A. structure:
- 100,000 km of pipes!
- total surface area 800–1000 m²
- 60,000 miles of capillaries
- diameters from 10 μm to 2 cm
- double network connected at smallest scale (anastomosed)

B. function:
- provide nutrients, oxygen to tissues and remove waste
- self-regulation/homeostasis, tissue remodeling and healing
- cellular, molecular trafficking

C. mechanics:
- Pressure: 5 – 120 mmHg
- Flow: 0.03 – 40 cm/s
Development of the Vasculature

Chicken embryos

Yolk sac vessels just after the onset of perfusion.

Connected tube formed.

Embryo 26 hours later than in A

Hierarchical structure formed.

(le Noble, Development 2004)
Development of the Vasculature

Mouse embryos:
- Normal
- Impaired heart function (impaired contractility \( Mlc2a^{-/-} \)).

When heart function is impaired, hierarchical branching does not develop.

Flow and hydraulic pressure control vascular structure.

(Lucitti, Development 2007)
A Typical Artery and a Typical Vein
Pressure and blood flow

Poiseuille’s relationship: \( \Delta P = \frac{8\mu lQ}{\pi r^4} \) (steady, laminar, pipe flow)

MRI, velocity mapping in thoracic aorta

Stenosis, w/o

Stenosis, 54%

(Canstein, MRM, 2006, 2007)
Mechanics: vessel wall

Longitudinal stress:
\[ \sigma_z = \frac{F}{A} = \frac{Pd^2}{((d+2t)^2 - d^2)} \]

Radial tension:
\[ \sigma_r = P \]

Hoop stress:
\[ \sigma_\theta = \frac{PD_m}{2t} \]
Vessel Wall Associated Pathologies

1. Atherosclerosis
Vessel Wall Induced Pathologies

2. Hypertensive Vascular Disease
Vessel Wall Induced Pathologies

3. Aneurysms

High risk of rupture and bleeding
What are the structural components?

<table>
<thead>
<tr>
<th>ARTERY/VEIN</th>
<th>% H₂O</th>
<th>% COLLAGEN</th>
<th>% ELASTIN</th>
<th>C:E RATIO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta</td>
<td>70.4 ± 0.4</td>
<td>45.5 ± 1.7</td>
<td>30.1 ± 1.7</td>
<td>1.58 ± 0.15</td>
</tr>
<tr>
<td>Carotid</td>
<td>71.1 ± 0.1</td>
<td>50.7 ± 2.1</td>
<td>20.1 ± 1.0</td>
<td>2.55 ± 0.13</td>
</tr>
<tr>
<td>Coronary</td>
<td>63.2 ± 1.0</td>
<td>47.9 ± 2.6</td>
<td>15.6 ± 0.7</td>
<td>3.12 ± 0.12</td>
</tr>
<tr>
<td>Femoral</td>
<td>68.0 ± 0.3</td>
<td>44.5 ± 1.4</td>
<td>24.5 ± 1.6</td>
<td>1.89 ± 0.14</td>
</tr>
<tr>
<td>Mesentery</td>
<td>70.8 ± 0.5</td>
<td>38.1 ± 1.7</td>
<td>26.5 ± 1.7</td>
<td>1.51 ± 0.15</td>
</tr>
<tr>
<td>Renal</td>
<td>70.4 ± 0.7</td>
<td>42.6 ± 1.6</td>
<td>18.7 ± 1.8</td>
<td>2.46 ± 0.27</td>
</tr>
<tr>
<td>Vena cava</td>
<td>35.07 ± 2.1</td>
<td>21.0 ± 3.7</td>
<td>1.67 ± 0.18</td>
<td></td>
</tr>
<tr>
<td>Jugular vein</td>
<td>41.8 ± 2.8</td>
<td>47.1 ± 3.1</td>
<td>0.89 ± 0.09</td>
<td></td>
</tr>
<tr>
<td>Femoral vein</td>
<td>47.0 ± 4.7</td>
<td>45.3 ± 2.6</td>
<td>1.04 ± 0.11</td>
<td></td>
</tr>
</tbody>
</table>

