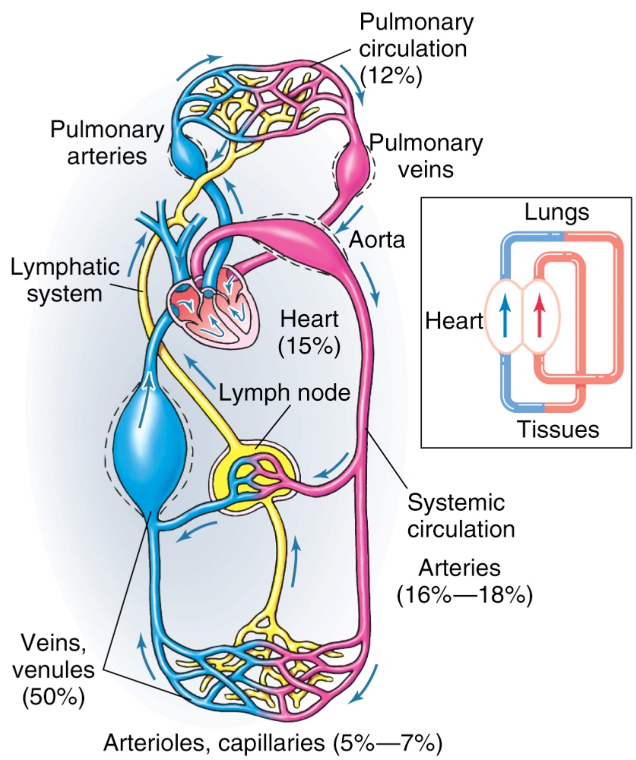
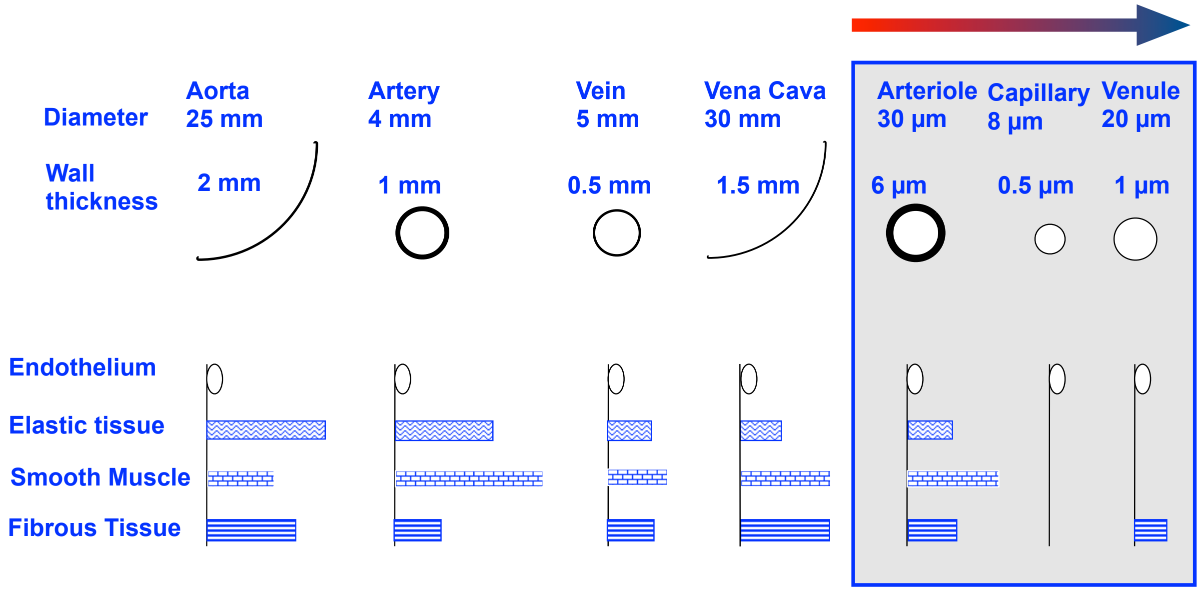
Microcirculation
Lecture Block 11
(contributions from Brett Burton)

Elements of Microcirculation

- Arterioles, capillaries, venules
- Structure and function: transport
- Fluid balance
- Lymph system



