

Kazan (Volga region) Federal University  
Institute of Fundamental Medicine and Biology  
Department of Morphology and General Pathology

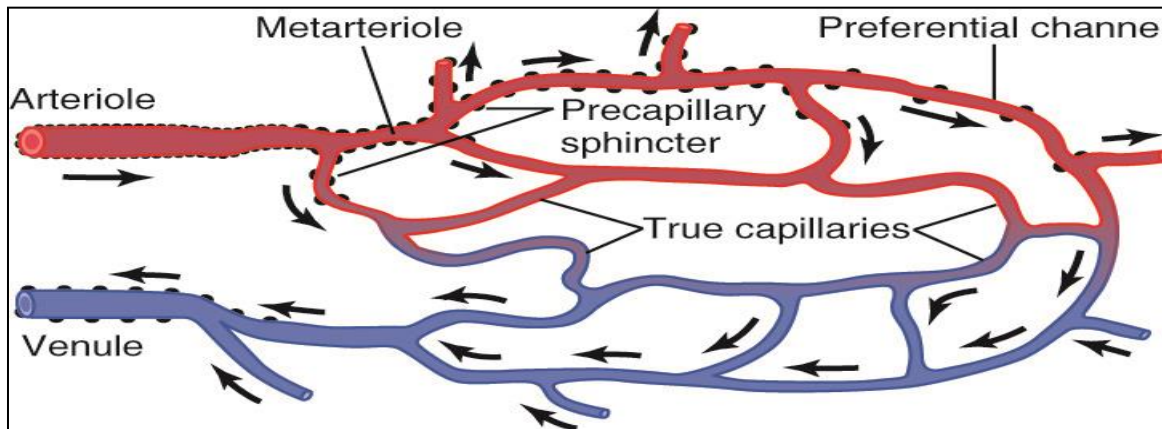
# Pathology of microcirculation

## Edema

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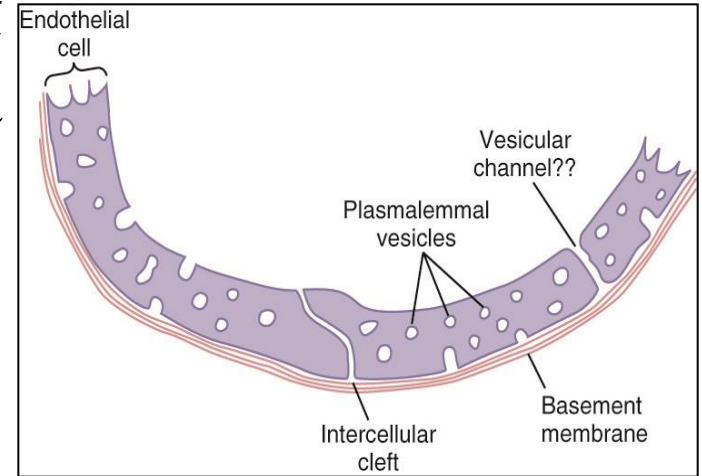
# The Microcirculation

- Important in the transport of nutrients to tissues.
- Site of waste product removal.
- Over 10 billion capillaries with surface area of 500-700 square meters perform function of solute and fluid exchange.



# Structure of Capillary Wall

- Composed of unicellular layer of endothelial cells surrounded by a basement membrane.
- Diameter of capillaries is 4 to 9 microns.
- Solute and water move across capillary wall via *intercellular cleft* (space between cells) or by *plasmalemma vesicles*.



# Pathology of microcirculation includes:

- 1) Edema
- 2) Disturbances of blood filling (ischemia, arterial/venous hyperemia)
- 3) Disturbances of vessel wall permeability (bleeding, hemorrhaging, plasmorrhagia)
- 4) Disturbances of blood stream (stasis, thrombosis, embolism)

# Fluid in organism

Total water quantity is 60-65% of body weight:

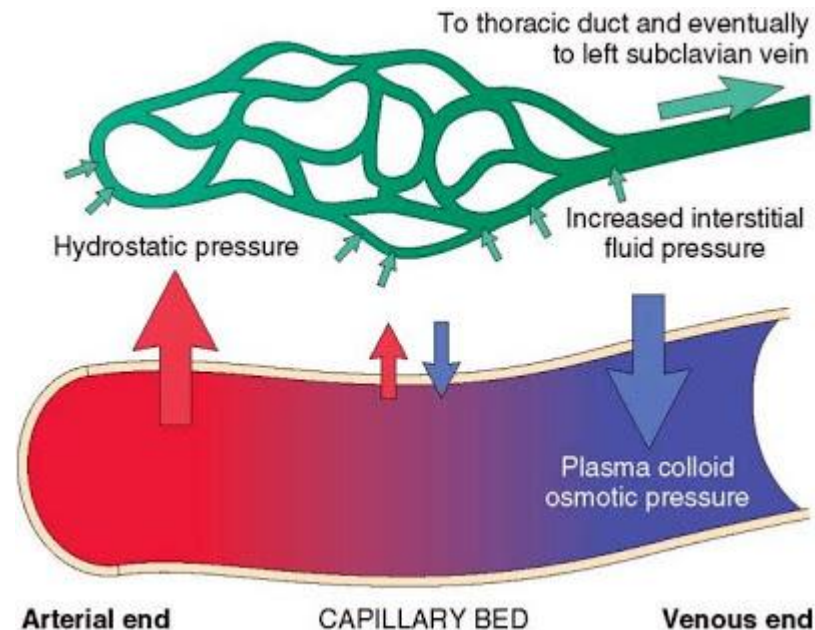
1) Intracellular fluid – 30-40% of body weight

2) Extracellular fluid – 15-20%:

- Interstitial fluid (11-12 l.)
- Intravascular fluid (5-6 l.)

# Definition of edema

- Edema is an abnormal presence of excessive fluid in the interstitial space.



# Classification

- 1) According to pathophysiological mechanism:
  - a) Transudate (low protein content)
  - b) Exudate (high protein content)
- 2) According to location:
  - a) Localized
  - b) Generalized
- 3) According to time of development:
  - a) Peracute (seconds)
  - b) Acute (minutes, hours, days)
  - c) Chronic (weeks, months)

# Classification

## 4) According to the cause of edema:

- a) Renal edema
- b) Hepatic edema
- c) Cardiac edema
- d) Malnutritional edema
- e) lymphedema



# Clinical Causes of Edema

## **Systemic edema**

- Congestive heart failure
- Cirrhosis
- Nephrotic syndrome/other hypoalbuminemia
- Drug-induced
- Idiopathic

## **Localized edema**

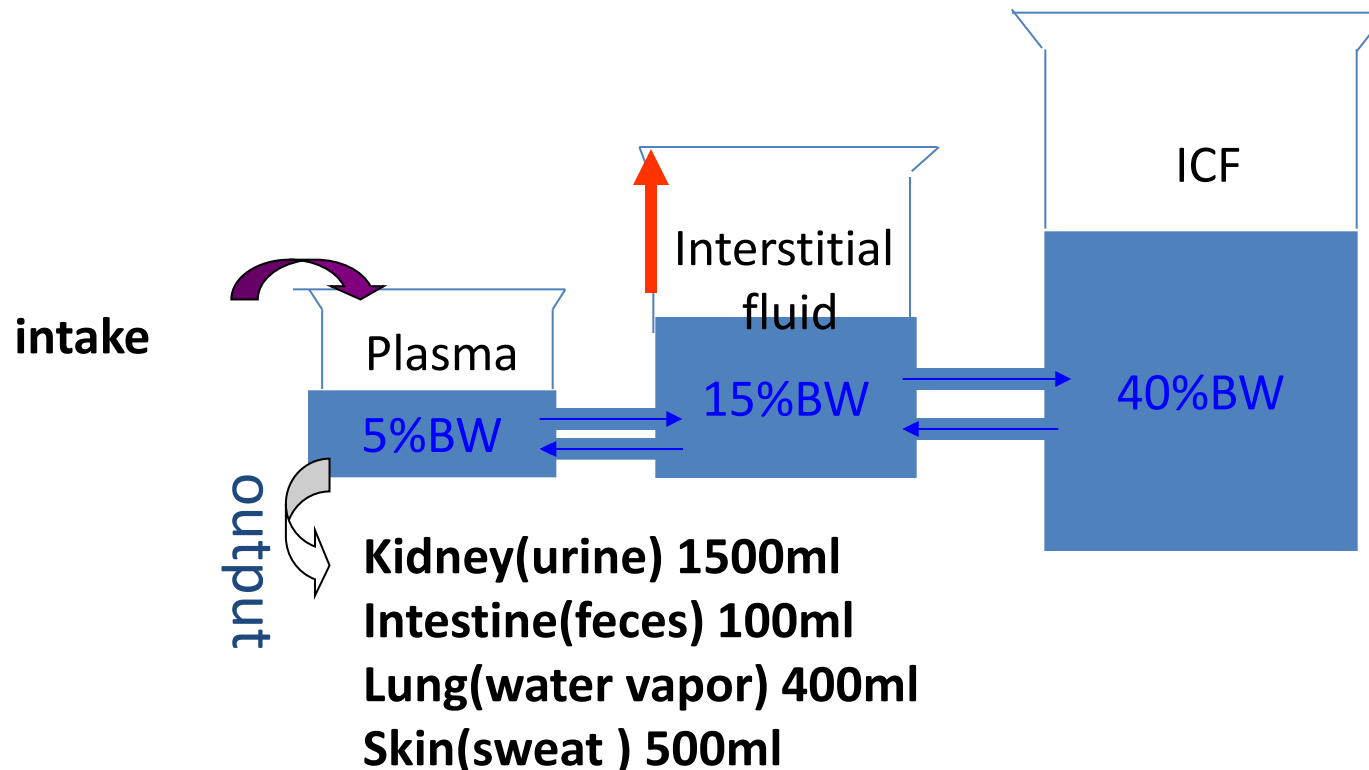
- Venous/lymphatic obstruction

# III . Etiology and pathogenesis

- **Im**balance of fluid exchange between plasma and interstitial compartment

- **Im**balance of fluid exchange between extra- and intra-body

Renal retention of sodium and water



$$\text{NFP} = (\text{BHP} + \text{IFOP}) - (\text{BCOP} + \text{IFHP})$$

- ✓ Net filtration pressure (NFP) balance of 2 pressures
- ✓ Two pressures promote *filtration*
  1. **Blood hydrostatic pressure** (BHP) generated by pumping action of heart  
Falls over capillary bed from 35 to 16 mmHg
  2. **Interstitial fluid osmotic pressure** (IFOP) 1 mmHg

