Vascular Endothelium

<table>
<thead>
<tr>
<th>Vasodilators</th>
<th>Vasoconstrictors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitric Oxide</td>
<td>Endothelin-1</td>
</tr>
<tr>
<td>Prostacyclin</td>
<td>Angiotensin II</td>
</tr>
<tr>
<td>Endothelium-derived hyperpolarizing</td>
<td></td>
</tr>
<tr>
<td>factor</td>
<td></td>
</tr>
<tr>
<td>Bradykinin</td>
<td></td>
</tr>
</tbody>
</table>

Wilson SH, Lerman A.  
Heart Physiology and Pathophysiology, Academic Press  
(edited by Sperelakis N.) 473-480
Nitric Oxide (NO) Function

- Vasodilator
- Inhibitor of vascular smooth muscle cell proliferation
- Inhibitor of platelet adherence/aggregation
- Inhibitor of leukocyte/endothelial interactions
Endothelial Dysfunction

Atherosclerotic risk factors

- Decreased NO bioavailability
- Increased levels of ET-1
Distribution of blood volume in a resting man (5.5 litres)

Palpated Pulse
Posterior Tibial Artery

Dorsalis Pedis Artery

http://www.med.umich.edu/lrc/courses/M1/anatomy/html/surface/pulses/pulses.html
shows the common sites where the pulse is felt.
1. Temporal artery at the temple above and to the outer side of the eye
2. External maxillary (facial) artery at the point of crossing the mandible (lower jaw)
3. Carotid artery on the side of the neck
4. Brachial artery on the inner side of the biceps
5. Radial artery on the radial bone side of the wrist
6. Femoral artery in the groin
7. Popliteal artery behind the knee
8. Posterior tibial pulse behind the inner ankle
9. Dorsalis pedis artery on the upper front part (anteriosuperior aspect) of the foot
Your pulse is the rate at which your heart beats.

Your pulse is usually called your heart rate, which is the number of times your heart beats each minute (bpm).

Example:
Given the following data:
Mean Blood Pressure = 100 mmHg
Diastolic Blood Pressure = 90 mmHg
Pulse rate [PR] = 25 pulses/15 seconds

\[
PR = \left( \frac{25 \text{ pulses}}{15 \text{ seconds}} \right) \times \left( \frac{60 \text{ seconds}}{1 \text{ minute}} \right) = 100 \text{ pulses / minute}
\]

\[
HR = \text{pulse rate} = 100 \text{ b/min}
\]
At normal resting heart rates $MAP$ can be approximated using the more easily measured systolic and diastolic pressures, $SP$ and $DP$:

$$MAP \approx DP + \frac{1}{3}(SP - DP)$$

or equivalently

$$MAP \approx \frac{(2 \times DP) + SP}{3}$$

or equivalently

$$MAP \approx DP + \frac{1}{3}PP$$

where $PP$ is the pulse pressure, $SP - DP$
• Blood Pressure = Cardiac Output x Total Peripheral Resistance

or

• BP = CO x TPR
The main factors influencing blood pressure are:

- Cardiac output (CO)
- Peripheral resistance (PR)
- Blood volume

**Blood pressure** = CO x PR

Blood pressure varies directly with CO, PR, and blood volume.
- **Stroke Volume (SV)** = EDV – ESV
- **Ejection Fraction (EF)** = (SV / EDV) × 100%
- **Cardiac Output (Q)** = SV × HR
- **Cardiac Index (CI)** = Q / Body Surface Area (BSA) = SV × HR/BSA

HR is Heart Rate, expressed as BPM (Beats Per Minute) BSA is Body Surface Area in square metres.
• Flow = Pressure/Resistance
• $Q_{[co]} = (\text{MAP} - \text{RAP})/\text{TPR}$

Where MAP = Mean Aortic (or Arterial) Blood Pressure in mmHg,

• RAP = Mean Right Atrial Pressure in mmHg and TPR = Total Peripheral Resistance in dynes-sec-cm$^{-5}$.