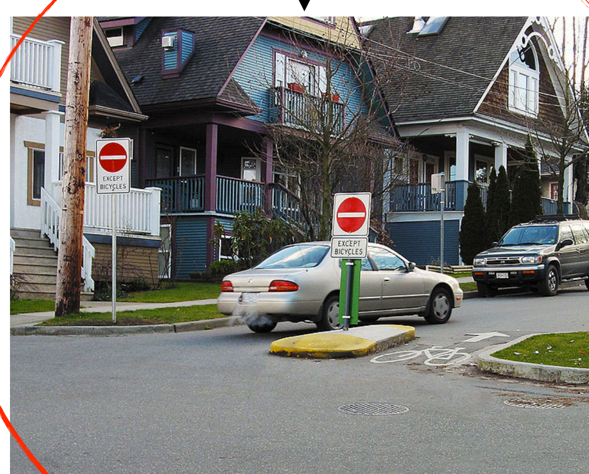
Vessels of the Circulatory System



Built to Transport

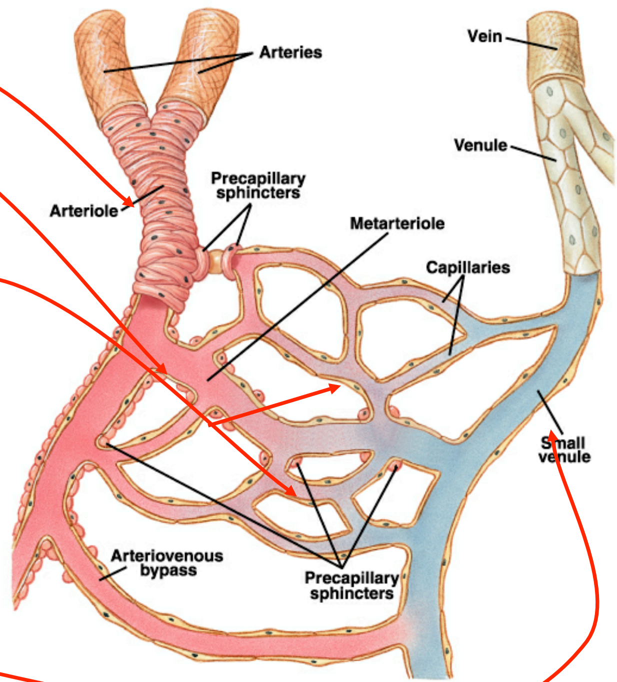
Arteries and Veins

Arterioles, Venules, Capillaries



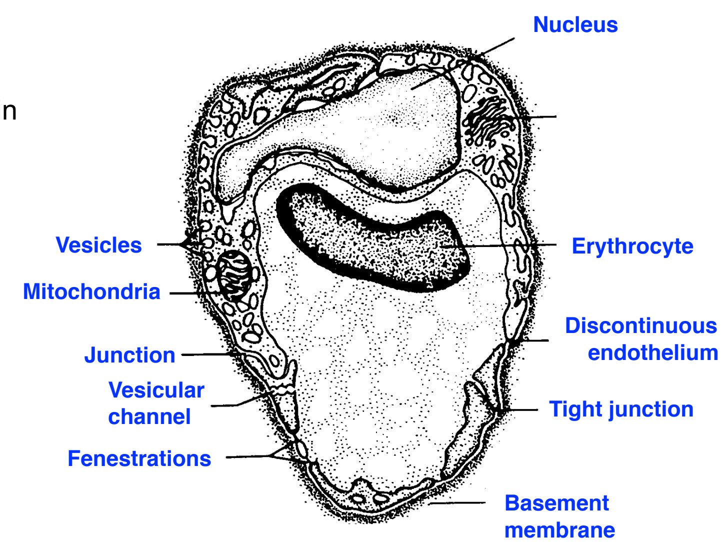
Structure of the Capillary System

- Arterioles
  - < 40 µm diameter
  - thick smooth muscle layer
- Metarterioles
  - connect arterioles and capillaries
  - discontinuous smooth muscle layer
  - serve as shunts
- Capillaries
  - approx. 10 billion in the body
  - 500-700 m^2 surface area
  - <30 µm from any cell to a cap
  - 4-9 µm diameter, 1 mm long
  - no smooth muscle, contractile endothelial cells but not clear if functional
- Venules
  - larger than arterioles
  - weak smooth muscle layer

