Hormonal BP regulation,

Capillaries and Lymphatics

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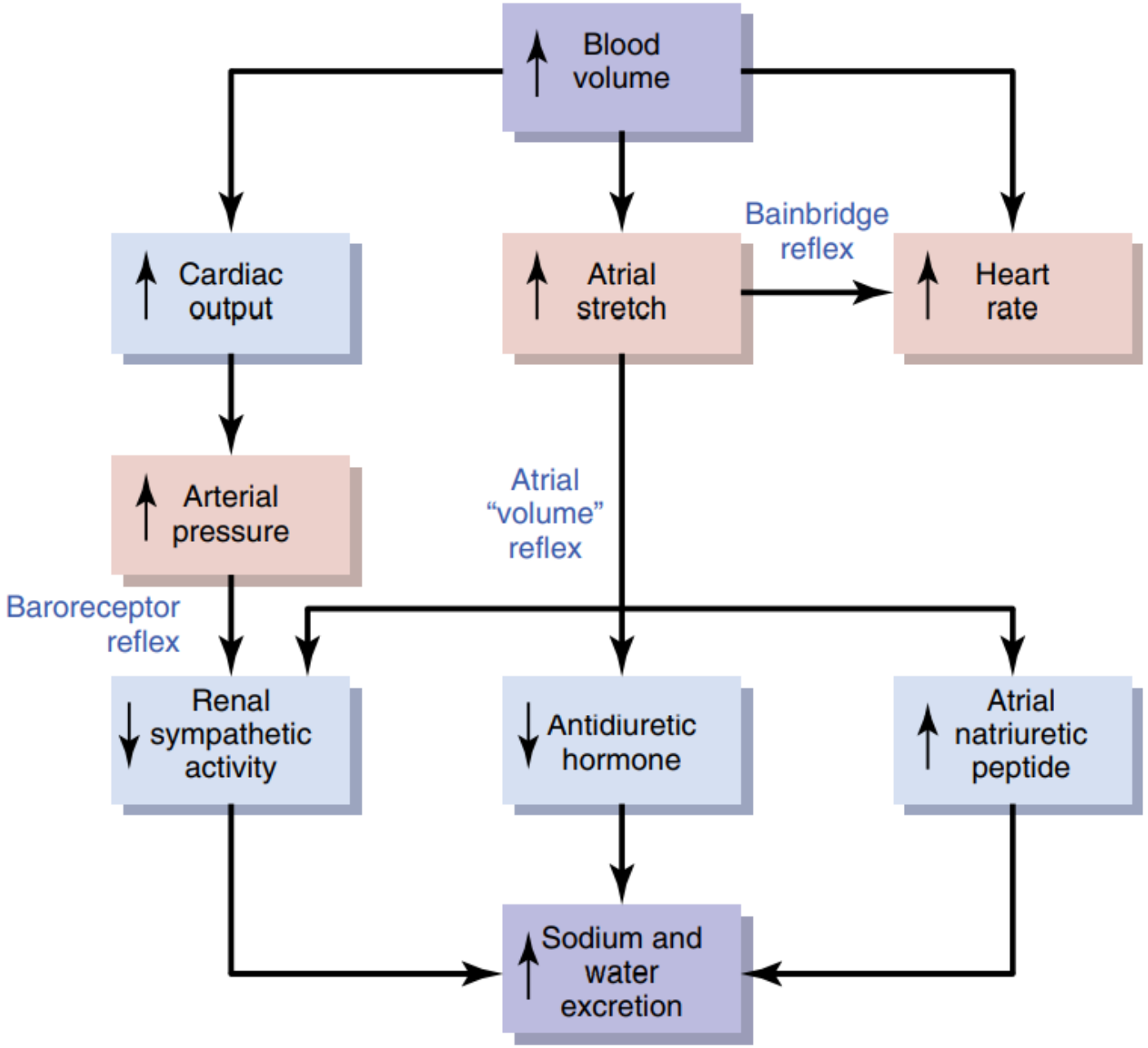
BP control by Atrial reflexes

- In their walls they (and pulmonary arteries) have stretch receptors called **low-pressure baroreceptors**.