$$\text{NFP} = (\text{BHP} + \text{IFOP}) - (\text{BCOP} + \text{IFHP})$$

2. Two pressures promote *reabsorption*

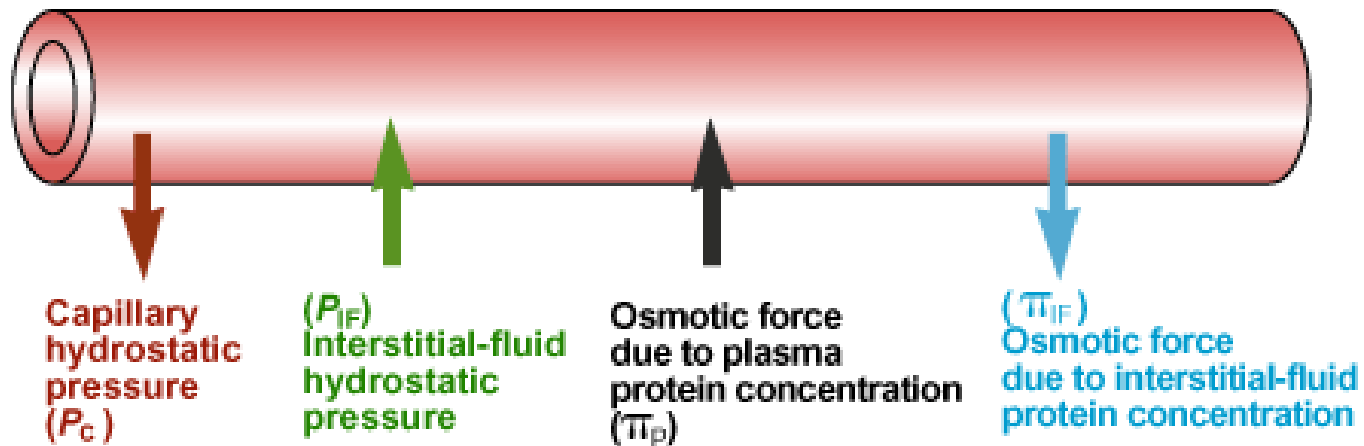
**1. Blood colloid osmotic pressure (BCOP)**

promotes reabsorption

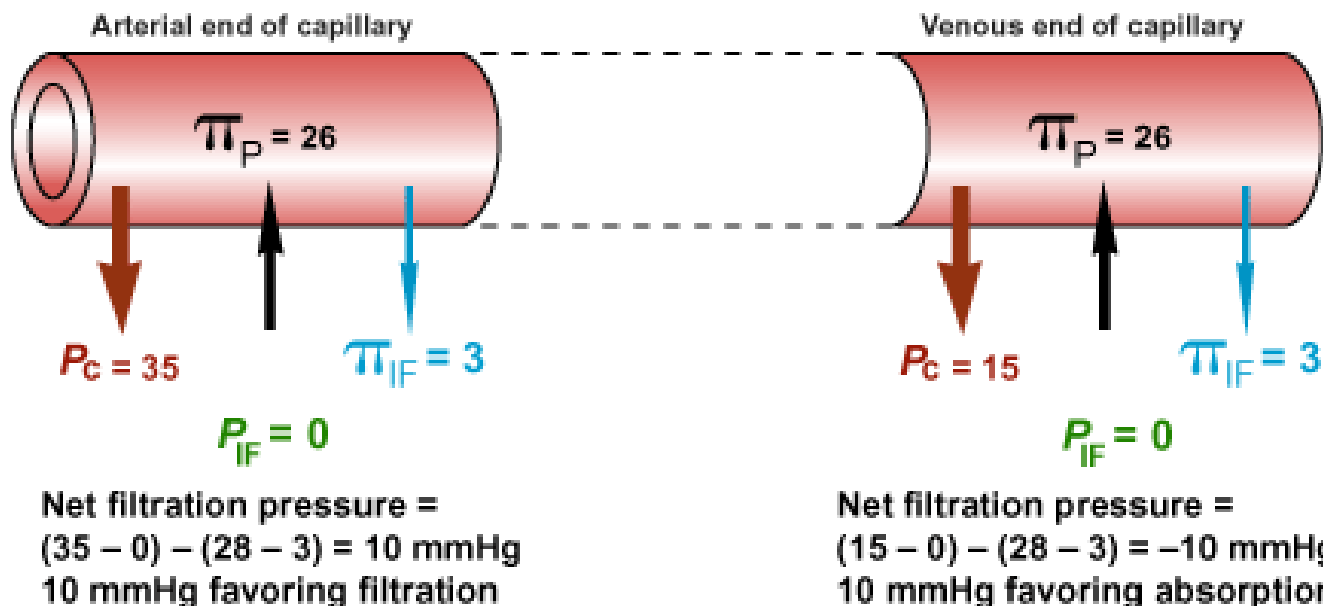
- Averages 36 mmHg
- Due to presence of blood plasma proteins too large to cross walls