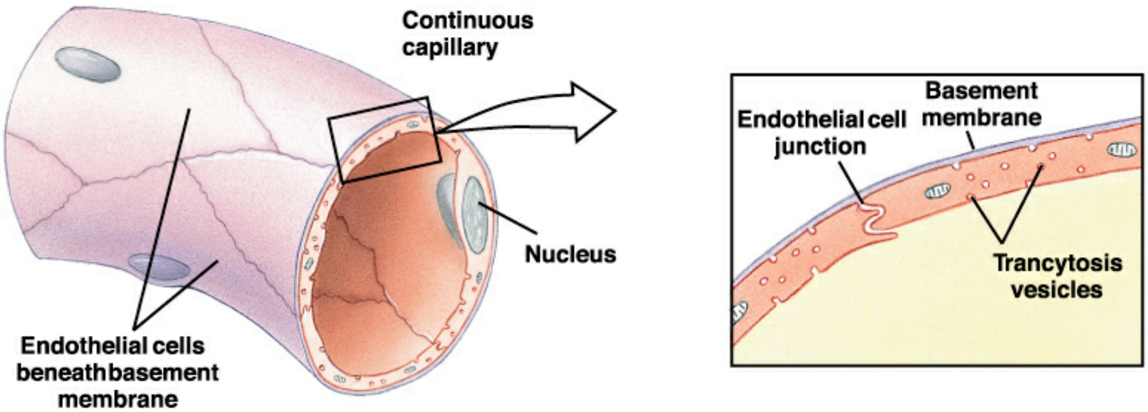


Capillary Wall Structure

- Intercellular cleft (Junctions):
  - 6-7 nm space between adjacent endothelial cells
  - site of transport, although only 1/1000th of surface area
  - reduced in size in brain (blood-brain barrier)
- Discontinuous endothelium
  - large spaces between endothelial cells
  - found in liver
- Pinocytic vessicles
  - Transport system for large molecules/solids
- Fenestra
  - Membrane “windows“ with permeable membrane cover
  - Found in kidneys, permit much higher transport levels

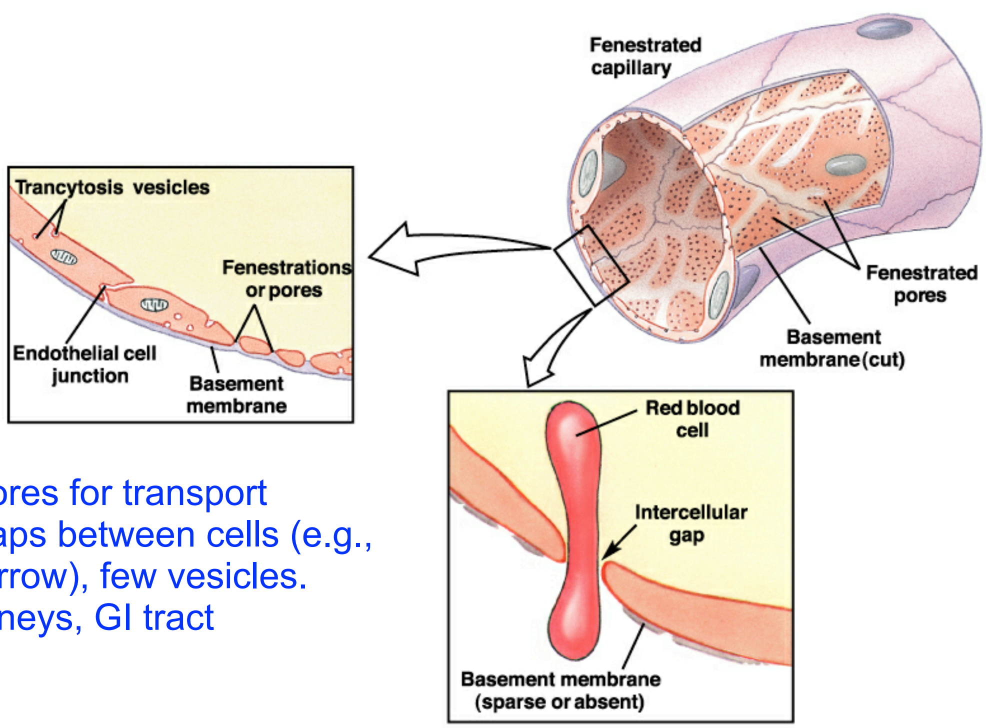


Continuous Capillary



Tight junctions between cells
Transport via vesicles
E.g., blood-brain barrier (extremely tight junctions)