- play an important role, especially in minimizing arterial pressure changes in response to changes in blood volume.

- also causes reflex reductions in renal sympathetic nerve activity, decreased tubular reabsorption, and dilation of afferent arterioles in the kidneys.


Blood volume
Cardiac output
Atrial stretch
Bainbridge reflex
Heart rate
Arterial pressure
Atrial "volume" reflex
Baroreceptor reflex
Renal sympathetic activity
Antidiuretic hormone
Atrial natriuretic peptide
Sodium and water excretion

Atrial reflexes

- **Increased heart rate.**
- Information from the low pressure atrial receptors travels in the vagus nerve to the nucleus tractus solitarius.

- The difference lies in the response of the medullary cardiovascular centers to the low- and high-pressure receptors.

- an increase in pressure at the venous low-pressure receptors produces an increase in heart rate (**Bainbridge reflex**).

Hormonal BP control

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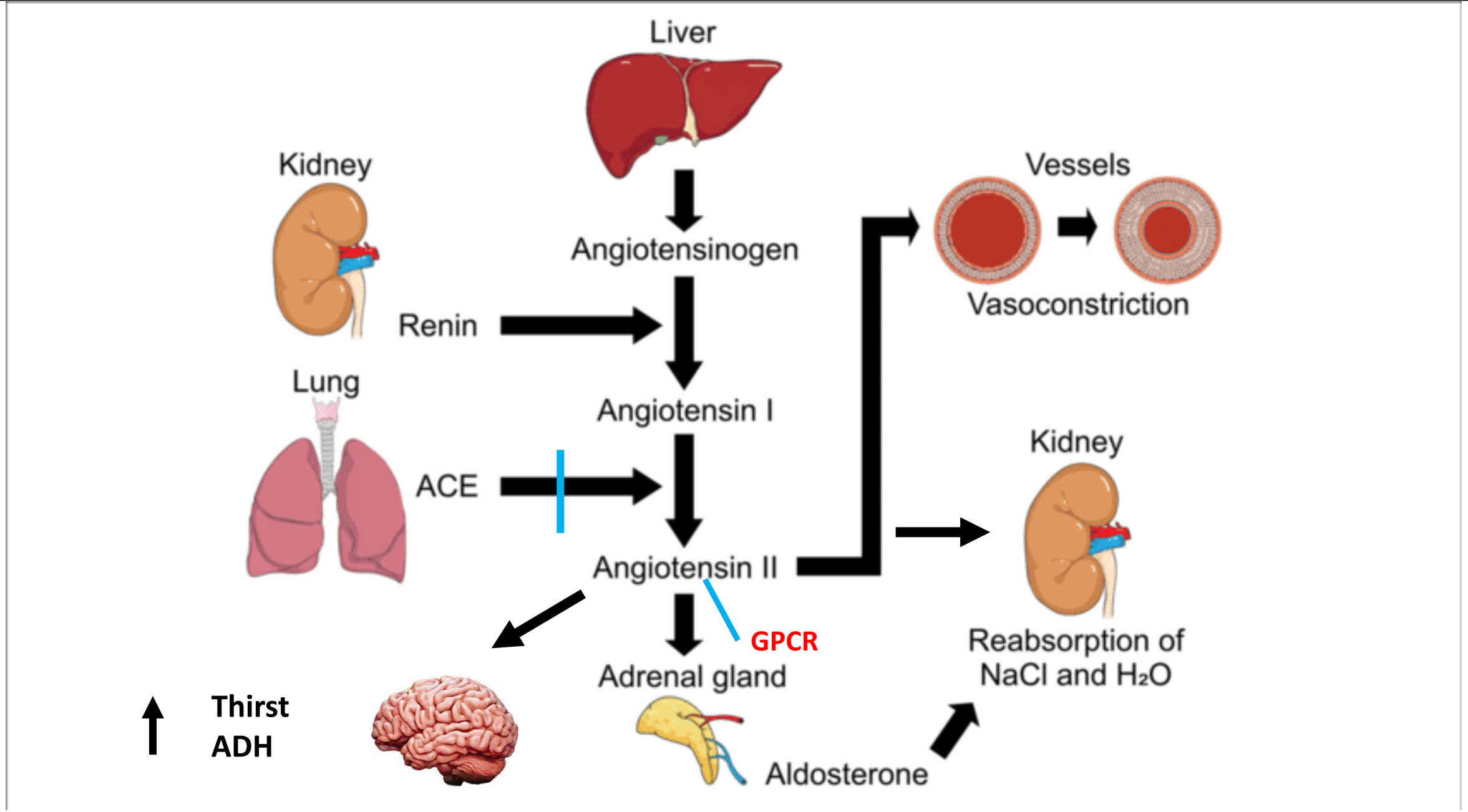
  - Renin- Angiotensin- Aldosterone system (RAAS).