**2. Interstitial fluid hydrostatic pressure (IFHP)**

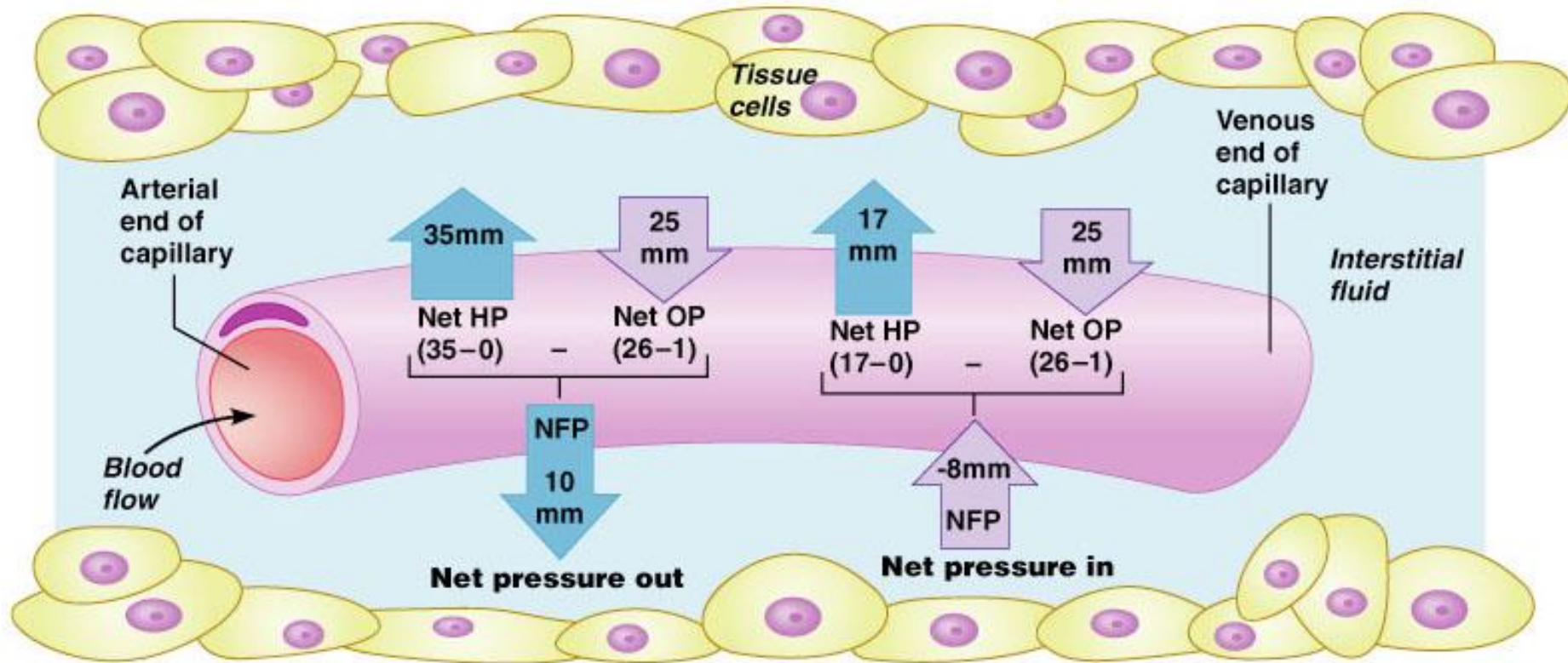
- Close to zero mmHg



$$\text{Net filtration pressure} = (P_c - P_{if}) - (\pi_P - \pi_{if})$$



# 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  
 $OP_c$  = 26 mm Hg

$OP_{if}$  = 1 mm Hg

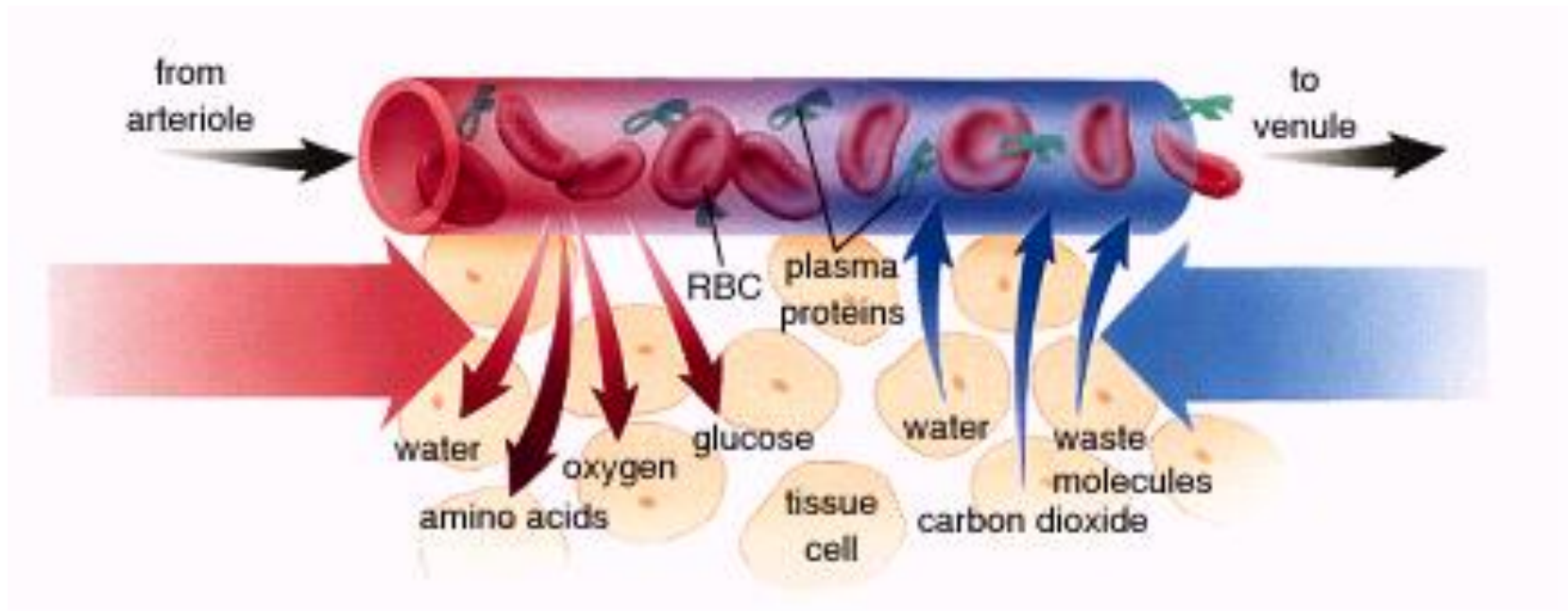
# Starling's Law

- ❖ Nearly as much reabsorbed as filtered
  - ❖ At the arterial end, net outward pressure of 10 mmHg and fluid leaves capillary (filtration)
  - ❖ At the venous end, fluid moves in (reabsorption) due to -9 mmHg
  - ❖ On average, about 85% of fluid filtered in reabsorbed
  - ❖ Excess enters lymphatic capillaries (about 3L/ day) to be eventually returned to blood

Imbalance of fluid exchange between plasma and  
interstitial compartment

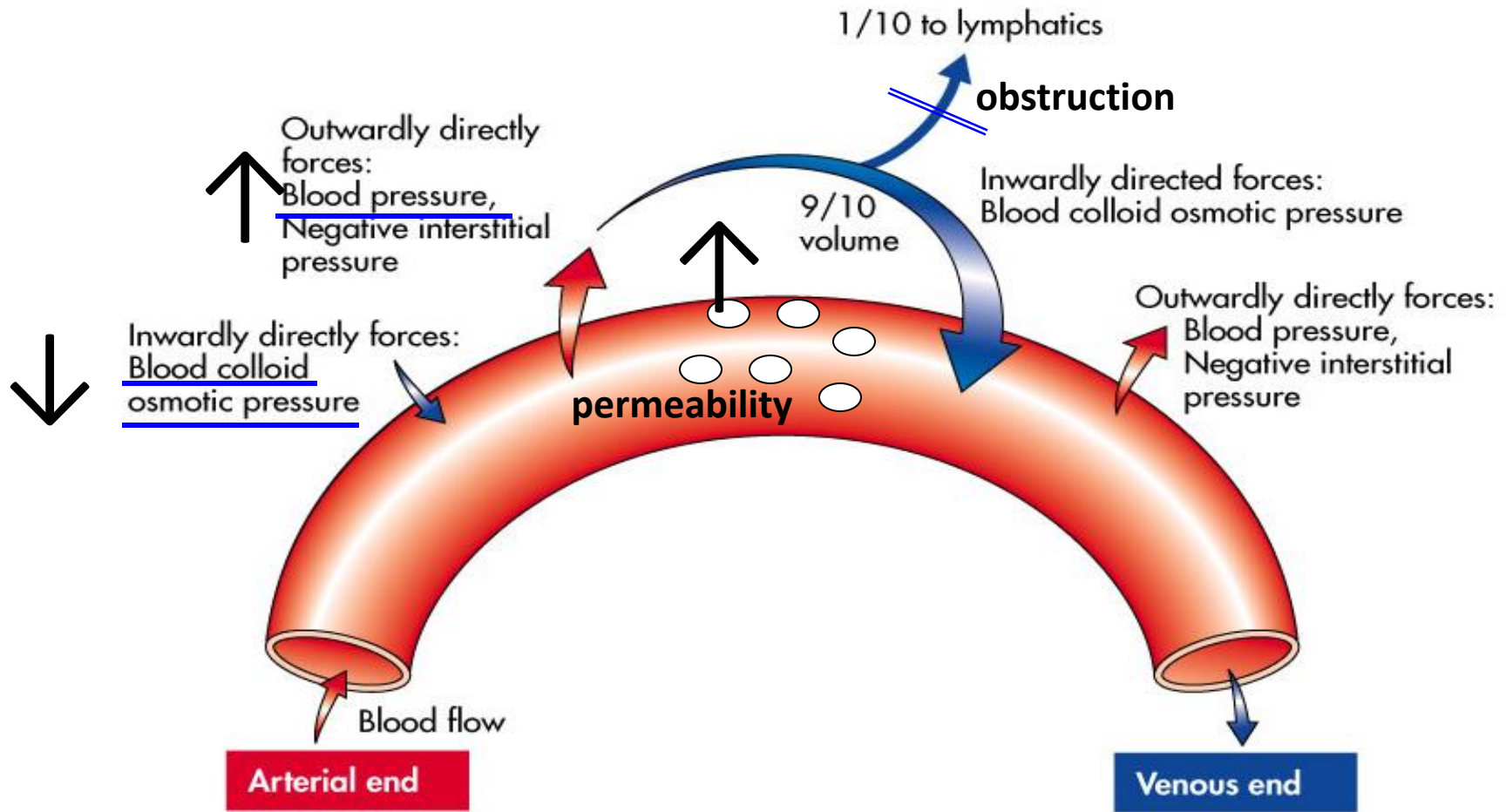


# capillaries



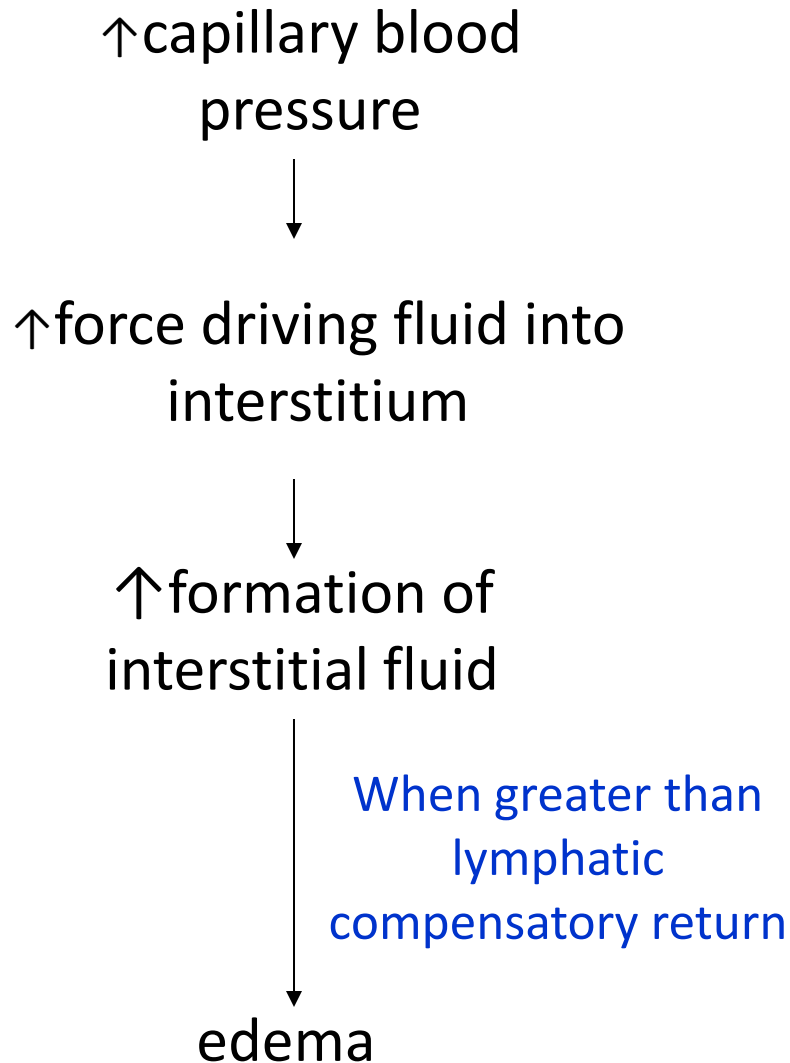
When blood flows through capillary, fluid exchange, including water and some small molecules that can pass through the capillary wall, will happen between plasma and interstitial compartment.