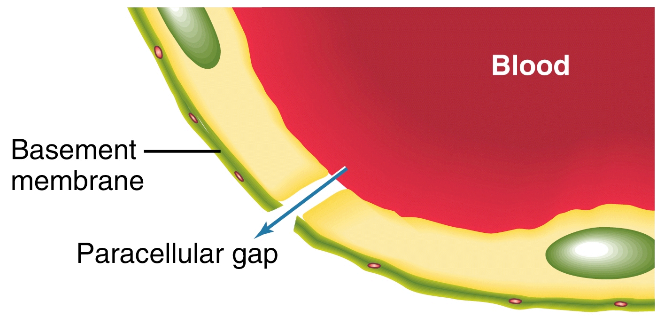
Fenestrated Capillary



Large pores for transport
Large gaps between cells (e.g., bone marrow), few vesicles.
E.g., kidneys, GI tract

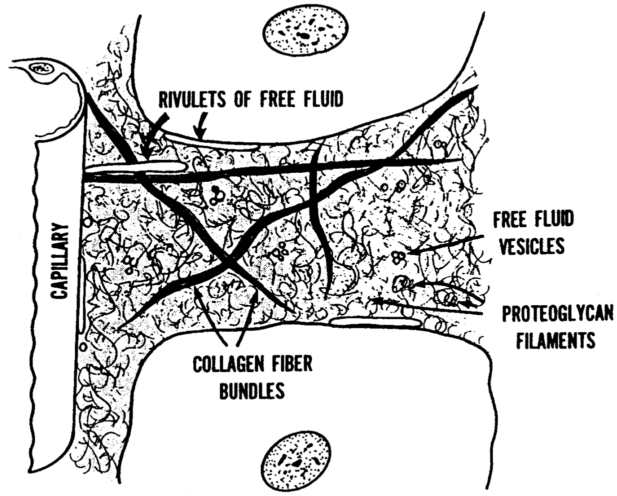
Sinusoidal Capillary

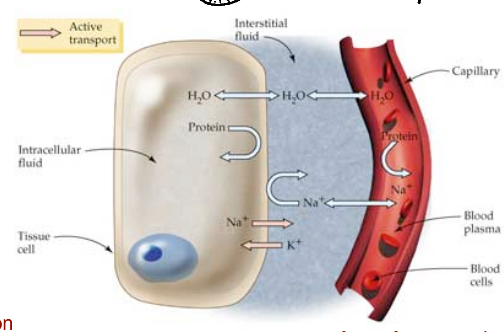
- Most porous of the caps
- Paracellular gaps and no vesicles.
- Liver, bone marrow, spleen, lymph nodes.
- Plasma and interstitial fluid in equilibrium.



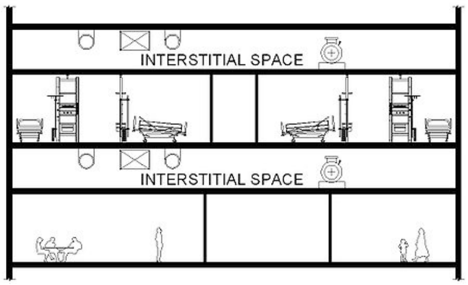
Interstitium and Interstitial Fluid

- 12 liters (1/6th of the body)
- Collagen bundles
  - provide structure, tension
- Proteoglycan filaments
  - thin, coiled shape (small)
  - “brush pile”of the interstitium
- Interstitial fluid
  - ultrafiltrate of plasma
  - trapped by proteoglycan filaments -> gel
  - slow flow through the gel
  - fast diffusion of water and electrolytes
- Free liquid
  - small rivulets along collagen and cell edges
  - water reservoir for interchange with capillaries
  - increases drastically in edema