Renin-Angiotensin-Aldosterone System

- The renin–angiotensin II–aldosterone system regulates BP primarily **by regulating blood volume**.

- This system is much **slower** than the baroreceptor reflex because it is hormonally, rather than neurally, mediated.

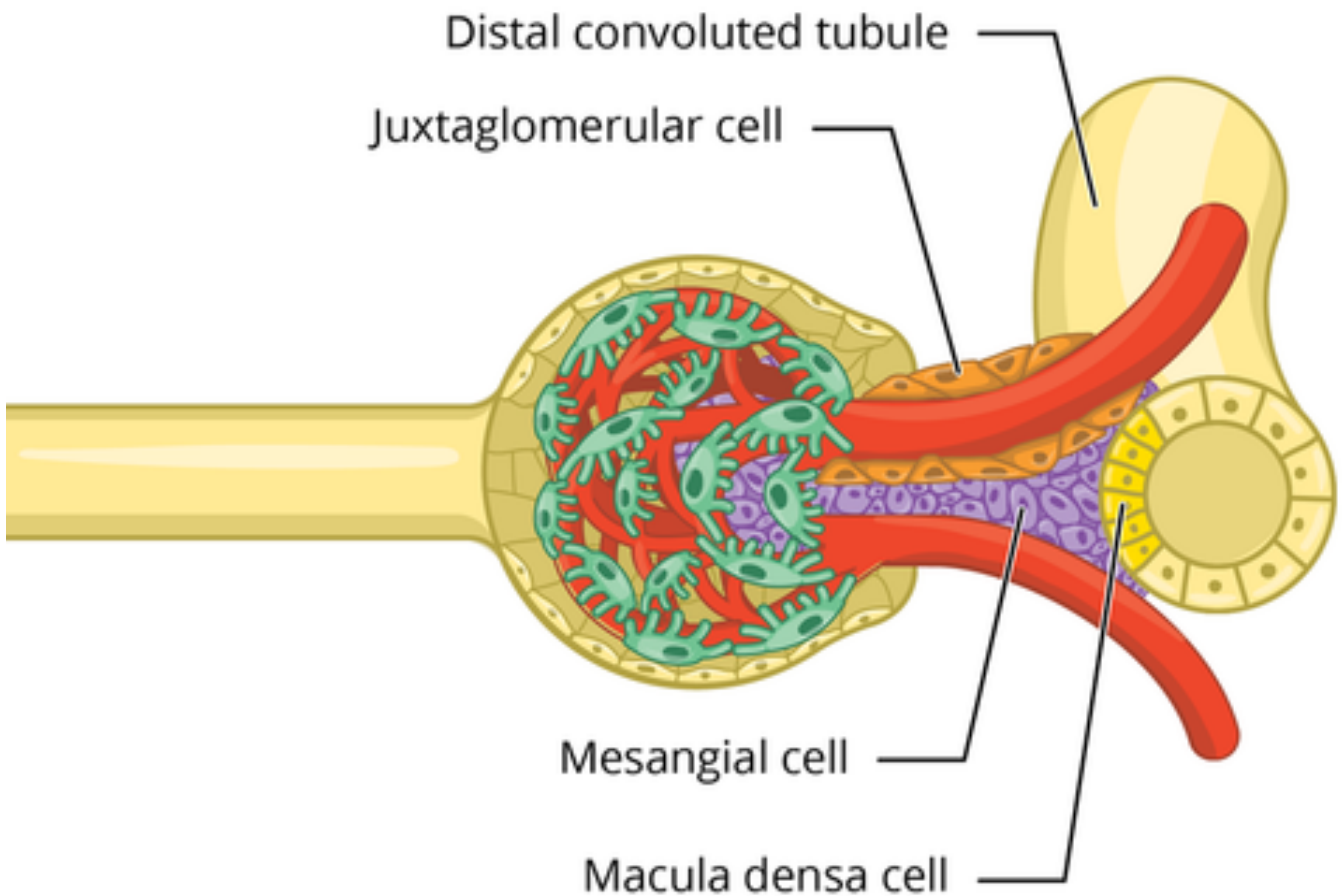
- RAAS is **activated in response to a decrease in the BP**.