# Total Pressure Differences Inside and Outside Capillary



The force promoting fluid outshift from capillary to interstitial compartment includes blood pressure and negative interstitial pressure. The force attracting fluid from interstitial compartment to capillary is blood colloid osmotic pressure. At the arterial end, the sum of the forces causes fluid to move from the capillary into the tissue. At the venous end, the sum of the forces causes fluid to move into the capillary. About nine-tenths of the fluid that leaves the capillary at its arterial end reenters the capillary at its venous end. About one-tenth of fluid passes into the lymphatics.

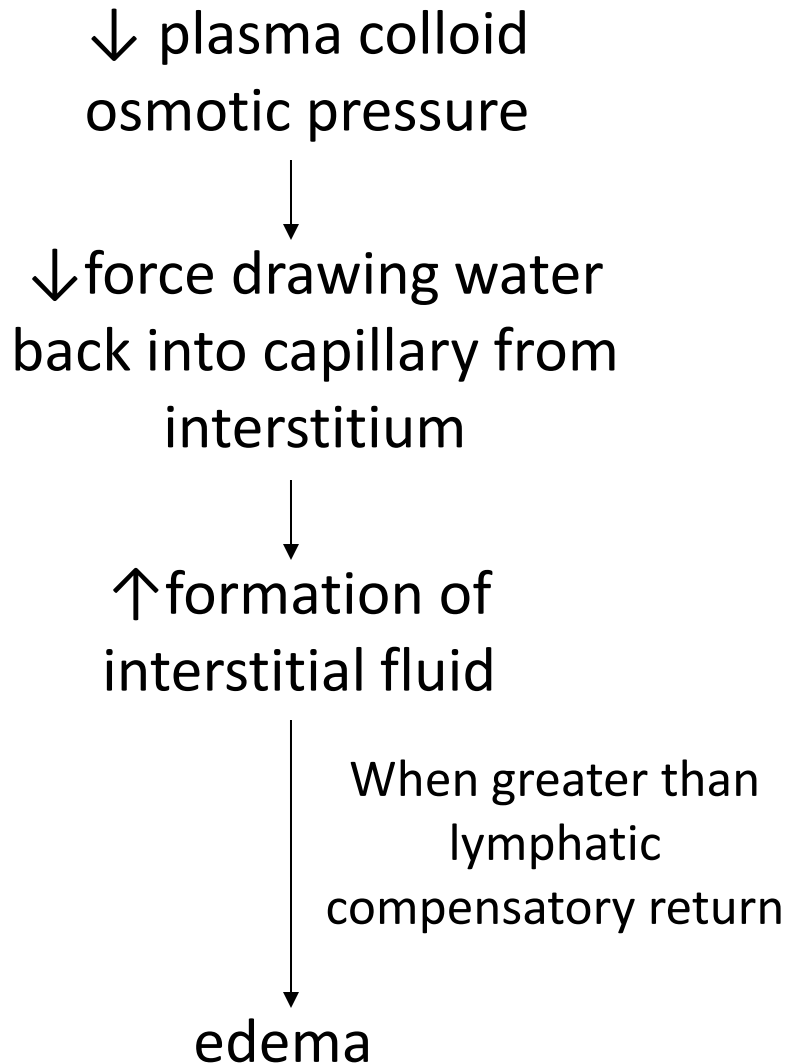
# 1. Increased capillary blood pressure



## Causes:

- Elevated plasma volume
- Increased venous pressure
  - Increased general venous pressure, i.e. congestive heart failure
  - Increased local venous pressure, i.e. venous thrombosis
- Arteriolar dilation i.e. acute inflammation

## 2. Decreased plasma colloid osmotic pressure



Causes: plasma albumin content decrease

- Decrease of protein production  
i.e. hepatic cirrhosis, malnutrition
- Excessive loss of protein  
i.e. nephrosis
- Elevated catabolism of protein  
i.e. chronic debilitating diseases, such as malignant tumor

### 3. Obstruction of lymphatic

During the process of interstitial fluid formation, one-tenth of fluid that leaves the capillary at its arterial end returns to the venous circulation via lymphatics. So obstruction of lymphatic will result in edema.

#### Causes:

- Blockage by cancer
- Blockage by infection, especially with filarial

## 4. Increased capillary permeability

↑capillary permeability



Filtration of more protein from  
capillary to interstitium



↓Plasma colloid osmotic pressure



↑formation of interstitial fluid



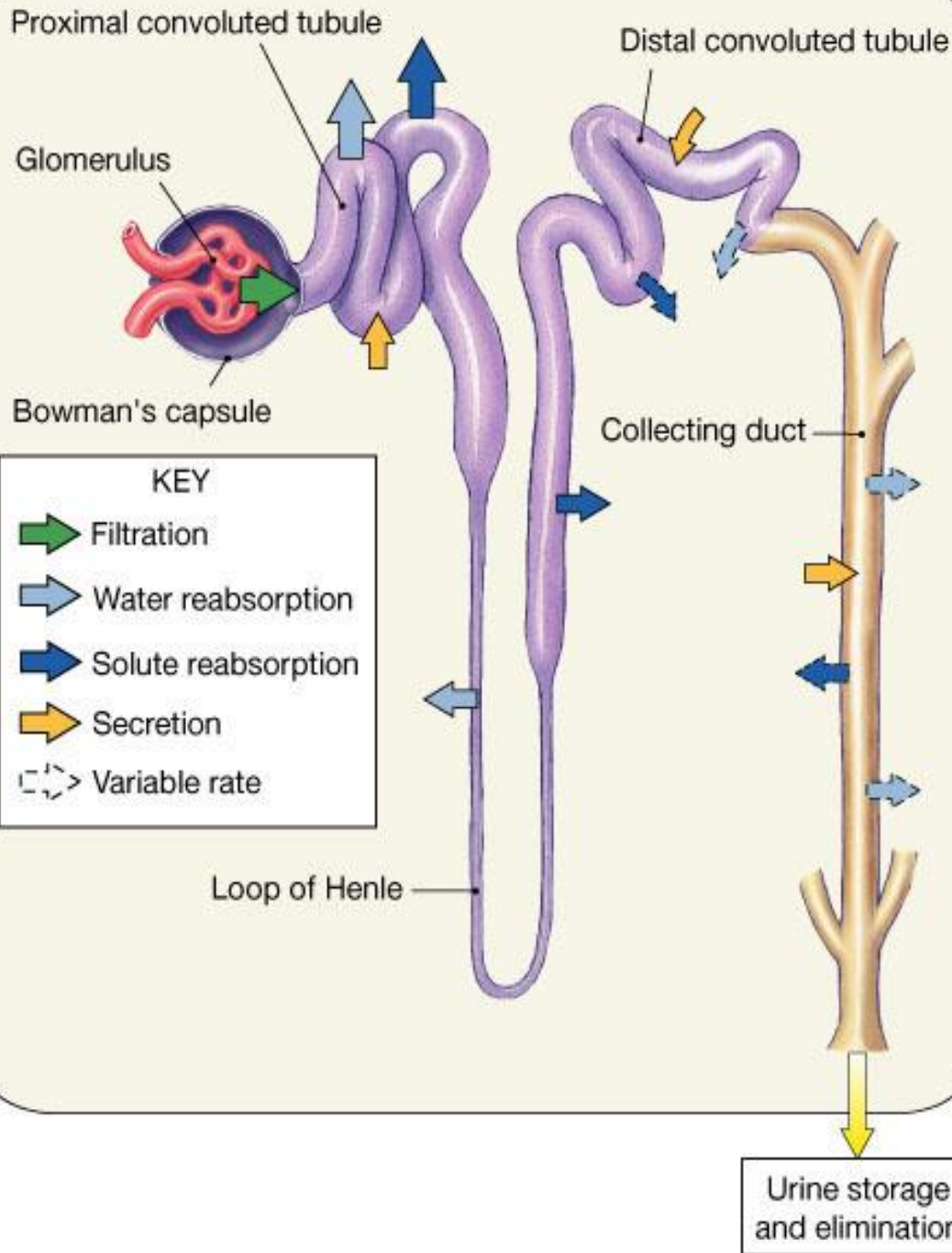
When greater than  
lymphatic  
compensatory return

edema

Causes: inflammation

- Infection
- Burn
- Allergic response
- Trauma
- Anoxia
- Acidosis

Imbalance of fluid exchange between extra-  
and intra-body



## Glomerular( filtration) and tubular (reabsorption) balance

(G-T balance)

- In normal condition, 99-99.5% of total volume of sodium and water filtrated via glomeruli are reabsorbed by tubules.
- 60-70% of filtrates are actively reabsorbed by proximal convoluted tubule.
- The reabsorptions of sodium and water at distal tubule and collectiong duct are regulated by hormone.