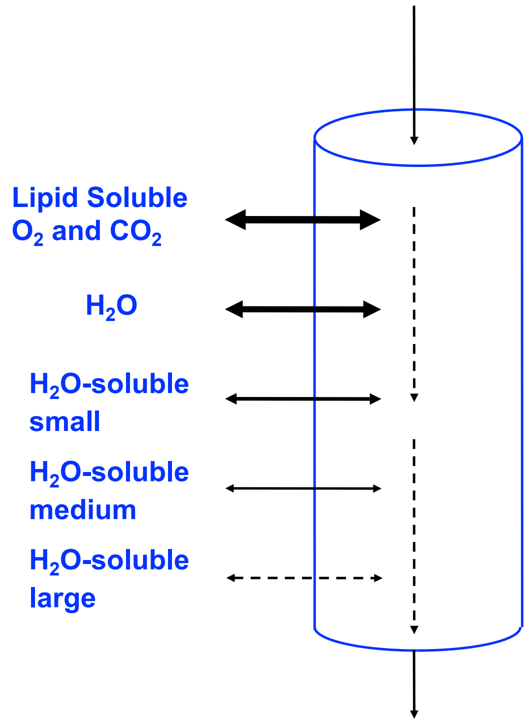
Other Interstitial Spaces



Capillary Diffusion and Water Balance

Diffusion through Capillaries

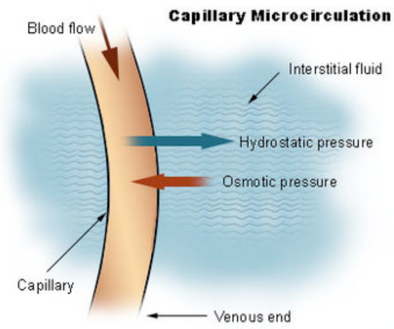
- Dominant mechanism, rate varies by tissue
- Diffusion of water 40-80 times faster than flow
- 2/3 of blood volume diffuses per minute
- Driven by concentration gradient:
  J = -DA dc/dx
  D = diffusion constant, A = area, c = concentration
- Flow limited: transport rate is fast enough for equilibrium
- Diffusion limited: equilibrium never established

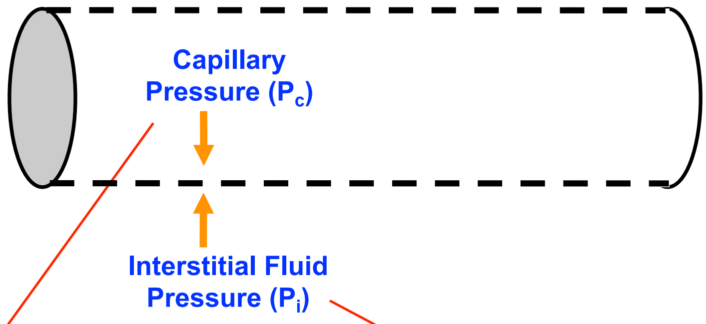


Fluid Balance

- Goal: what is the overall purpose of the system
  - Maintain correct amount of fluid in blood, interstitium, (and body)
- Process Steps: the set of steps that produce something
  - How is water controlled?
- Points of Regulation: where can we alter the process?
  - Where is are fluid levels controlled?
- Sensor types and locations: the measurement system(s)?
  - How do we sense fluid levels?
- Feedback mechanisms: how do sensors communicate with points of regulation to alter the process?
  - What connects sensors, regulation, process?

Fluid Balance: Hydrostatic Pressure

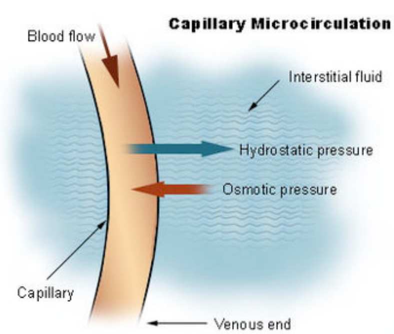


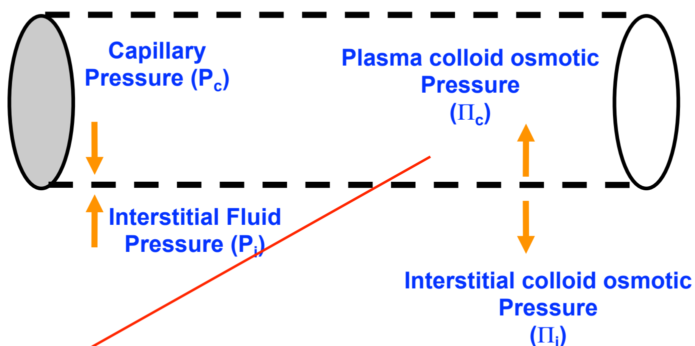


- Direct measures: 30--40 mm Hg arterial, 10--15 venous, 25 in the middle
- Functional measures: 17 mm Hg mean

- Near zero in healthy state
- Free fluid pressure
  - small but negative(2-7 mm Hg), helps to hold interstitium together
  - determines the tendency for edema
- Gel pressure
  - positive and static