(Fischer GM & Llaurado JG, 1966; Zocalo, ISRN Physiology, 2013)
Structure of aorta

(Wolinsky, Cir Res, 1964)

(Wolinsky, Cir Res, 1964)

Medial tension

\[ T_{AA} = T_{PT} \]

\[ T_{AA} = 6T_{PT} \]

(Leung, Cir Res, 1977)
Vessel wall composition – aortic elastin

(Wolinsky, Cir Res, 1964)
Vessel wall composition – aortic elastin

(Sokolis, J Biomechanics, 2006)
Aortic wall composition – elastin

Longitudinal section

P=0

P=250 mmHg

(Sokolis, J Biomechanics, 2006)
Aortic wall composition – elastin

circumferential section

(Sokolis, J Biomechanics, 2006)
Aortic wall composition – collagen

Longitudinal section

P=0

P=250 mmHg

(Sokolis, J Biomechanics, 2006)
Aortic wall composition – collagen

circumferential section

(Sokolis, J Biomechanics, 2006)
Vessel wall – Non-linear elasticity

Heterogeneity: Two-phase materials

Collagen: $E = 10^9$ dynes/cm$^2$
Elastin: $E = 3 \times 10^6$ dynes/cm$^2$

$$\sigma = E \varepsilon$$

(Wagenseil, Mecham, 2005)
Diminished windkessel effect, hardening of the artery (fragmentation and loss of elastin)

(Wagenseil and Mecham, Physiol Rev 2009)
Vessel wall function - disease

pulmonary arteries – rat smoking.

(Liu and Fung, J Biomechanics, 1992)
Vessel wall function - hypertension

Rat cerebral artery  3-order resistive vessel

(Dunn, Hypertension, 1997)
Vessel wall function - disease

σ

Calcified portion ruptures

Calcified portion is recruited

Load-free extension

ε
What causes the change of vessel structure and function?

Learn from the development:
In 1893, Thomas:

- Vessel lumen size depends on blood flow
- Vessel length depends on longitudinal force on connective tissues
- Vessel wall thickness depend on pressure
Changes by the cells

ECs:

short term -> secrete vasoconstrictor or vasodilator to constrict or relax the smooth muscle cells

long term -> generate basement membrane

SMCs:

short term -> change diameter of artery wall in response to flow change.

long term -> change of elastin/collagen content (aneurysm), SMC replication

Collagen: I, III, V -> fibril-forming, responsible for vessel strength
Mechanotransduction of ECs

Ion channels, integrins, receptor Tyr kinases, apical glycocalyx, primary cilia, heterotrimeric G proteins, PECAM1, VE cadherin

(Hahn and Schwartz, Nat Rev Mol Cell Biology, 2009)
Mechanotransduction of SMCs

What do they sense:

- Transmural pressure (120/80 mmHg in arteries, 30-40 mmHg in capillaries)
- Vascular wall strain by pulsative pressure (coronary artery, carotid artery)
  - Circumferential, axial wall tension; radial compression
- Passive or active mechanics, myogenic tone
- Shear stress from luminal flow

Results: thicken, stiffen, lengthen the vessel wall.

- SMC replication
- Elastin/collagen secretion
- Vessel tortuosity
Mechanotransduction of SMCs

How do they sense:

- Increased transmural pressure
- VSM membrane depolarization
- Activating calcium entry
  - Leading to Vessel constriction

[Diagram illustrating the process]

GCaMP2 Transgenic Mice, Ach stimulation

(Tallini, Circ Res, 2007)

- Hyperpolarization
  - Activation of $K_{ca}$ channels
Application and Vascular Engineering

Acute hypertension

Atherosclerosis – SMC proliferation, matrix calcification

Coronary bypass vein grafts – when veins becomes artery – VSM induced fibrosis (collagen deposition)

Engineered vessel grafts always lack of elastin