- GFR is decreased, while tubular reabsorption is not decreased accordingly;
- Tubular reabsorption increases, while GFR isn't increased.



G-T imbalance

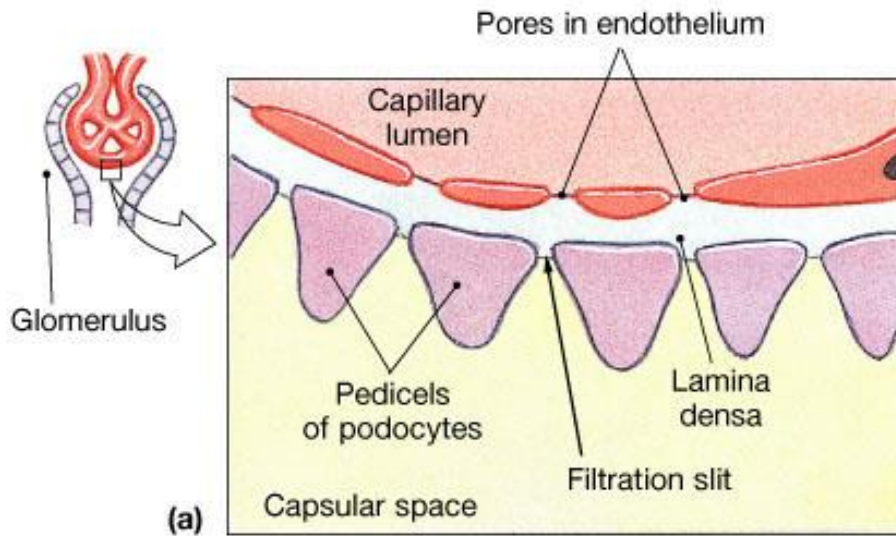


Retention of sodium and water

- ↓ GFR
- ↑ Reabsorption of proximal tubule
- ↑ Reabsorption of distal tubule and collection tubule

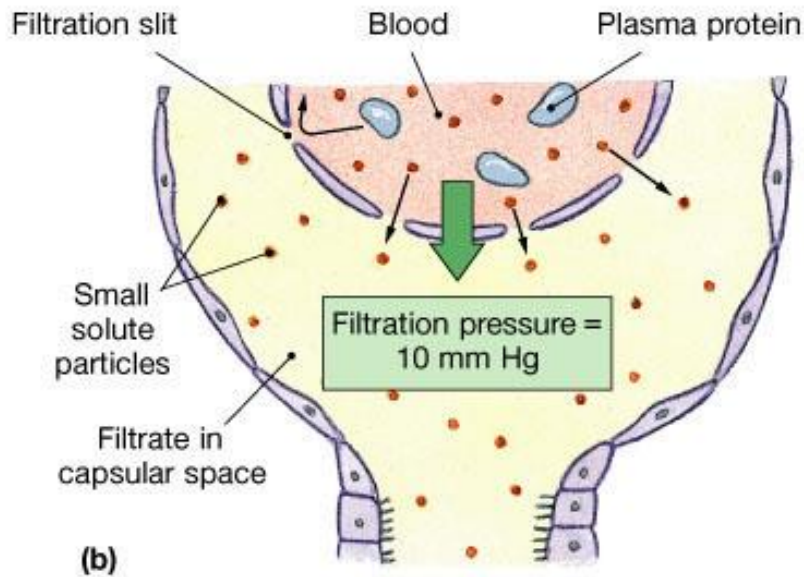
# 1. Decreased glomerular filtration rate (GFR)

- When decreased GFR is not accompanied with decreased tubular reabsorption, retention of sodium and water will be caused.



## Factors determining the GFR:

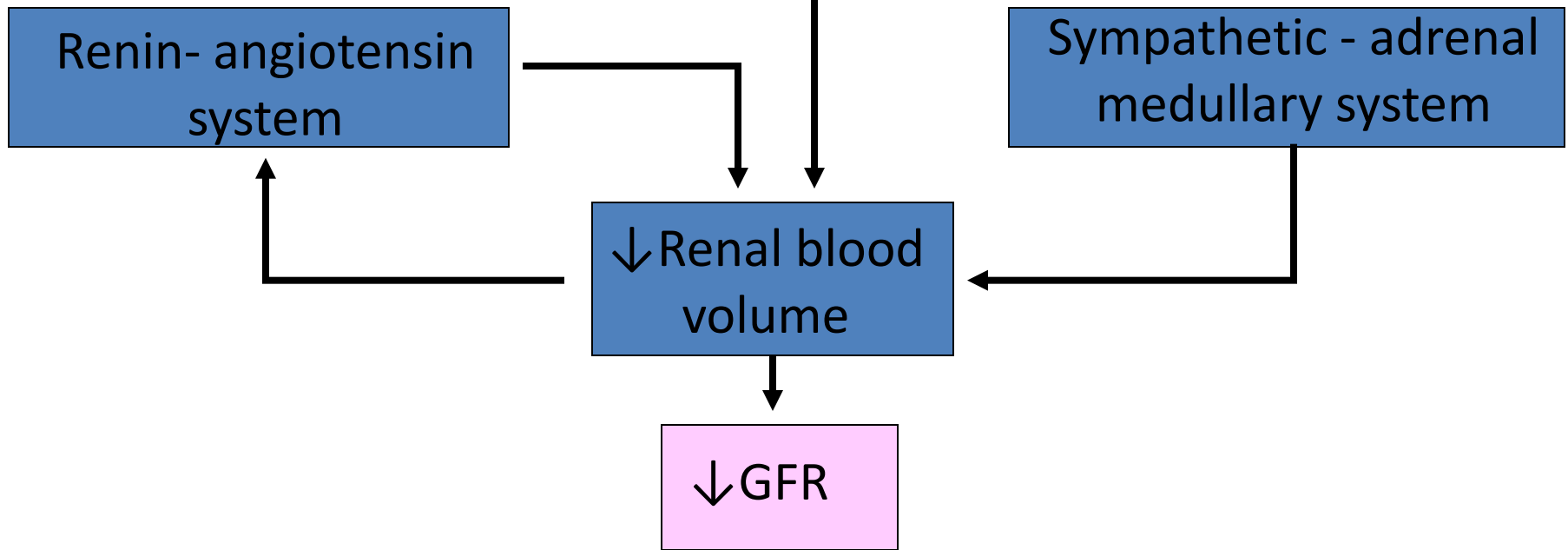
- Filtration area and membrane permeability
- Filtration pressure
- Effective circulating blood volume or renal blood volume



# 1. ↓GFR

## Causes

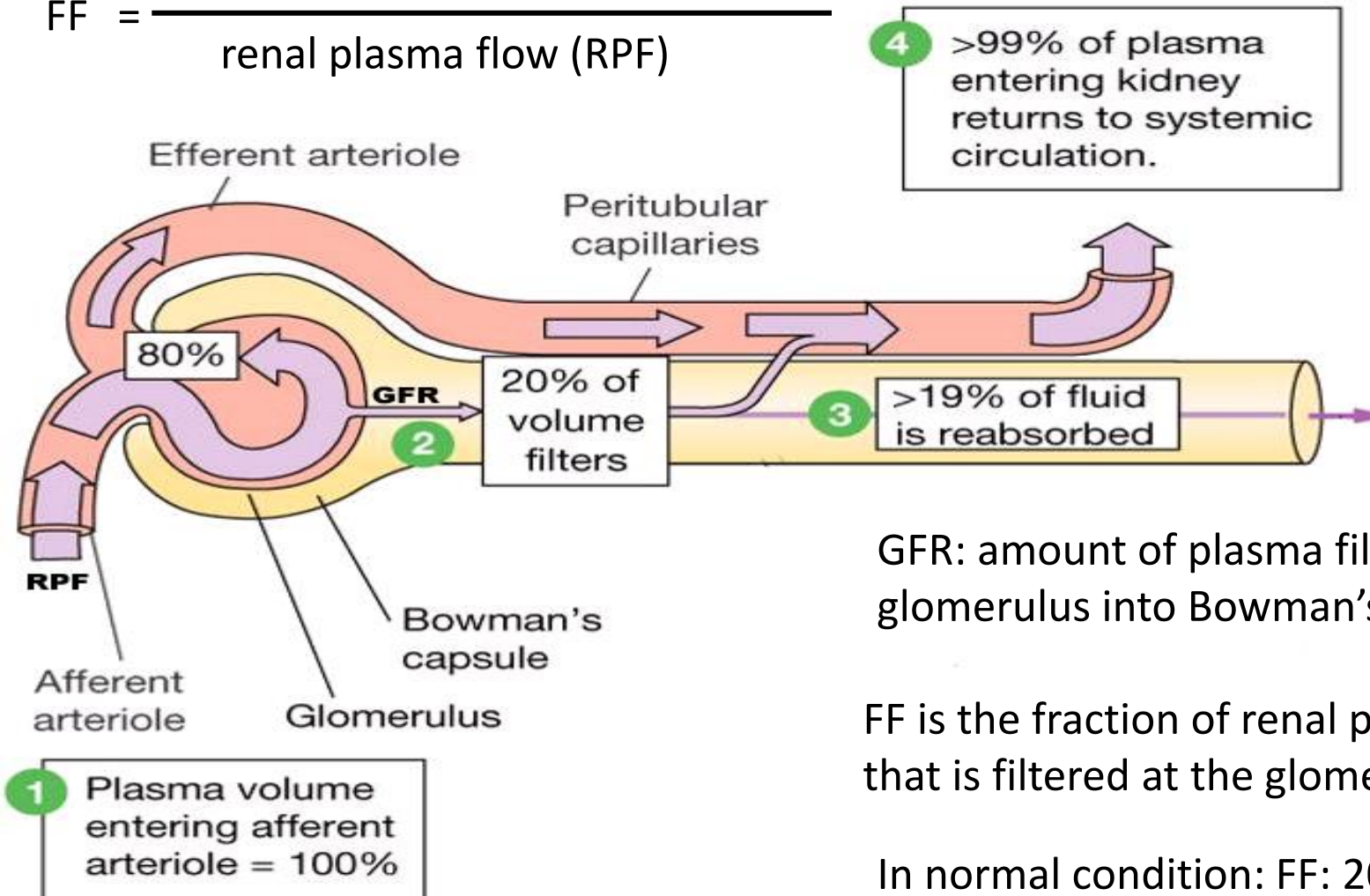
- Extensive glomerular damage  
i.e. Acute or chronic glomerulonephritis
- Decrease of effective circulating blood volume  
i.e. congestive heart failure, nephrotic syndrome