Fluid Balance: Osmotic Pressure

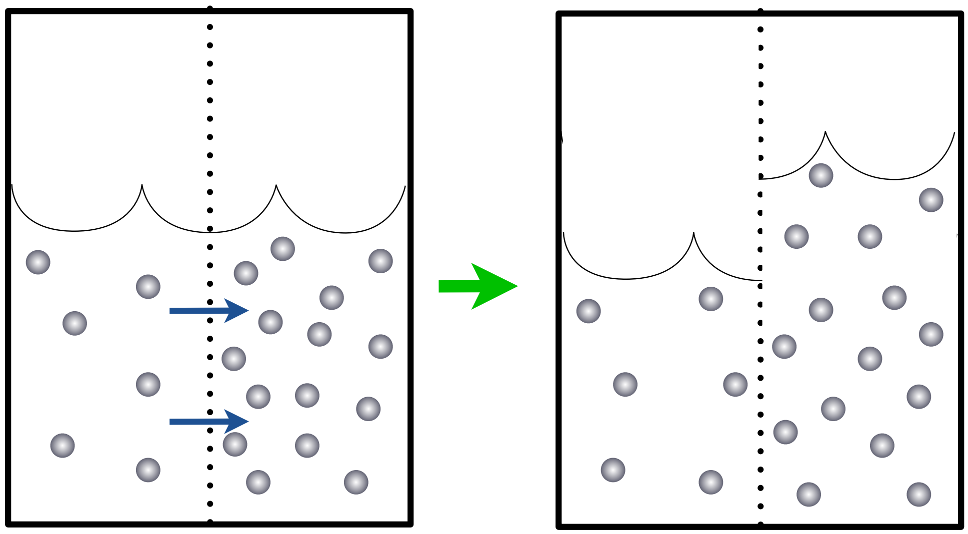




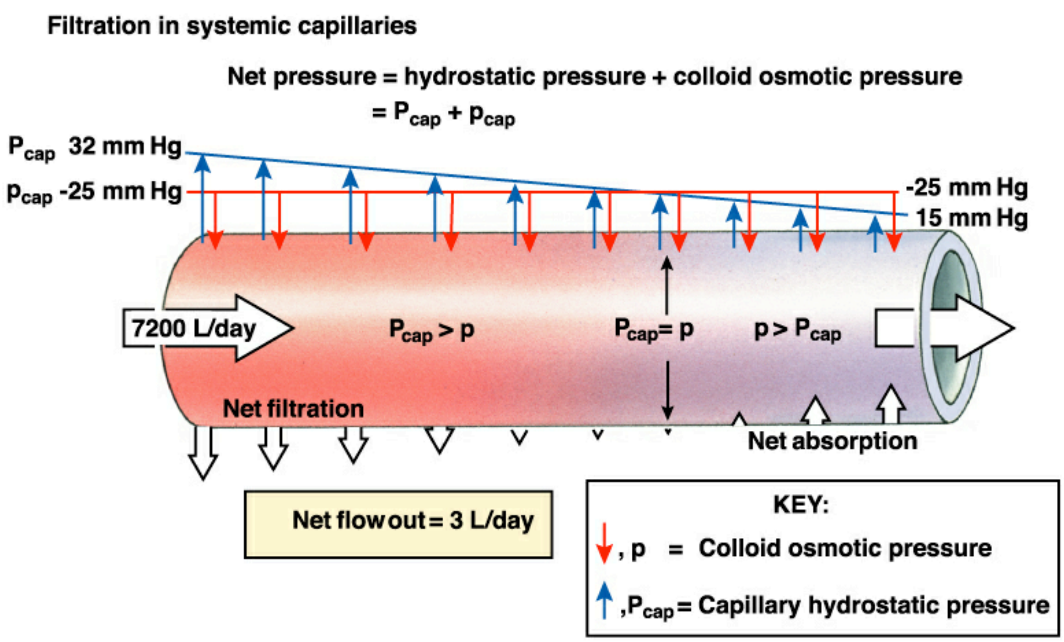
- Proteins diffuse poorly out of blood
- Plasma: 7.3 g/dl; IF: 2--3 g/dl
- Donnan Effect:
  - negatively charged proteins attract, but do not bind, ions
  - result is higher osmotic pressure
  - in humans: 28 mm Hg vs.19 from protein

- Only small amount of protein in the IF
- 6 mm Hg pressure.