Jose R. Vargas-Rodriguez et al. Hyperglycemia and Angiotensin-Converting Enzyme 2 in Pulmonary Function in the Context of SARS-CoV-2 Infectionc, 2022

Renin-Angiotensin-Aldosterone System

- Renin is an enzyme.
- In plasma, renin catalyzes the conversion of angiotensinogen (renin substrate) to angiotensin I.
- Angiotensin I has little biologic activity, other than to serve as a precursor to angiotensin II.


Distal convoluted tubule
Juxtaglomerular cell
Mesangial cell
Macula densa cell

Renin-Angiotensin-Aldosterone System

- Angiotensin II is an octapeptide with the following biologic actions in the adrenal cortex, vascular smooth muscle, kidneys, and brain, where it activates type 1 G protein–coupled angiotensin II receptors (AT1 receptors).

- Inhibitors of AT1 receptors, such as losartan, block the actions of angiotensin II at the level of the target tissues.

Renin-Angiotensin-Aldosterone System

- A decrease in BP causes a decrease in renal perfusion pressure, which is sensed by mechanoreceptors in afferent arterioles of the kidney.
- The decrease in BP causes prorenin to be converted to renin in the juxtaglomerular cells.
- Renin secretion by the juxtaglomerular cells is also increased by stimulation of renal sympathetic nerves.

Renin-Angiotensin-Aldosterone System

- In the lungs and kidneys, angiotensin I is converted to angiotensin II, catalyzed by angiotensin-converting enzyme (ACE).

- An angiotensin-converting enzyme inhibitor (ACEi), such as captopril, blocks the production of angiotensin II and all of its physiologic actions.

Renin-Angiotensin-Aldosterone System

- Angiotensin II acts on the zona glomerulosa cells of the adrenal cortex to stimulate the synthesis and secretion of aldosterone.

- Aldosterone then acts on the principal cells of the renal distal tubule and collecting duct to increase Na+ reabsorption and, thereby, to increase ECF volume and blood volume.

- These processes require hours to days to occur and account for the slow response time of the renin–angiotensin II–aldosterone system.

Renin-Angiotensin-Aldosterone System

- Angiotensin II also has its own direct action on the kidney, independent of its actions through aldosterone.

- Angiotensin II stimulates Na+ -H+ exchange in the renal proximal tubule and increases the reabsorption of Na+ and HCO3

Renin-Angiotensin-Aldosterone System

- Angiotensin II also acts directly on the arterioles by binding to G protein–coupled AT1 receptors to cause vasoconstriction.

- The resulting increase in TPR leads to an increase in BP.

Renin-Angiotensin-Aldosterone System

- Angiotensin II acts on the hypothalamus to increase thirst and water intake. It also stimulates secretion of antidiuretic hormone (ADH), which increases water reabsorption in collecting ducts.

- By increasing total body water, these effects complement the increases in Na+ reabsorption (caused by aldosterone and Na+ -H+ exchange), thereby increasing ECF volume, blood volume, and blood pressure.

DESCRIPTION OF CASE. A 65-year-old woman visits her physician complaining of "not feeling well" and decreased urination. Her diastolic blood pressure is elevated at 115 mm Hg, and she has abdominal bruits (sounds). She is immediately admitted to the hospital and has a workup for hypertension.

Laboratory tests reveal the following information: Her blood pressure continues to be dangerously elevated, and her glomerular filtration rate (GFR) is significantly decreased, at 30 mL/min. Renal vascular disease is suspected. Renal angiography shows 90% stenosis of the right renal artery. Her plasma renin activity is elevated, and renin levels are much higher in right renal venous blood than in left renal venous blood.