## 2. Increased filtration fraction (FF)

-Increased reabsorption in proximal tubule

$$FF = \frac{\text{glomerular filtration rate (GFR)}}{\text{renal plasma flow (RPF)}}$$

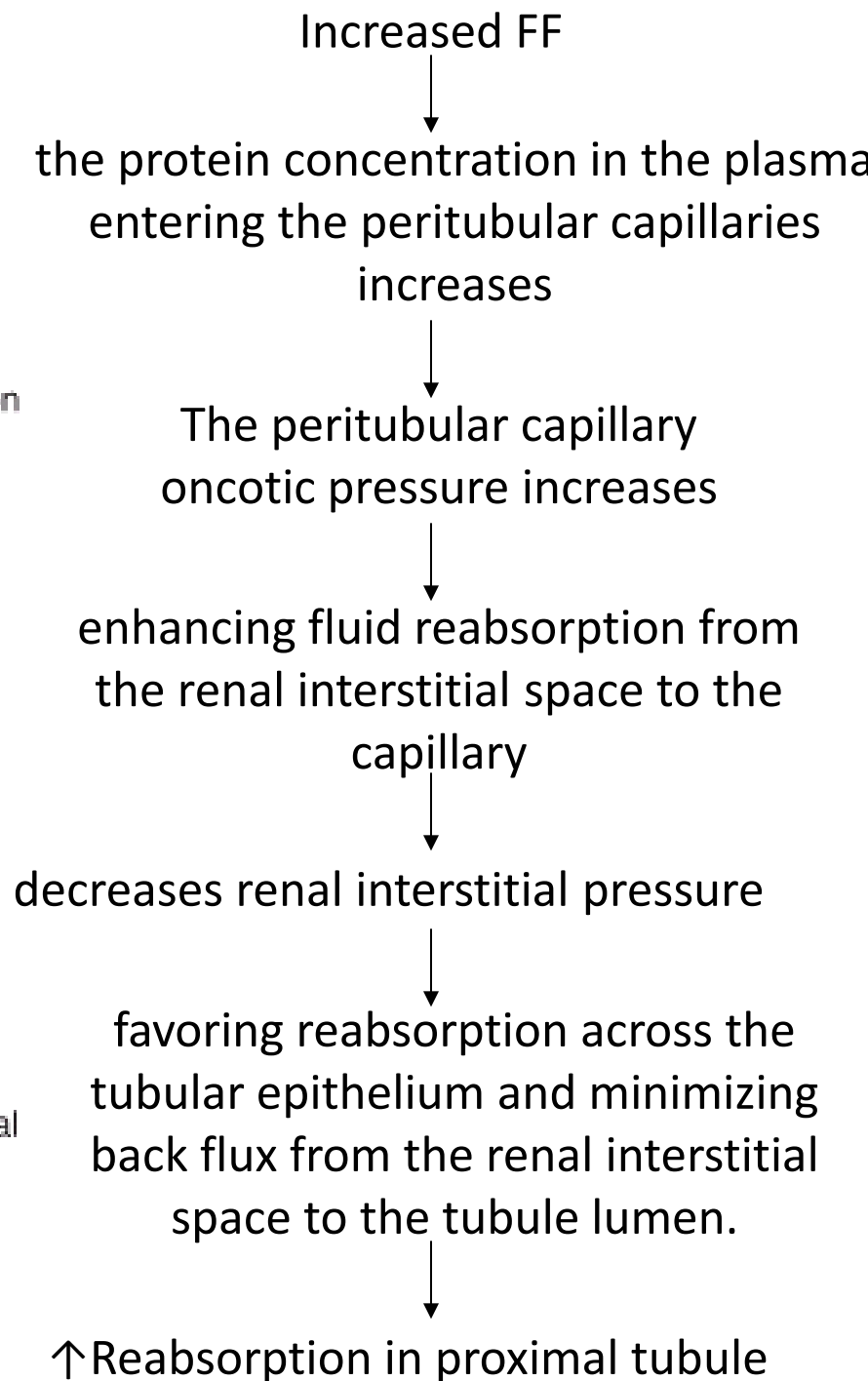
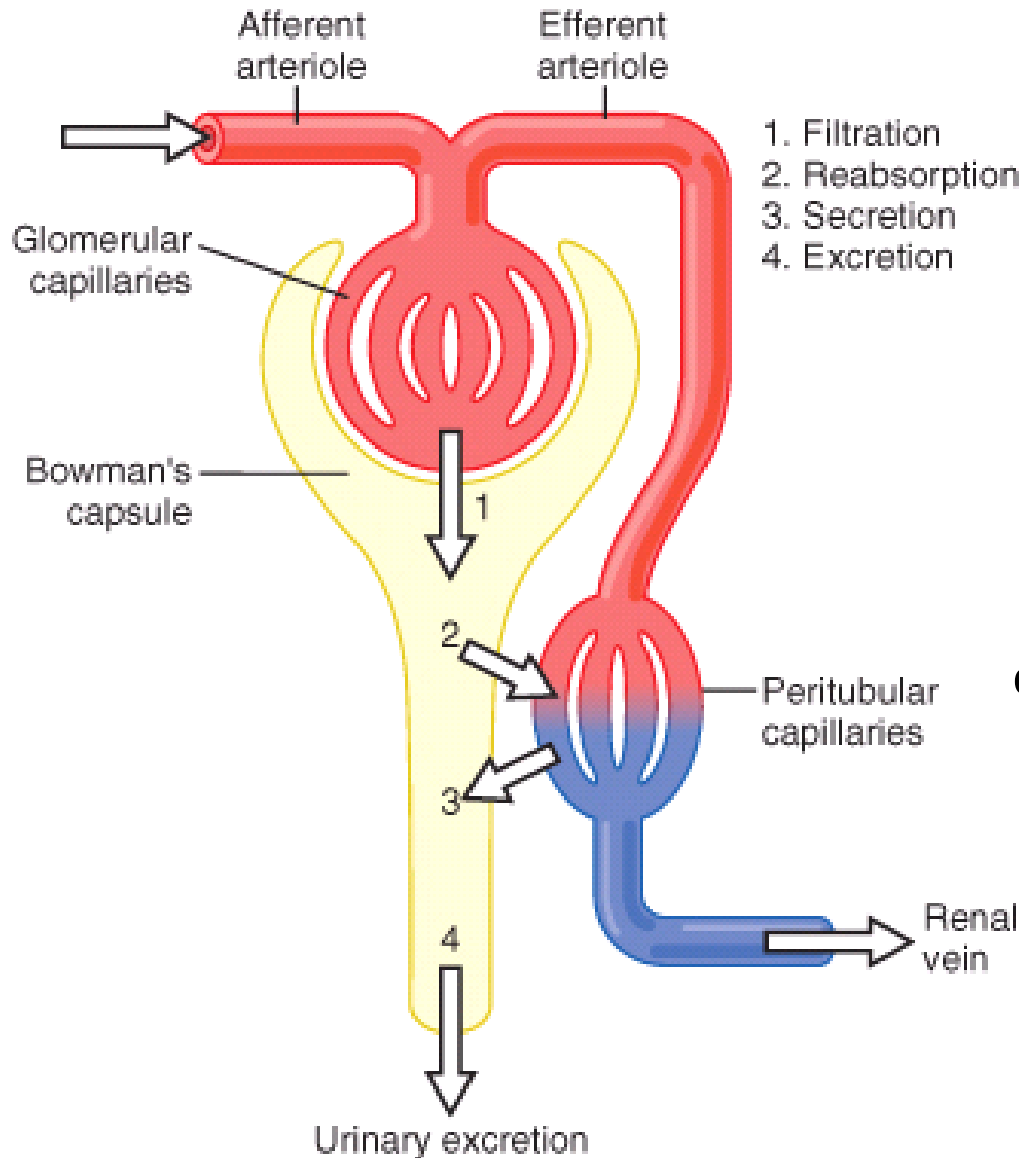