Fluid Balance: Osmotic Pressure



Fluid Balance



Fluid Balance Example

Arterial End

Hydrostatic Pressure		mm Hg
	Capillary	30
	Interstitial	-5.3
Subtotal (positive = outwards)		35.3
Osmotic Pressure		
	Capillary	-28
	Interstitial	-6
Subtotal (positive = outwards)		-22
Total (positive = outwards)		13.3

Venous End

Hydrostatic Pressure		mm Hg
	Capillary	10
	Interstitial	-5.3
Subtotal (positive = outwards)		15.3
Osmotic Pressure		
	Capillary	-28
	Interstitial	-6
Subtotal (positive = outwards)		-22
Total (positive = outwards)		-6.7

Fluid Balance Example

Mean Values

Hydrostatic Pressure		mm Hg
	Capillary	17
	Interstitial	-5.3
Subtotal (positive = outwards)		22.3
Osmotic Pressure		
	Capillary	-28
	Interstitial	-6
Subtotal (positive = outwards)		-22
Total (positive = outwards)		0.3

- Starling Equilibrium
  - 0.3 mm Hg net outward pressure
  - 2 ml/min net outflow
  - Difference goes to lymphatics

Example of Imbalance: Starvation and fluid balance
- reduction in blood protein
- drop in capillary osmotic pressure
- water leaves blood and gathers in abdomen

Fluid Movement Equation

$$Q_{tc} = KA(P_c - P_i + \Pi_c - \Pi_i)$$

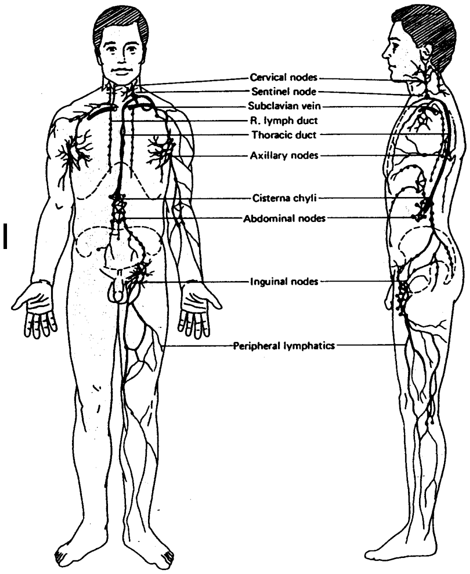
$K =$	capillary permeability
$A =$	surface area
$P_c =$	capillary pressure
$P_i =$	interstitial pressure
$\Pi_c =$	capillary colloid osmotic pressure
$\Pi_i =$	interstitial colloid osmotic pressure

Is $Q_{tc} = 0$?

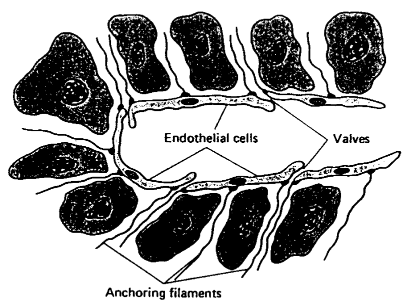
Lymphatic System

The Lymphatic System

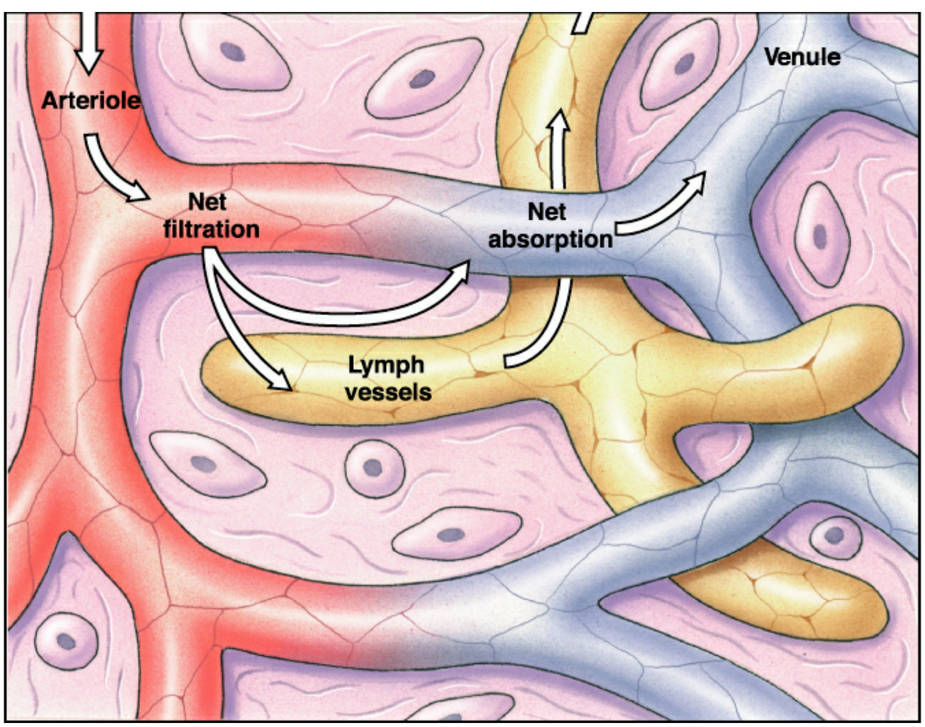
- Role
  - fluid balance
  - fat absorption from GI
  - immune response: bacteria