An attempt to dilate the right renal artery with angioplasty is unsuccessful. The woman is treated with captopril, an ACEi.

EXPLANATION OF CASE. The woman has stenosis of her right renal artery, which reduces blood flow to her right kidney. The abdominal bruits are heard because blood flow through the stenosed renal artery is turbulent (i.e., Reynolds number is increased). As a result of the decreased renal blood flow, her GFR and her urine output are decreased.

The woman's hypertension is secondary to the decrease in renal blood flow. Renal perfusion pressure to the right kidney is significantly decreased. The right kidney "thinks" that arterial pressure is low and that aldosterone is needed. Thus renin secretion by the right kidney increases, which results in renin levels in the right renal vein higher than those in the left renal vein. Increased circulating renin activity results in increased production of angiotensin II and aldosterone. Angiotensin II causes vasoconstriction of arterioles, which elevates TPR and mean arterial pressure. Aldosterone increases renal Na^+ reabsorption, elevating total body Na^+ content, ECF volume, and blood volume. The increase in blood volume leads to the increased diastolic blood pressure.

TREATMENT. Because an attempt to dilate the stenosed renal artery is unsuccessful, the woman is treated with an ACEi to interrupt the cycle that produced the hypertension (i.e., to block the conversion of angiotensin I to angiotensin II). Although the right kidney will continue to secrete high levels of renin and plasma renin activity will continue to be elevated, angiotensin II will not be produced if the ACE is inhibited. Likewise, aldosterone secretion will decrease, and Na^+ reabsorption also will decrease.

Microcirculation

Exchange of substances across the capillary wall

- Blood flow to the capillaries is intermittent due to vasomotion.
- The exchange of solutes and gases across the capillary wall occurs by **simple diffusion**.
- Some solutes can diffuse through the endothelial cells, and others must diffuse between the cells, depending on whether the solute or gas is lipid soluble.

Exchange of substances across the capillary wall

- **Gases** such as O2 and CO2 are highly lipid soluble.
- These gases readily cross the capillary wall by diffusing through the endothelial cells; diffusion is driven by the partial pressure gradient for the individual gas.

- the **rate of diffusion** depends on the driving force (the **partial pressure difference** for the gas) and the surface area available for diffusion. Thus, the greater the number of open capillaries, the greater the **surface area for diffusion**.

Exchange of substances across the capillary wall

- **Water-soluble substances** such as water itself, ions, glucose, and amino acids are not lipid soluble; thus they cannot cross the endothelial cell membranes.

- The **diffusion** of water-soluble substances **is limited to the aqueous clefts between endothelial cells**; hence, the surface area for their diffusion is much less than that for the lipid-soluble gases.

Exchange of substances across the capillary wall

- Proteins are generally too large to cross the capillary walls via the clefts between endothelial cells and are retained in the vascular compartment.

- In some tissues, such as brain, the clefts are particularly “tight,” and little protein leaves these capillaries.

- In the kidney and intestine, the capillaries are fenestrated or perforated, which permits the passage of limited amounts of protein.

Starling Equation

- The Starling equation states that fluid movement across a capillary wall is determined by the net pressure across the wall, which is the sum of hydrostatic pressure and oncotic pressures

$$J_v = K_f[(P_c - P_i) - (\pi_c - \pi_i)]$$

where

J_v = Fluid movement (mL/min)

K_f = Hydraulic conductance (mL/min per mm Hg)

P_c = Capillary hydrostatic pressure (mm Hg)

P_i = Interstitial hydrostatic pressure (mm Hg)

π_c = Capillary oncotic pressure (mm Hg)

π_i = Interstitial oncotic pressure (mm Hg)

Starling Equation

- The direction of fluid movement can be either into or out of the capillary.

- When net fluid movement is out of the capillary into the interstitial fluid, it is called filtration; when net fluid movement is from the interstitium into the capillary, it is called absorption.

Changes in Starling forces

- Changes in Starling forces can influence the direction and magnitude of fluid movement across capillaries.