GFR: amount of plasma filtered at glomerulus into Bowman's capsule

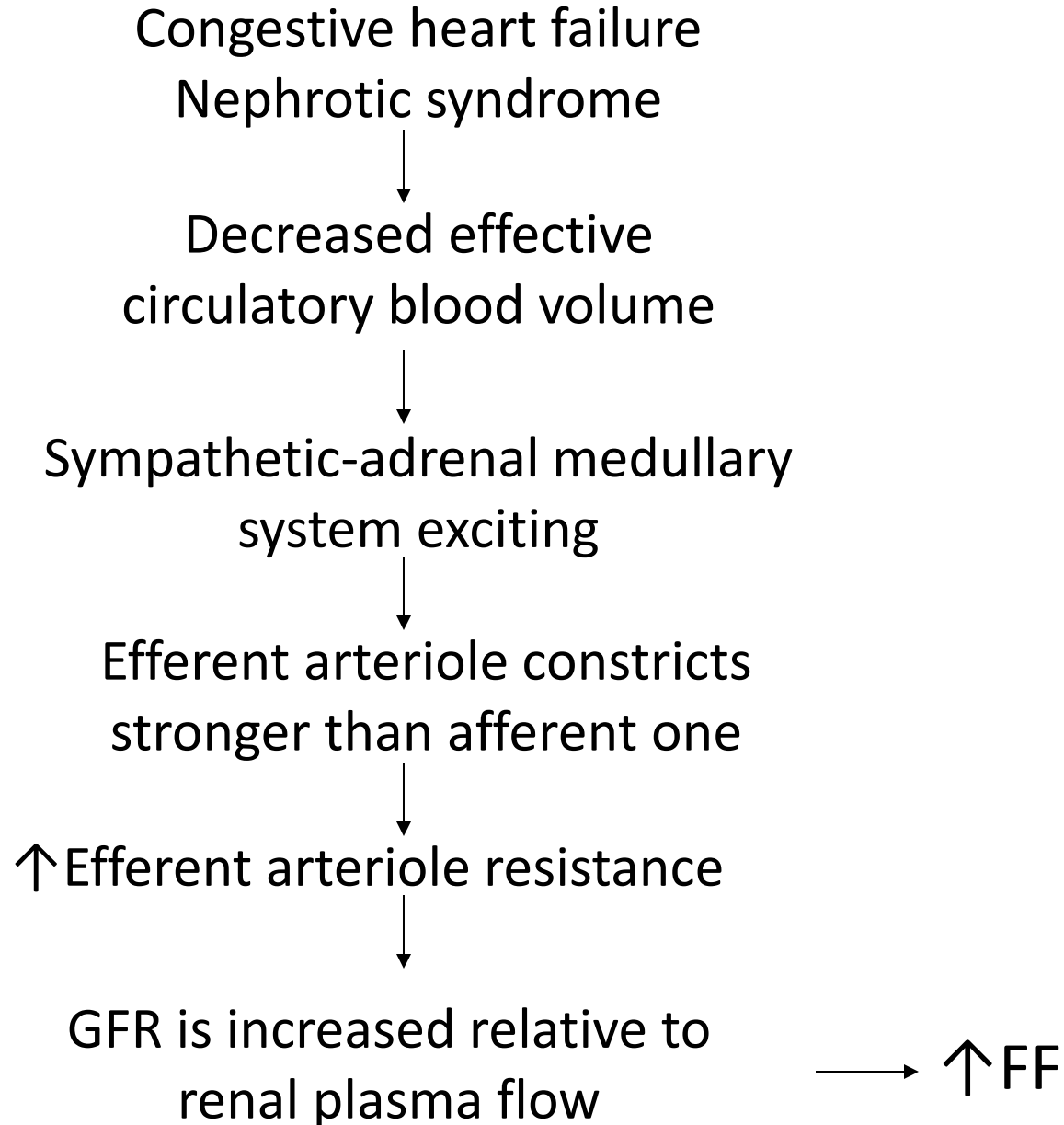
FF is the fraction of renal plasma flow that is filtered at the glomerulus

