tissue blood flow (review)

Pressure gradients:
- Systemic pressure (MAP - CVP*)
- Capillary pressures

Arterial resistance:
- Autoregulation (e.g., pO₂, pCO₂, pH, lactic acid)
- Vasoactive factors
  - (e.g., histamine, bradykinin, angiotensin II, vasopressin)
- Myogenic tone

\[ \text{Flow} = \frac{\Delta \text{Pressure}}{\text{Resistance}} \]

*Central venous pressure ~ right atrial pressure
# Vasoactive compounds (examples)

<table>
<thead>
<tr>
<th>Vasoconstrictors</th>
<th>Vasodilators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norephinephrine and Epinephrine (via $\alpha_1$-AR)</td>
<td>Epinephrine (via $\beta_2$-AR)</td>
</tr>
<tr>
<td>Serotonin</td>
<td>Histamine</td>
</tr>
<tr>
<td>Angiotensin II (via AT$_1$ receptors)</td>
<td>Atrial natriuretic peptide (ANP)</td>
</tr>
<tr>
<td>Endothelin (ET$_1$ receptors)</td>
<td>Bradykinin</td>
</tr>
<tr>
<td>Vasopressin (or ADH)</td>
<td>PGE$_2$ (prostaglandin)</td>
</tr>
<tr>
<td></td>
<td>PGI$_2$ (prostacyclin)</td>
</tr>
<tr>
<td></td>
<td>NO (nitric oxide)</td>
</tr>
<tr>
<td></td>
<td>ACh (acetylcholine)</td>
</tr>
<tr>
<td></td>
<td>-in some vessels</td>
</tr>
</tbody>
</table>

Important: different vascular beds have different receptors!!
Review of sympathetic nervous system effects on heart and vasculature

A. Effects of norepinephrine

- Feedback inhibition
- Smooth muscle
- Sympathetic neuron
- Decreased cAMP
- NE
- Heart
- + Inotropic
- + Chronotropic
Regulation of Systemic Blood Pressure

Short-term regulation (neural)
Reflexes "negative feedback mechanisms"

- Baroreceptors
- Chemoreceptors
- Cerebral ischemic response
- Higher brain functions (e.g., anticipation)

Long-term regulation (renal)

- Renal control of blood volume
- Atrial stretch*
Nervous system control of arterial pressure (short-term (seconds to hours))

Higher brain areas

Vasomotor center (medulla and pons)

Systemic responses e.g., baroreceptors

↓ HR
(ACh on nodal cells)

↑ HR, ↑ contraction
↑ TPR
↑ venous return (NE/Epi)

vagus n.

sympathetic n.

(-)↑↓ (-)
Medullary center

Baroreceptor afferents

Carotid sinus

Aortic arch

Heart

Sympathetic (NE)

Vagus (ACh)

Adrenal medulla (releases Epi/NE)

Arterioles/veins

Ganong Fig 31-7
Baroreceptors respond to stretch

Carotid sinus

Aortic arch

Neural signals to medullary control center

Sherwood Fig 10-37
Baroreceptors are not involved in long-term control: quickly readjust to higher pressure

Ganong Fig 31-11
Parasympathetic stimulation → Heart → ↓ Heart rate → ↓ Cardiac output → ↓ Blood pressure

Sympathetic stimulation → Heart → ↑ Heart rate
  → ↑ Contractile strength of heart
  → ↑ Stroke volume
  → ↑ Cardiac output → ↑ Blood pressure

Heart → Arterioles → ↑ Vasoconstriction
  → ↑ Vasoconstriction

Veins → ↑ Vasoconstriction
  → ↑ Venous return
  → ↑ Stroke volume
  → ↑ Cardiac output → ↑ Blood pressure

“afterload”

 preload

venoconstriction

Sherwood Fig 10-39
When blood pressure becomes elevated above normal

↓ Carotid sinus and aortic arch receptor potential

↑ Rate of firing in afferent nerves

Cardiovascular center

↓ Sympathetic cardiac nerve activity and 
↓ sympathetic vasoconstrictor nerve activity and
↑ parasympathetic nerve activity

↓ Heart rate and 
↓ stroke volume and arteriolar and venous vasodilation

↓ Cardiac output and 
↓ total peripheral resistance

Blood pressure decreased toward normal

Sherwood Fig 10-40
Explain cardiovascular responses if your patient is taken from a horizontal position to a 60° position (head up) on a tilt table

Initial ΔBP? Decreased because of gravity (hydrostatic pressure)

Reflex response? Dec baroreceptor firing rate turns on Symp response

Outcome? Inc CO through (B1 - AR), vasoconstriction (A1), Inc Venous return b/c of venoconstriction, inc BP
Explain cardiovascular responses upon standing up abruptly from a supine position (any differences from tilt table experiment?)
Summary of neural control of MAP
Chemoreceptor reflex

Chemoreceptors in carotid and aortic bodies
Sensitive to:

\[ \downarrow \text{pO}_2 \]
\[ \uparrow \text{CO}_2 \]
\[ \downarrow \text{pH} \]

\[ \downarrow \text{Blood flow} \rightarrow \text{Activate vasomotor center} \rightarrow \uparrow \text{BP} \]
(aortic, carotid)

