Vascular Biology I - Components of the Vascular System

Functions of Vascular system:

1-Active transport of substances through the body
(small organisms have mostly passive transport): Nutrients (glucose, ATP), Oxygen, waste, hormones
(chemical signals), host defenses (WBC, platelets, globulins … etc)

2 - Regulation of that flow:
Arterial “shunts” to distribute blood flow to organs that need it the most (eg – blood flow to the brain and
heart must be maintained at all costs, so in the event of blood loss, vasoconstriction occurs).
“Basal tone” – tonic contraction of vessel smooth muscle in the absence of external stimulation.

3 – Thermal regulation:
Blood flow through skin -> heat radiation -> cooling (quite efficient). By redirecting flow, you can cool
down or heat up internal organs.

→ maintenance of homeostasis
Distribution of systematic blood flow

<table>
<thead>
<tr>
<th>Organ</th>
<th>Flow Rate at Rest (ml/min)</th>
<th>% of Total Flow</th>
<th>Flow Rate with Strenuous Exercise (ml/min)</th>
<th>% of Total Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain</td>
<td>650</td>
<td>13</td>
<td>750</td>
<td>4</td>
</tr>
<tr>
<td>Heart</td>
<td>215</td>
<td>4</td>
<td>750</td>
<td>4</td>
</tr>
<tr>
<td>Skel. Musc.</td>
<td>1,030</td>
<td>20</td>
<td>12,500</td>
<td>73</td>
</tr>
<tr>
<td>Skin</td>
<td>430</td>
<td>9</td>
<td>1,900</td>
<td>11</td>
</tr>
<tr>
<td>Kidney</td>
<td>950</td>
<td>20</td>
<td>600</td>
<td>3</td>
</tr>
<tr>
<td>Abd. Organs</td>
<td>1,200</td>
<td>24</td>
<td>600</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>545</td>
<td>10</td>
<td>400</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>5,000</td>
<td>100</td>
<td>17,500</td>
<td>100</td>
</tr>
</tbody>
</table>

Components of the Cardiovascular System

1. Heart – obviously the pump that drives the system (more details elsewhere)
2. Blood- main components:
   a. Erythrocytes (Red Blood Cells) – Carry oxygen bound to hemoglobin molecules, Hematocrit” = % of blood volume made up by erythrocytes.
   c. Plasma – the solvent. Contains mostly water, proteins, dissolved gasses, nutrients, hormones, waste products …
   d. Platelets. Responsible for clotting (repair of damaged tissue, plug for hemorrhages…) The clotting process consists of a complex cascade of chemical signals.
3. Lymphatic system: endothelial filtration can produce excess water and other materials, mostly protein: “lymph”. Parallel vascular system that returns this fluid into the venous system at the junctions of subclavian and jugular veins. Flow is passive, powered by muscle contractions and guided by one-way valves. Proteins go from blood to lymph because of osmotic gradient. Need lymphatic system to return them to the blood.
4. Vasculature : arteries (input to tissue) and veins (output from tissue), capillaries (site of exchange)
b - Vascular Components – Macroscopic level

Distribution of Blood through vascular system and maintain pressure, pulsatility, etc.
-Components (the different types of vessels)

1. Aorta, arteries: very elastic- they store the cardiac stroke volume until it can flow through the system. As you get further from heart, the pressure waves become more smoothed out (they act as a low pass filter because of their compliance)

2. Arterioles: local control of blood flow by regulating the amount of flow to individual organs through arterial sphincters. They are responsible for maintaining the peripheral resistance

3. Capillaries: Are the site of chemical exchanges between blood and tissue (Oxygen, nutrients, ions …). Pulmonary vessels are where oxygen enters the blood stream.

4. Venules: collect capillary blood and direct it into the veins

5. Veins: Take the deoxygenated blood back to the heart. Very compliant, little resistance (passive). Not much muscle tone. The inner walls have pockets that act as one-way valves (not 100%). Return blood flow is often aided by skeletal muscles’s actions (eg- some people faint after standing for a long time, because leg muscles help the blood return to the heart)