• $Q \approx (\text{HR} \times \text{SV}) \approx \text{MAP} / \text{TPR}$
Cardiac Output (CO)

**Figure 19.7**

- **BP activates cardiac centers in medulla**
- **Parasympathetic activity**
- **Sympathetic activity**

- **Activity of respiratory pump (ventral body cavity pressure)**
- **Activity of muscular pump (skeletal muscles)**
- **Sympathetic vasoconstriction**

- **Epinephrine in blood**

- **Venous return**
- **Contractility of cardiac muscle**

- **EDV**
- **ESV**

- **Stroke volume (SV)**
- **Heart rate (HR)**

**Key:**
- **Increased**
- **Decreased**

- **Initial stimulus**
- **Physiological response**
- **Result**

**Cardiac output (CO = SV x HR)**
Blood Flow

- Actual volume of blood flowing through a vessel, an organ, or the entire circulation in a given period:
  - Is measured in ml per min.
  - Is equivalent to cardiac output (CO), considering the entire vascular system.
  - Is relatively constant when at rest.
  - Varies widely through individual organs.

Blood Flow
Blood flow (F) is directly proportional to the difference in blood pressure (ΔP) between two points in the circulation.

- If ΔP increases, blood flow speeds up; if ΔP decreases, blood flow declines.

Blood flow is inversely proportional to resistance (R).

- If R increases, blood flow decreases.

R is more important than ΔP in influencing local blood pressure.
Flow rate through blood vessels
• directly proportional to the pressure gradient
• inversely proportional to vascular resistance
Blood Flow

Blood flow (F) depends on:

1. Pressure Gradient ($\Delta P$) - heart
2. Resistance (R) - blood vessels
   * viscosity
   * vessel length
   * vessel diameter

Vessel diameter is the main determinant of vascular resistance.
Resistance factors that remain relatively constant are:

- **Blood viscosity** – “stickiness” of the blood
- **Blood vessel length** – the longer the vessel, the greater the resistance encountered
• Force per unit area exerted on the wall of a blood vessel by its contained blood
  ◦ Expressed in millimeters of mercury (mm Hg)
  ◦ Measured in reference to systemic arterial BP in large arteries near the heart
• The differences in BP within the vascular system provide the driving force that keeps blood moving from higher to lower pressure areas
Normal blood pressures are said to range from 100/60 mmHg to 150/90 mmHg.

Table 1. Some 'average' blood pressures relating to age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Systolic pressure (mmHg)</th>
<th>Diastolic pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>New-born</td>
<td>80</td>
<td>46</td>
</tr>
<tr>
<td>10</td>
<td>103</td>
<td>70</td>
</tr>
<tr>
<td>20</td>
<td>120</td>
<td>80</td>
</tr>
<tr>
<td>40</td>
<td>126</td>
<td>84</td>
</tr>
<tr>
<td>60</td>
<td>135</td>
<td>89</td>
</tr>
</tbody>
</table>
● **Systemic pressure:**
  ◦ Is highest in the aorta
  ◦ Declines throughout the length of the pathway
  ◦ **Is 0 mm Hg in the right atrium**
● **The steepest change in blood pressure occurs in the arterioles**
• **Systolic pressure** – pressure exerted on arterial walls during ventricular contraction

• **Diastolic pressure** – lowest level of arterial pressure during a ventricular cycle

• **Pulse pressure** – the difference between systolic and diastolic pressure

• **Mean arterial pressure (MAP)** – pressure that propels the blood to the tissues

• **MAP** = diastolic pressure + 1/3 pulse pressure[systolic]
Capillary Blood Pressure

- Capillary BP ranges from 20 to 40 mm Hg
- Low capillary pressure is desirable because high BP would rupture fragile, thin-walled capillaries
- Low BP is sufficient to force filtrate out into interstitial space and distribute nutrients, gases, and hormones between blood and tissues
Venous BP is steady and changes little during the cardiac cycle

- **The pressure gradient in the venous system is only about 20 mm Hg**
- A cut vein has even blood flow; a lacerated artery flows in spurts
Direction and amount of fluid flow depends upon the difference between:

- Capillary hydrostatic pressure ($HP_c$)
- Capillary colloid osmotic pressure ($OP_c$)

$HP_c$ – pressure of blood against the capillary walls:
- Tends to force fluids through the capillary walls
- Is greater at the arterial end of a bed than at the venule end

$OP_c$ – created by nondiffusible plasma proteins, which draw water toward themselves
• NFP – all the forces acting on a capillary bed
• \( NFP = (HP_c - HP_{if}) - (OP_c - OP_{if}) \)
• At the arterial end of a bed, hydrostatic forces dominate (fluids flow out)
Net Filtration Pressure (NFP)