- Increase in filtration happens if increase in any of the forces that favor filtration or by a decrease the ones that favor absorption:

- increases in arterial pressure or venous pressure (but more so from increases in venous pressure).
- decreases in πc resulting from dilution of plasma protein concentration.

Starling Equation

- **Pc, capillary hydrostatic pressure**, is a force favoring filtration out of the capillary.
- The value for Pc is determined by both arterial and venous pressures (the capillary being interposed between the arteries and veins), although the value for Pc is closer to arterial pressure than to venous pressure.
- Furthermore, Pc is more affected by changes in venous pressure than by changes in arterial pressure. Except in glomerular capillaries, Pc declines along the length of the capillary because of the filtration of fluid.
- Therefore, Pc is highest at the arteriolar end of the capillary and lowest at the venous end.

Starling Equation

- **Pi, interstitial hydrostatic pressure**, is a force opposing filtration. Normally, Pi is nearly zero, or it may be slightly negative.

- **πi, interstitial oncotic pressure**, is a force favoring filtration.
- πi is determined by the interstitial fluid protein concentration. Normally, because there is little loss of protein from capillaries, there is little protein in interstitial fluid, making πi quite **low**.

Starling Equation

- **πc, capillary oncotic pressure**, is a force opposing filtration.

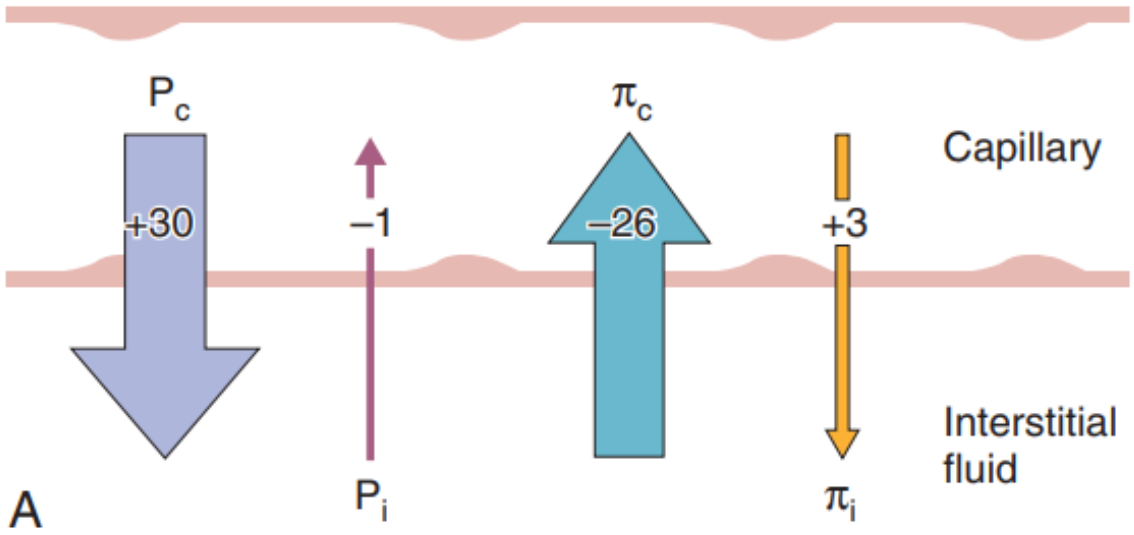
- πc is the effective osmotic pressure of capillary blood due to the presence of plasma proteins, and it is determined by the protein concentration of capillary blood.

- Therefore increases in protein concentration of blood cause increases in πc and decrease filtration, and decreases in protein concentration of blood cause decreases in πc and increase filtration.