6. Lymphatic system: carries interstitial fluid / excess protein into the venous return so that they can enter the vascular system. Similar to veinous network (not identical, though). Flow is driven by oncotic pressure, muscle movement, contractions of lymphatic vessels, and one way valves. Lyphatic system enters veinous system at the junction of sub-clvian and jugular veins.
Cross-sectional area of the various blood vessels in the systemic and pulmonary circulation along with the percentage volume of blood for a 20 kg dog. (From Milnor[1989] with permission from the author and Williams and Wilkins Co.)
Fig. 2A-1  A, Low-magnification electron micrograph of an arteriole in cross section (inner diameter of approximately 40 μm) in cat ile. The wall of the blood vessel is composed largely of vascular smooth muscle cells (SM) whose long axes are directed approximately circularly around the vessel. A single layer of endothelial cells (E) forms the innermost portion of the blood vessel. Connective tissue (CT) elements such as fibroblasts and collagen make up the adventitial layer at the periphery of the vessel; nerve bundles (N) also lie in this layer. EN, Endothelial cell nucleus. B, Detail of the wall of the blood vessel in panel A. This field contains a single endothelial layer (E), the medial smooth muscle layer (three smooth muscle cell profiles; SM₁, SM₂, SM₃), and the adventitial layer (fibroblasts [N] and connective tissue [CT]). SMN, Smooth muscle nucleus. C, Another region of the arteriole, showing the area between the endothelial (E) and smooth muscle (SM) layers that are apposed. A projection of an endothelial cell (between arrows) is closely associated to the surface of the overlying smooth muscle, forming a "myoendothelial junction." Plasmalemmal vesicles are prominent in the endothelium (V) and the smooth muscle cell (where such vesicles are known as "caveolae" [C]).
a. Vascular components: Microscopic level endothelium, connective tissue, VSM.
   i). Endothelium: lining tissue (endothelial cells). lots of functions;
      - Liner for the interior of the blood vessels. Non reactive to RBCs.
      - Barrier between blood and tissue. Materials penetrate tissues through pores (4 nm diameter), or junctions between endothelial cells, EXCEPT for brain. “brain blood barrier”.
      - Passive Transport: sum of the following:
        - Diffusion \( (J = D*A* \frac{dc}{dx} = P*S*(Cout - Cin)) \)
        - Hydrostatic pressure (pushes fluid out of capillaries - strongest)
        - Osmotic pressure (keeps fluid in capillaries).
      (“Starling Hypothesis”: transport can be calculated as the sum of all of the above.)
      - “leftovers’ accumulate in the interstitial space end get taken up by lymphatic system.
      
      - Active (as in pinocytosis)
      - Angiogenesis – generation of new vessels. (also helps produce VSM)
      - Produce vasoconstriction/dilation factors that signal VSM to act. (Endothelial Derived Contracting Factor, EDRelaxingF)

ii)- Connective Tissues
Maintain the vessels in place and provide the structure to support the intra-cascular pressure.
   - Elastin: polypeptide molecules with spring-like properties, give the tissue its elasticity. “stretchable”
   - Collagen Fibers: another peptide. Long, Rigid molecules. It’s used all over the body to give structure. Eg – fascia, tendons …

iii) – Vascular Smooth Muscle:

   a. Functions
      - Regulate the diameter (-> resistance to flow) of the vessel by constriction / dilation.
        Regulates where blood flow goes.
      - There can be one or more layers of it around the vessels.
      - Wraps around the vessels in a helical pattern. (Remember schwann cells?)
      - Slow reaction to signals relative to skeletal muscle.
        - Capable of sustaining contractions for extended periods of time.
        -

   b. Contraction
- Passive stretching if increased BP
- Different from skeletal muscle: no clearly defined sarcomeres, but still uses “sliding filament” mechanism driven by phosphorylation of cross-bridges. (this is activated by the presence of Ca++ ions in the myoplasm.)
- Difference from skeletal muscle: no troponin (this is what forms the cross bridges in skeletal muscle. In skeletal muscle, Ca++ ions trigger cross-bridge cycling of troponin directly).
  In VSM, Ca++ binds to calmodulin, this in turn leads to phosphorylation of myosin light chains: cross-bridge cycling.
- “latch state”: Can stay contracted with little phosphorylation activity once it gets contracted -> Easy to maintain tone.

c. Contraction signals:
- Direct factors (no intermediaries):
  - Hormones: epinephrine, norepinephrine, angiotensin … operate on receptor gated Ca++ channels
  - Pharmacological agents (receptor gated Ca++ channels)
  - Nervous input (voltage gated Ca++ channels)
- Indirect factors (cause endothelial tissue to release contracting/relaxing factors EDCF, EDRF). Some additional chemical factors may affect the action of different agents (block binding sites … etc) or change the availability of Ca++ locally.

<table>
<thead>
<tr>
<th>Smooth</th>
<th>Skeletal</th>
</tr>
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<tbody>
<tr>
<td>Coordinated activity</td>
<td>Individual Recruitment of Cells</td>
</tr>
<tr>
<td>Poor Efficiency</td>
<td>High Efficiency</td>
</tr>
<tr>
<td>Indirect Activation by Ca++</td>
<td>Direct activation by Ca++</td>
</tr>
<tr>
<td>Variable/graded contraction</td>
<td>On/Off</td>
</tr>
<tr>
<td>Low energy for sustained contraction</td>
<td>High energy for sustained contraction</td>
</tr>
<tr>
<td>Non-striated tissue</td>
<td>Striated sarcomeres</td>
</tr>
<tr>
<td>Actin &gt;&gt; Myosin</td>
<td>Actin ~ Myosin</td>
</tr>
</tbody>
</table>