Less sensitive than baroreceptors
Responds mostly to low BP
Start here

Carotid and Aortic bodies
chemoreceptors

↓$P_{CO_2}$

Lung stretch

↑Ventilation

Central chemoreceptor

↓$P_{O_2}$  ↑$P_{CO_2}$  ↓pH

Heart

↑Cardiac Output

improves metabolic status

Medullary vagal control center
Cerebral Ischemia Reflex

↓ Blood flow → ↑↑↑ Activate vasomotor center → ↑ BP

Extremely powerful response

Preserves blood flow to brain

May completely shut down urine output and peripheral circulation
Short-Term and Long-Term Control of Blood Pressure

Maximum feedback gain

Acute Change in Pressure at This Time

CNS ischemic response

Baroreceptors

Chemoreceptors

Renal Body-fluid

Time After Sudden drop in Pressure

Seconds
Minutes
Hours
Days

modified from G&H
Your 67 year old patient has experienced bouts of syncope, particularly when she gets up from watching TV to answer the phone. She has been previously diagnosed with significant bilateral carotid artery atherosclerosis (plaque formation), and arteriosclerosis (decreased arterial compliance).

What do you suspect is happening?
Long-term control of blood pressure

Involves signals to kidney that BP is changed
e.g., ↓BP → ↓ renal perfusion

Physiological:
e.g., ↓ blood volume

Pathophysiiological:
e.g., renal artery stenosis

arterial resistance may be different at different sites
Renal Physiology
101

G&H Fig 26-3
Only ~20% gets filtered each time through kidney.
Possible outcomes of substance handling

**Freely filtered**
- Not secreted
- Not reabsorbed

**Freely filtered**
- Not secreted
- Fully reabsorbed

**Freely filtered**
- Not secreted
- Partially reabsorbed

**Freely filtered**
- Secreted
- Not reabsorbed

*(some substances are too big to be filtered)*
Aldosterone (ALD)
Na⁺ reabsorption
K⁺ secretion

Antidiuretic hormone (ADH)
Water reabsorption

modified Katzung Fig 15-1
G&H Figure 26-17 Structure of the juxtaglomerular apparatus regulates renin secretion
Macula densa feedback mechanism for autoregulation of glomerular hydrostatic pressure and glomerular filtration rate (GFR) during decreased renal arterial pressure.

*systemic response is to ↑BP*

G&H Figure 26-18

Macula densa feedback mechanism for autoregulation of glomerular hydrostatic pressure and glomerular filtration rate (GFR) during decreased renal arterial pressure.
Response to drop in BP

ACE = angiotensin converting enzyme

Ganong Fig. 39-2
Response mediated by the sympathetic nervous system

Sympathetic activity

 Activation of $\beta_1$ adrenoceptors on heart

 Cardiac output

 Activation of $\alpha_1$ adrenoceptors on smooth muscle

 Peripheral resistance

 Increase in blood pressure

 Decrease in blood pressure

 Renal blood flow

 Renin

 Angiotensin II

 Aldosterone

 Glomerular filtration rate

 Sodium, water retention

 Blood volume

 Brain

 Thirst (drink)

Response mediated by the renin-angiotensin-aldosterone system

modified from Lippincott Fig 19-3
Increased blood pressure

(inhibits)

\[ \text{Angiotensinogen} \rightarrow \text{Renin (from kidney)} \rightarrow \text{Angiotensin I (inactive)} \rightarrow \text{Angiotensin II} \rightarrow \text{ACE} \rightarrow \text{Decreased aldosterone production} \rightarrow \text{Decreased blood pressure}

\[ \downarrow \text{Antidiuretic hormone (vasopressin)} \]

\[ \text{ACE} = \text{angiotensin converting enzyme} \]

Bradykinin is a vasodilator
Atrial reflexes

↑ Venous return → ↑ Atrial stretch → Hypothalamus

↑ HR (↑ SA nodal firing)

↑ Cardiac Output

↑ Renal filtration

Kidneys excrete Na⁺ and H₂O

↓ Blood Volume

Antidiuretic Hormone (ADH)

Release of Atrial Natriuretic Peptide (ANP)

Blood Volume

(↑)

Bainbridge reflex

'low pressure baroreceptors'
Response to ↑ blood volume & pressure

1. Sympathetic nerve activity → Brain
2. Brain → ADH
3. ADH → Kidneys
4. Kidneys → NaCl and H2O excretion
5. NaCl and H2O excretion → Blood volume and pressure

Response to ↓ blood volume & pressure

1. Sympathetic nerve activity → Brain
2. Brain → ADH
3. ADH → Kidneys
4. Kidneys → NaCl and H2O excretion
5. NaCl and H2O excretion → Blood volume and pressure

Netter Fig 4-20
Short-Term and Long-Term Control of Blood Pressure

- CNS ischemic response
- Baroreceptors
- Chemoreceptors
- Renal Body-fluid

Modified from G&H