$$J_v = K_f[(P_c - P_i) - (\pi_c - \pi_i)]$$

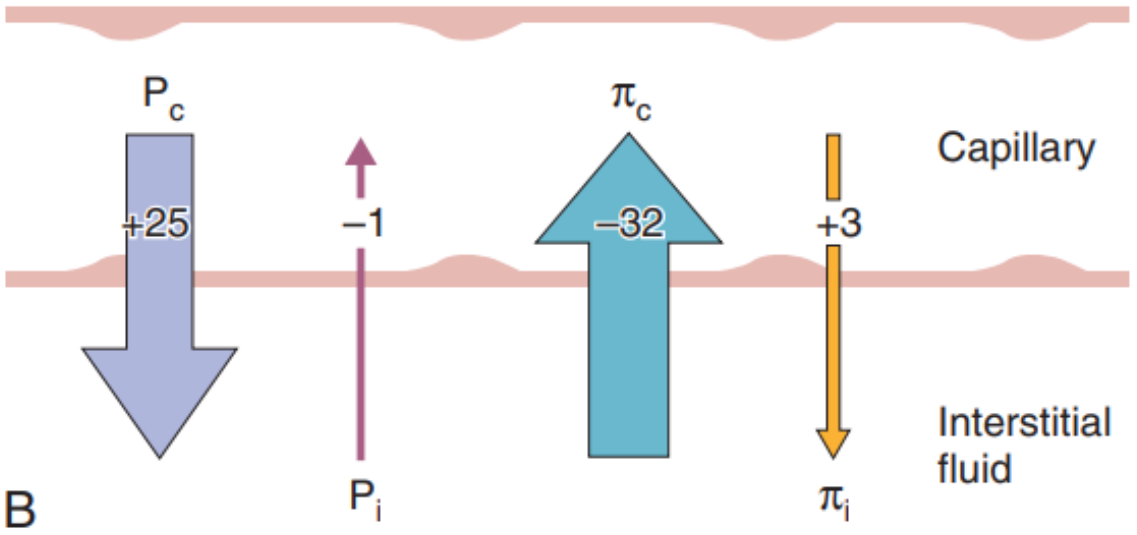
Net filtration

Net pressure = +6 mm Hg



Net absorption

Net pressure = −5 mm Hg



Starling Equation

- The **magnitude of fluid movement is determined by the hydraulic conductance, (water permeability**), of the capillary wall.

- The hydraulic conductance determines how much fluid movement will be produced for a given pressure difference.

Starling Equation

- Kf, hydraulic conductance, is the water permeability of the capillary wall.

- It varies among different types of tissues, depending on the anatomic characteristics of the capillary wall (e.g., the size of the clefts between endothelial cells; whether the capillaries are fenestrated).

- Therefore the magnitude of fluid movement for a given pressure difference is **largest** in capillaries with the highest Kf (e.g., **glomerular** capillaries), and it is **lowest** in capillaries with the lowest Kf (e.g., **cerebral** capillaries).

Starling Equation

- Kf is not influenced by such factors as changes in arteriolar resistance, hypoxia, or buildup of metabolites.