In normal condition: FF: 20%

# Increased FF make elevated reabsorption of proximal tubule

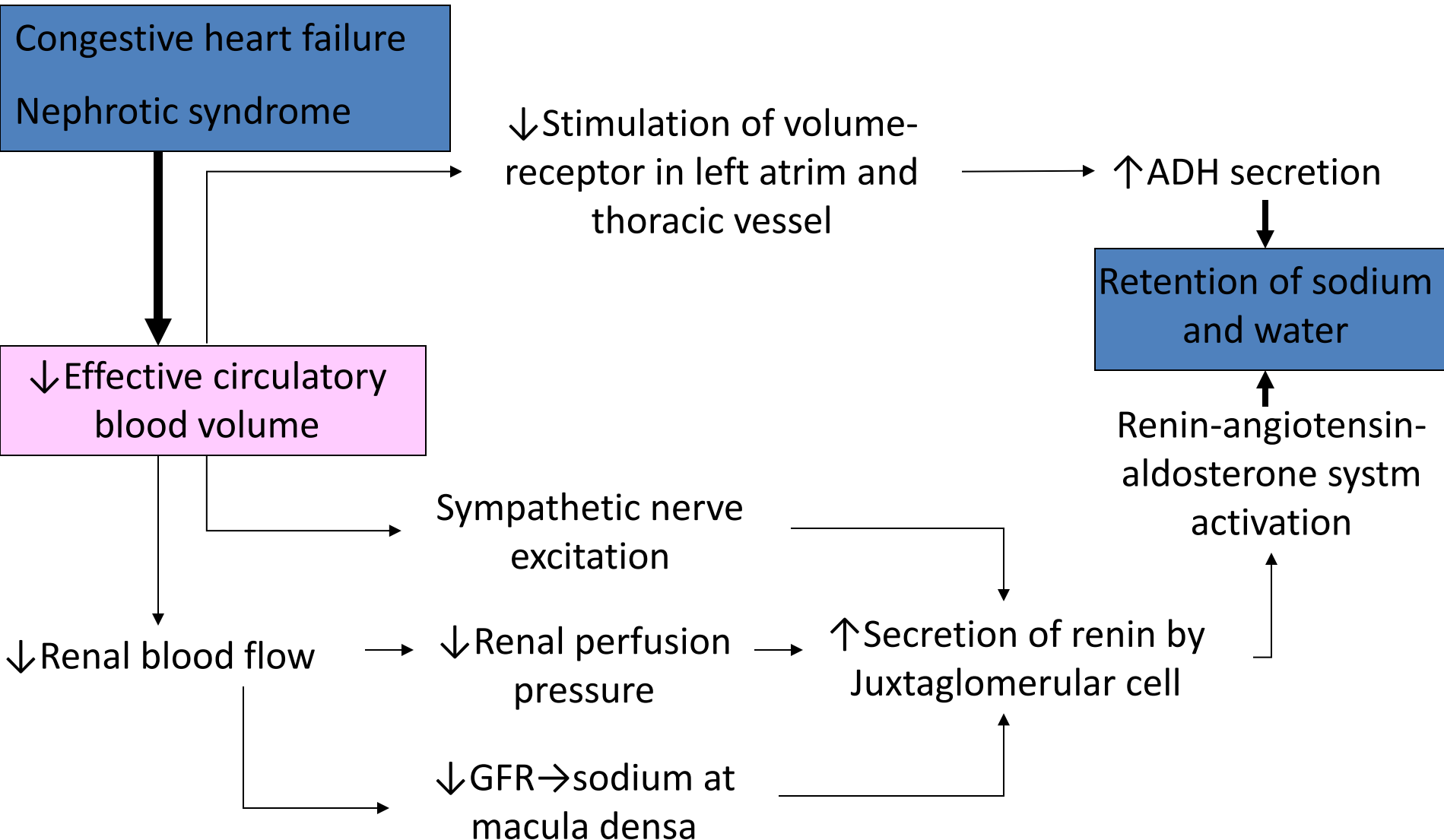


# Causes of FF increasing



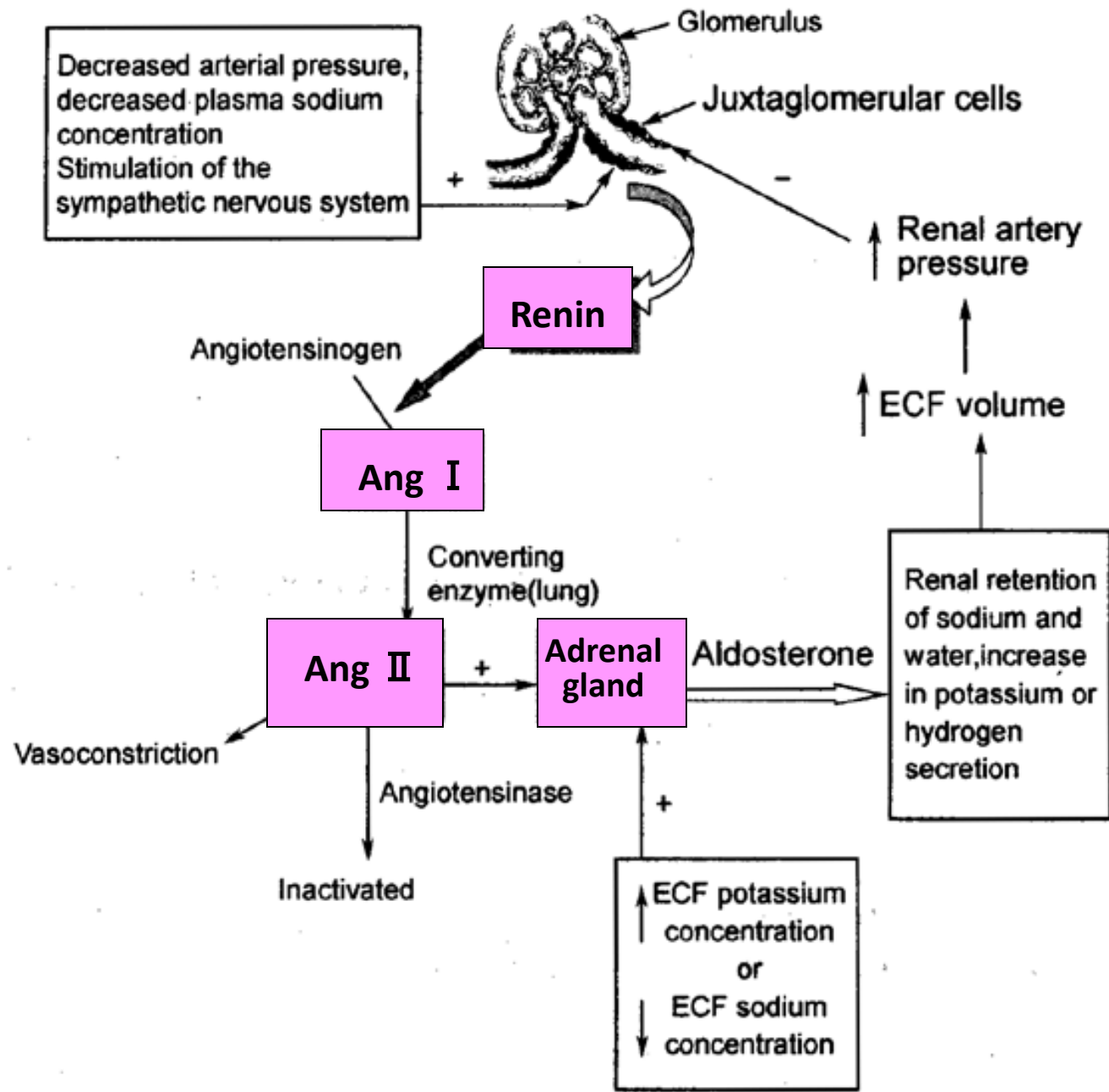
### 3. increased ADH and ADS secretion

-Increased reabsorption in distal tubule and collecting duct



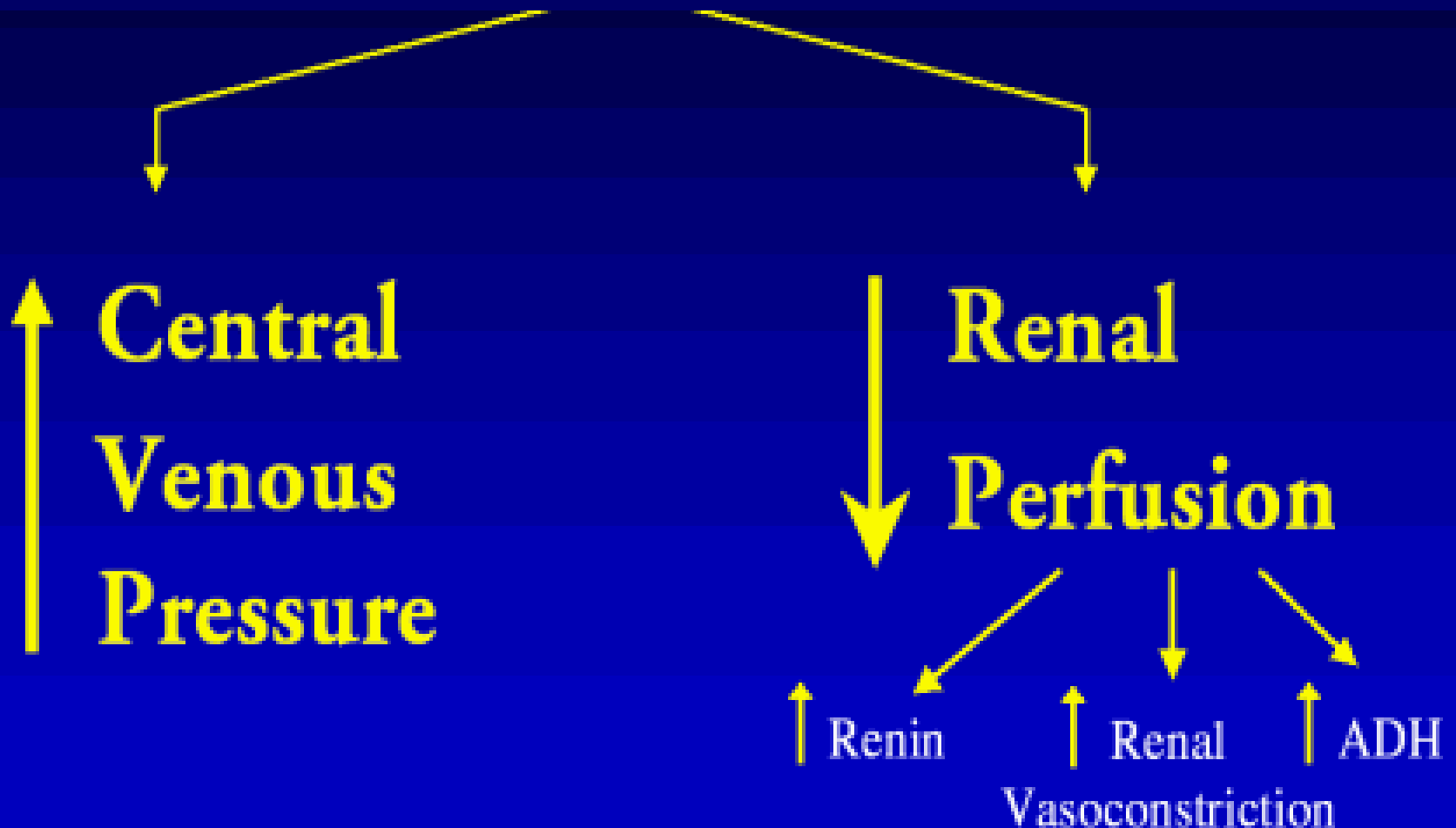


# The renin-angiotensin-aldosterone system



# Systemic Edema

## Congestive heart failure



**Portal Hypertension** ← **Cirrhosis**

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graph TD; Cirrhosis --> PortalHypertension[Portal Hypertension]; Cirrhosis --> SerumAlbumin[Serum Albumin]; Cirrhosis --> RenalPerfusion[Renal Perfusion]; PortalHypertension --> SinusoidalHypertension[Sinusoidal Hypertension]; SinusoidalHypertension --> HepaticLymph[Hepatic Lymph]; HepaticLymph --> Overwhelms[Overwhelms Thoracic Duct]; Overwhelms --> SystemicEdema[Systemic Edema]; SystemicEdema --> Ascites[ASCITES]; SerumAlbumin --> Ascites; RenalPerfusion --> Aldosterone[Aldosterone]; Aldosterone --> Ascites;
```

**Sinusoidal Hypertension**

**Serum Albumin**

**Renal Perfusion**

↑ **Hepatic Lymph** →

Overwhelms  
Thoracic Duct

↑ **Aldosterone**

**Systemic Edema**

**ASCITES**

# Nephrotic Syndrome/Hypoalbuminemic states

- The primary alteration: decreased colloid oncotic pressure

protein loss in the urine

severe nutritional deficiency

protein loss enteropathy

congenital hypoalbuminemia

liver cirrhosis

- Promotes fluid move into the interstitium

- Causes hypovolemia



salt/water retention    activation RAAS etc

Alterations of metabolism and function

# 1. The feature of edema fluid

- Transudates
  - Formed under almost normal capillary permeability
  - Low content of cells and protein
    - Exception: edema fluid due to lymphatic obstruction
- Exudates
  - Resulted from an increase in capillary permeability
  - Contain plentiful cells and a large amount of protein
  - Usually seen in inflammation

## 2. The cutaneous characters of edema

- Pitting edema
  - a tissue area is pressed by thumb and after the thumb is removed, a pit is left at the pressed site for a few seconds.
- Recessive edema
  - Edema without pit.
  - Before pitting edema emergeing, excessive interstitial fluids already exist in generalized edema patient.



Increased extra interstitial fluid is bound in a proteoglycan filament messwork of tissue, so that this gel fluid does not flow easily through the tissues.

### 3. Distribution character of generalize edema

#### Influencing factors

- Gravity
- Structure of tissue
- Local hemodynamics

- Cardiac edema: ankle
- Renal edema: eyelids and face
- Hepatic edema: ascites