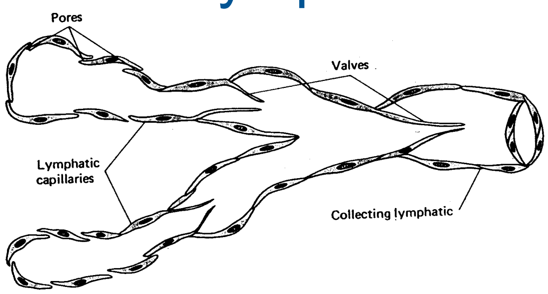
- Lymphatic capillaries
  - endothelial flaps
  - valves to collectors
  - driven by skeletal muscle contraction



Fluid Balance and Lymphatics



Lymphatic Flow



- Interstitial Pressure
  - negative pressure permits flow
  - at positive pressures capacity for flow saturates
- Lymphatic pump
  - valves block backflow
  - lymphatics contract when filled
  - external pressure moves lymph
  - 4-150 ml/hr flow (1/6000 of cardiac output) = total plasma volume in 1 day

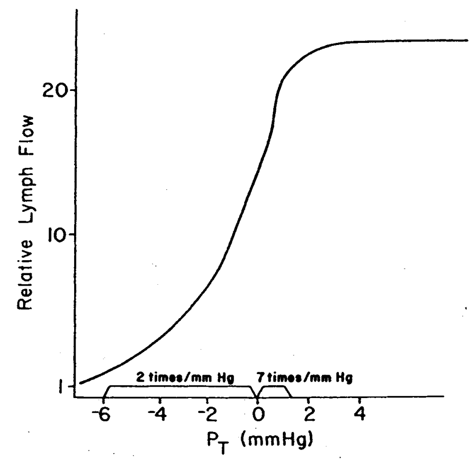


Figure 31–4. Relationship between interstitial fluid pressure and lymph flow. Note that lymph flow reaches a maximum as the interstitial pressure rises slightly above atmospheric pressure (0 mm Hg). (Courtesy of Drs. Harry Gibson and Aubrey Taylor.)

Fluid Balance

- Goal: what is the overall purpose of the system
  - Maintain correct amount of fluid in blood, interstitium, (and body)
- Process Steps: the set of steps that produce something
  - Diffusion across capillaries
  - Removal of water from tissue (lymphatics) and body (kidney)
- Points of Regulation: where can we alter the process?
  - Blood pressure
  - Colloid pressure (osmotic forces)
  - Kidney
- Sensor types and locations: the measurement system(s)?
  - Numerous (stay tuned)
- Feedback mechanisms: how do sensors communicate with points of regulation to alter the process?
  - Numerous, involving both nervous and endocrine and local

Stay Tuned!

Pulmonary Edema

- Causes:
  - Increase in pulmonary capillary pressure (e.g., reduced left ventricular function).
  - Increased permeability of pulmonary capillaries (e.g., exposure to noxious gases or chemicals).
  - Decrease in plasma colloid pressure (rare)
- Effects:
  - Alveolar edema: membranes break easily and fluid gushes into the alveoli, blocking exchange
  - Lymphatic compensation: lymphatics increase in size/capacity
  - Rapid death: With acute LV failure, pressure can rise to 50 mm Hg within minutes and death can follow within a half hour.
- Safety factors:
  - Negative interstitial pressure
  - Lymphatic flow capacity
  - Lymphatic washout of proteins