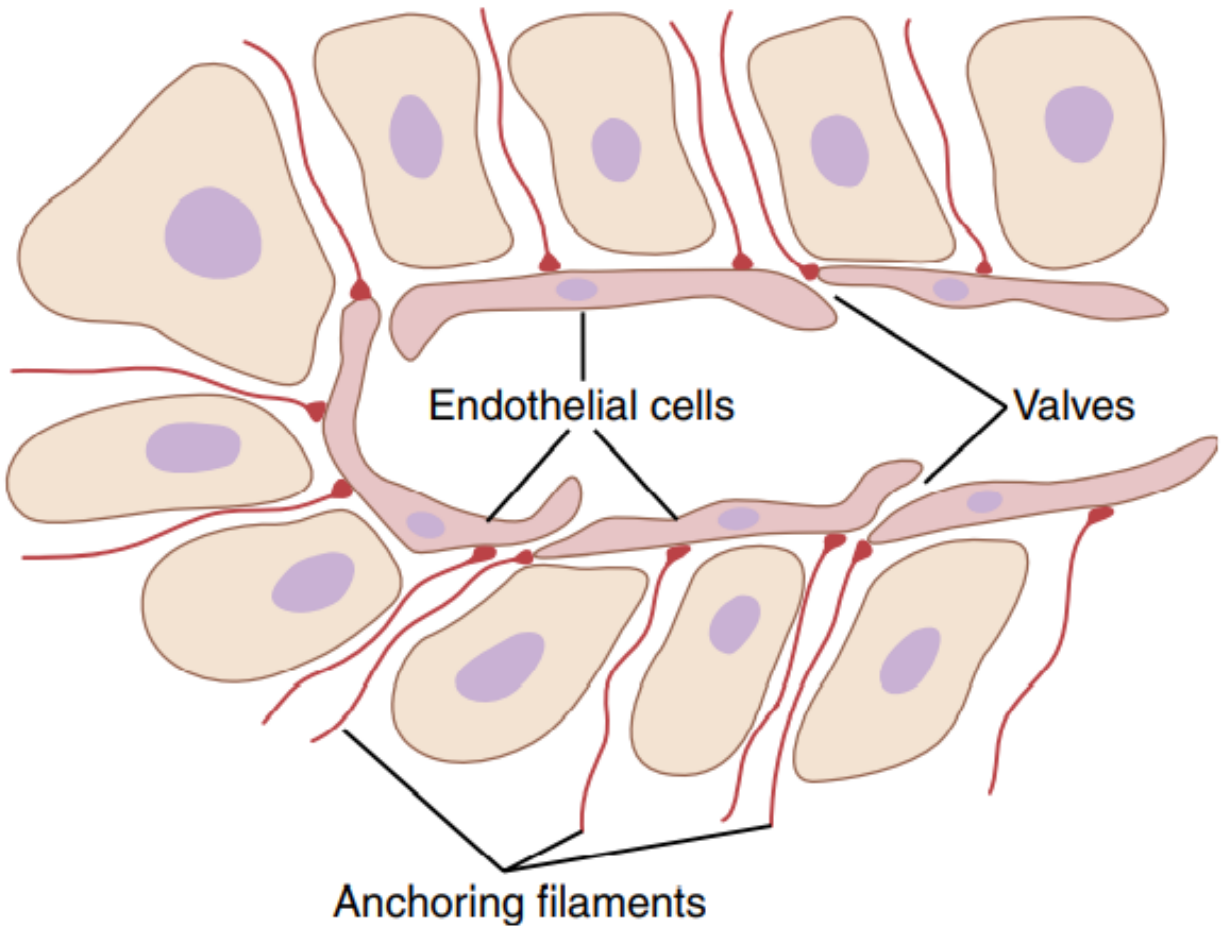
- However, Kf is increased in capillary injury (e.g., toxins or in burns). Such increases in Kf will increase the capillary permeability to water and also will result in the loss of protein from the capillary.

Lymph

- The lymphatic system is responsible for returning interstitial fluid and proteins to the vascular compartment.

- The lymphatic capillaries lie in the interstitial fluid, close to the vascular capillaries.

- The lymphatic capillaries possess **one-way flap valves**, which permit interstitial fluid and protein to enter, but not leave, the capillaries.


Endothelial cells
Valves
Anchoring filaments

Lymph

- These capillaries merge into larger lymphatic vessels and eventually into the largest lymphatic vessel, the thoracic duct, which empties lymph into the large veins.

- The lymphatic vessels have a smooth muscle wall, which has intrinsic contractile ability.

- Lymph flow back to the thoracic duct is promoted by contraction of the smooth muscle in the lymph vessels and by compression of the lymph vessels by activity of the surrounding skeletal muscle.

Lymph

- factors that determine **lymph flow** are

- (1) the interstitial fluid pressure
- (2) the activity of the lymphatic pump

Edema

- An increase in interstitial fluid volume is called edema (swelling).

- By definition, edema forms when the volume of interstitial fluid (due to filtration out of the capillaries) exceeds the ability of the lymphatics to return it to the circulation.

- Thus edema can form when there is increased filtration or when lymphatic drainage is impaired.

TABLE 4.6 Causes and Examples of Edema Formation

Cause	Examples
↑ P_c (capillary hydrostatic pressure)	Arteriolar dilation Venous constriction Increased venous pressure Heart failure Extracellular fluid volume expansion
↓ π_c (capillary oncotic pressure)	Decreased plasma protein concentration Severe liver failure (failure to synthesize protein) Protein malnutrition Nephrotic syndrome (loss of protein in urine)
↑ K_f (hydraulic conductance)	Burn Inflammation (release of histamine; cytokines)
Impaired lymphatic drainage	Standing (lack of skeletal muscle compression of lymphatics) Removal or irradiation of lymph nodes Parasitic infection of lymph nodes

Thank you