Key to pressure values:
- $HP_c$ at arterial end = 35 mm Hg
- $HP_c$ at venous end = 17 mm Hg
- $HP_if = 0$ mm Hg
- $OP_if = 1$ mm Hg
- $OP_c = 26$ mm Hg

Figure 19.16
Blood Flow: Heart

- Small vessel coronary circulation is influenced by:
  - Aortic pressure
  - The pumping activity of the ventricles

- During ventricular systole:
  - Coronary vessels compress
  - Myocardial blood flow ceases
  - Stored myoglobin supplies sufficient oxygen

- During ventricular diastole, oxygen and nutrients are carried to the heart
Factors Aiding Venous Return

- Valve (open)
- Contracted skeletal muscle
- Valve (closed)
- Vein
- Direction of blood flow
Inadequate blood perfusion or excessively high arterial pressure:
  ◦ Are autoregulatory
  ◦ Provoke myogenic responses – stimulation of vascular smooth muscle

Vascular muscle responds directly to:
  ◦ Increased vascular pressure with increased tone, which causes vasoconstriction
  ◦ Reduced stretch with vasodilation, which promotes increased blood flow to the tissue
Short-Term Mechanisms: Vasomotor Activity

- **Sympathetic activity causes:**
  - Vasoconstriction and a rise in BP if increased
  - BP to decline to basal levels if decreased

- **Vasomotor activity is modified by:**
  - Baroreceptors (pressure-sensitive), chemoreceptors (O₂, CO₂, and H⁺ sensitive), higher brain centers, bloodborne chemicals, and hormones
Stimulus: Rising blood pressure

Homeostasis: Blood pressure in normal range

Baroreceptors in carotid sinuses and aortic arch stimulated

Arterial blood pressure rises above normal range

Rate of vasomotor impulses allows vasodilation (vessel diameter)

Impulse traveling along afferent nerves from baroreceptors:
Stimulate cardio-inhibitory center (and inhibit cardio-acceleratory center)

Sympathetic impulses to heart
HR and contractility

CO and R return blood pressure to homeostatic range

Inhibit vasomotor center
Vasomotor fibers stimulate vasoconstriction.

CO and R return blood pressure to homeostatic range.

Cardiac output (CO).

Peripheral resistance (R).

Impulses from baroreceptors:
- Stimulate cardio-acceleratory center (and inhibit cardio-inhibitory center).

Stimulus: Declining blood pressure.

Arterial blood pressure falls below normal range.

Impulses to heart (HR and contractility).

Stimulate vasomotor center.

Baroreceptors in carotid sinuses and aortic arch inhibited.

Figure 19.8
Vasomotor fibers stimulate vasoconstriction. Stimulating vasomotor fibers return blood pressure to homeostatic range.

Cardiac output (CO) and peripheral resistance (R) return blood pressure to homeostatic range.

Impulse traveling along afferent nerves from baroreceptors:
- Stimulate cardio-inhibitory center (and inhibit cardio-acceleratory center).
- Stimulate cardio-acceleratory center (and inhibit cardio-inhibitory center).

Baroreceptors in carotid sinuses and aortic arch stimulated.

Arterial blood pressure rises above normal range.

Stimulus: Rising blood pressure.

Stimulate cardio-acceleratory center (and inhibit cardio-inhibitory center).

Rate of vasomotor impulses allows vasodilation (vessel diameter).

Sympathetic impulses to heart (HR and contractility).

Sympathetic impulses to inhibit vasomotor center.

Baroreceptors in carotid sinuses and aortic arch inhibited.

Arterial blood pressure falls below normal range.

Stimulus: Declining blood pressure.

Baroreceptors in carotid sinuses and aortic arch stimulated.

Arterial blood pressure rises above normal range.

Impulse traveling along afferent nerves from baroreceptors:
- Stimulate cardio-inhibitory center (and inhibit cardio-acceleratory center).
- Stimulate cardio-acceleratory center (and inhibit cardio-inhibitory center).

Stimulate cardio-acceleratory center (and inhibit cardio-inhibitory center).

Rate of vasomotor impulses allows vasodilation (vessel diameter).

Sympathetic impulses to heart (HR and contractility).

Sympathetic impulses to inhibit vasomotor center.

Homeostasis: Blood pressure in normal range.

Figure 19.8
Chemicals that Increase Blood Pressure

- **Adrenal medulla hormones** – norepinephrine and epinephrine increase blood pressure
- **Antidiuretic hormone (ADH)** – causes intense vasoconstriction in cases of extremely low BP
- **Angiotensin II** – kidney release of renin generates angiotensin II, which causes vasoconstriction
- **Endothelium-derived factors** – endothelin and prostaglandin-derived growth factor (PDGF) are both vasoconstrictors
• **Atrial natriuretic peptide (ANP)** – causes blood volume and pressure to decline
• **Nitric oxide (NO)** – is a brief but potent vasodilator
• **Inflammatory chemicals** – histamine, prostacyclin, and kinins are potent vasodilators
• **Alcohol** – causes BP to drop by inhibiting ADH

**Chemicals that Decrease Blood Pressure**
Long-term mechanisms control BP by altering blood volume

- **Baroreceptors adapt to chronic high or low BP**
  - Increased BP stimulates the kidneys to eliminate water, thus reducing BP
  - Decreased BP stimulates the kidneys to increase blood volume and BP
Kidney Action and Blood Pressure

Table 138. Clinical Evaluation of Patients at Increased Risk of Chronic Kidney Disease

**All Patients**
- Measurement of blood pressure
- Serum creatinine to estimate GFR
- Protein-to-creatinine ratio or albumin-to-creatinine ratio in a first-morning or random untimed “spot” urine specimen
- Examination of the urine sediment or dipstick for red blood cells and white blood cells

**Selected Patients, Depending on Risk Factors**
- Ultrasound imaging (for example, in patients with symptoms of urinary tract obstruction, infection or stone, or family history of polycystic kidney disease)
- Serum electrolytes (sodium, potassium, chloride and bicarbonate)
- Urinary concentration or dilution (specific gravity or osmolality)
- Urinary acidification (pH)

Key:
- Initial stimulus
- Physiological response
- Result
Blood flow to venous plexuses below the skin surface:

- Varies from 50 ml/min to 2500 ml/min, depending on body temperature
- Is controlled by sympathetic nervous system reflexes initiated by temperature receptors and the central nervous system
• As temperature rises (e.g., heat exposure, fever, vigorous exercise):
  ◦ Hypothalamic signals reduce vasomotor stimulation of the skin vessels
  ◦ Heat radiates from the skin
• Sweat also causes vasodilation via bradykinin in perspiration
  ◦ Bradykinin stimulates the release of NO
• As temperature decreases, blood is shunted to deeper, more vital organs
Blood flow in the pulmonary circulation is unusual in that:

- The pathway is short
- Arteries/arterioles are more like veins/venules (thin-walled, with large lumens)
- They have a much lower arterial pressure (24/8 mm Hg versus 120/80 mm Hg)
Three types include:

- Hypovolemic shock – results from large-scale blood loss
- Vascular shock – poor circulation resulting from extreme vasodilation
- Cardiogenic shock – the heart cannot sustain adequate circulation
Acute bleeding (or other events leading to blood volume loss) leads to:

1. Inadequate tissue perfusion → ↓ O₂ and nutrients to cells
2. Cells begin to metabolize anaerobically (without O₂) → lactic acid accumulates
3. Interstitial fluid moves into blood → tissues dehydrate

Compensatory mechanisms activated:

- Chemoreceptors activated (by ↓ in blood pH)
  - major effect: Activation of respiratory centers
  - minor effect: Cardioacceleratory and vasomotor centers activated
  - ↑ Rate and depth of breathing
  - CO₂ blown off; blood pH rises

- Baroreceptor firing reduced (by ↓ in blood volume and blood pressure)
  - Heart rate

- Hypothalamus activated (by ↓ pH and ↓ blood volume)
  - Intense vasoconstriction (only heart and brain spared)
  - Renal blood flow
  - Angiotensin II produced in the blood
  - Aldosterone released
  - Kidneys retain salt and water
  - ↓ Urine output

Brain

Thirst

Blood pressure maintained

ADH released

Kidney

Restlessness (early sign)

Central nervous system depressed

Coma (late sign)

Water retention

↑ Blood volume

↑ Urine output

If fluid volume continues to decrease, blood pressure ultimately drops. ↓ Blood pressure is a late sign.