GLOMERULAR FILTRATION RATE (GFR)

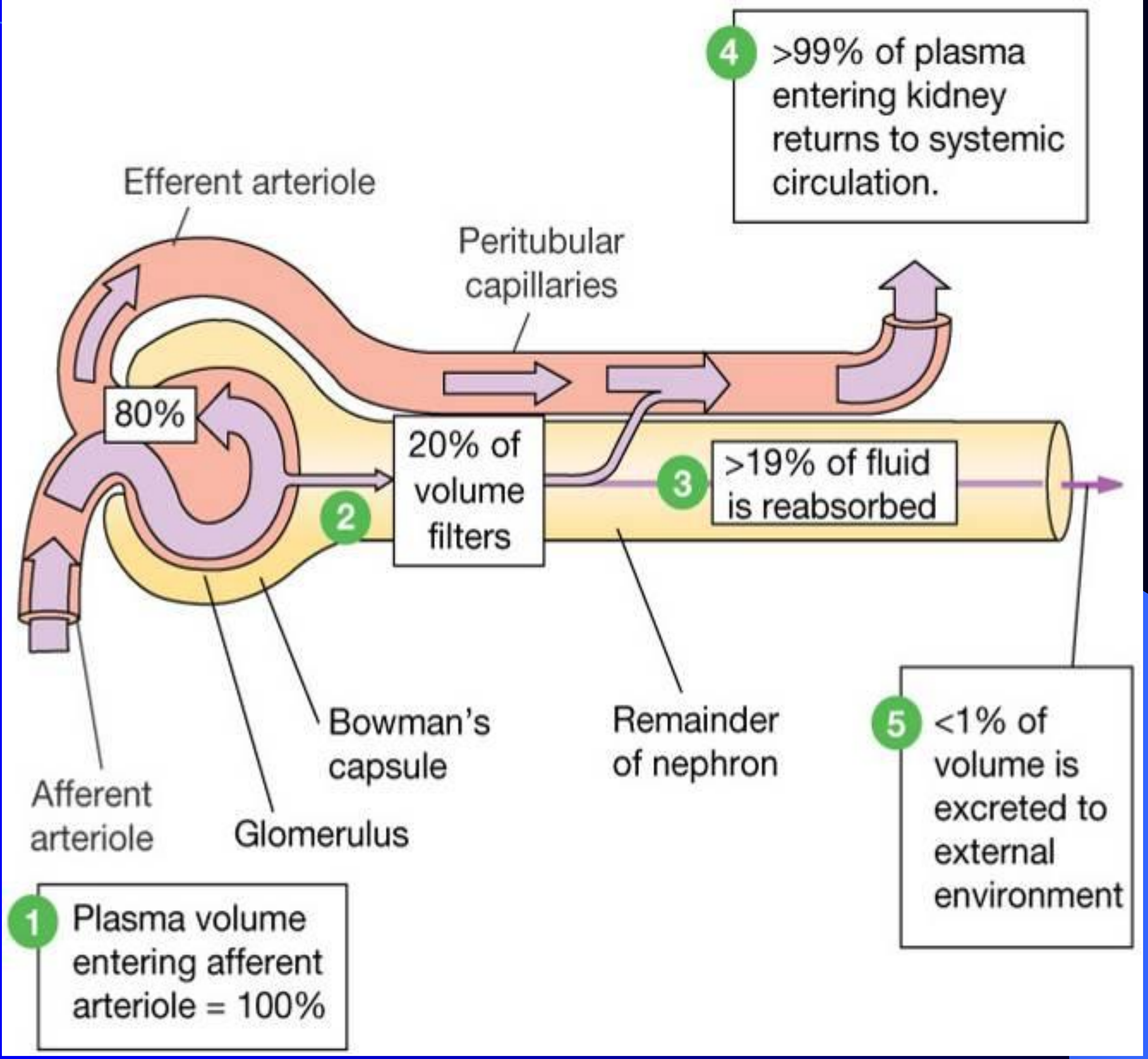
Glomerular filtration rate (GFR)

- **Definition:**
- **Is the volume of plasma filtered by all nephrons in both kidneys/unit time**
- **= 125ml/min**
- **GFR values = 180L/day**
- **Varies with kidney size and lean body weight**
- **Less in women**
- **Variation in GFR between different species depend on number of nephrons**

GFR ≈ 125 ml/min

(180L/day)

(about 1% is excreted)



GLOMERULAR FILTRATION

Depends on:

1- Pressure gradient across the filtration barrier (endothelium, basal membrane, epithelium = podocytes)

2- Blood circulation throughout the kidneys

3- Permeability of the filtration barrier

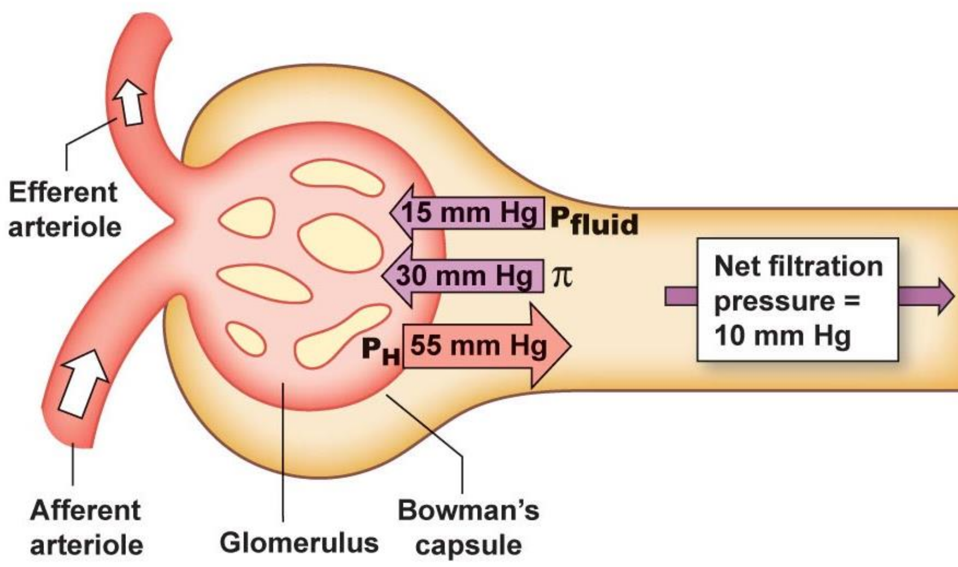
4- Filtration membrane surface area

The solution after filtration is very similar to plasma, but should be WITHOUT PROTEIN

Nephron
Glomerular Filtration

Forces

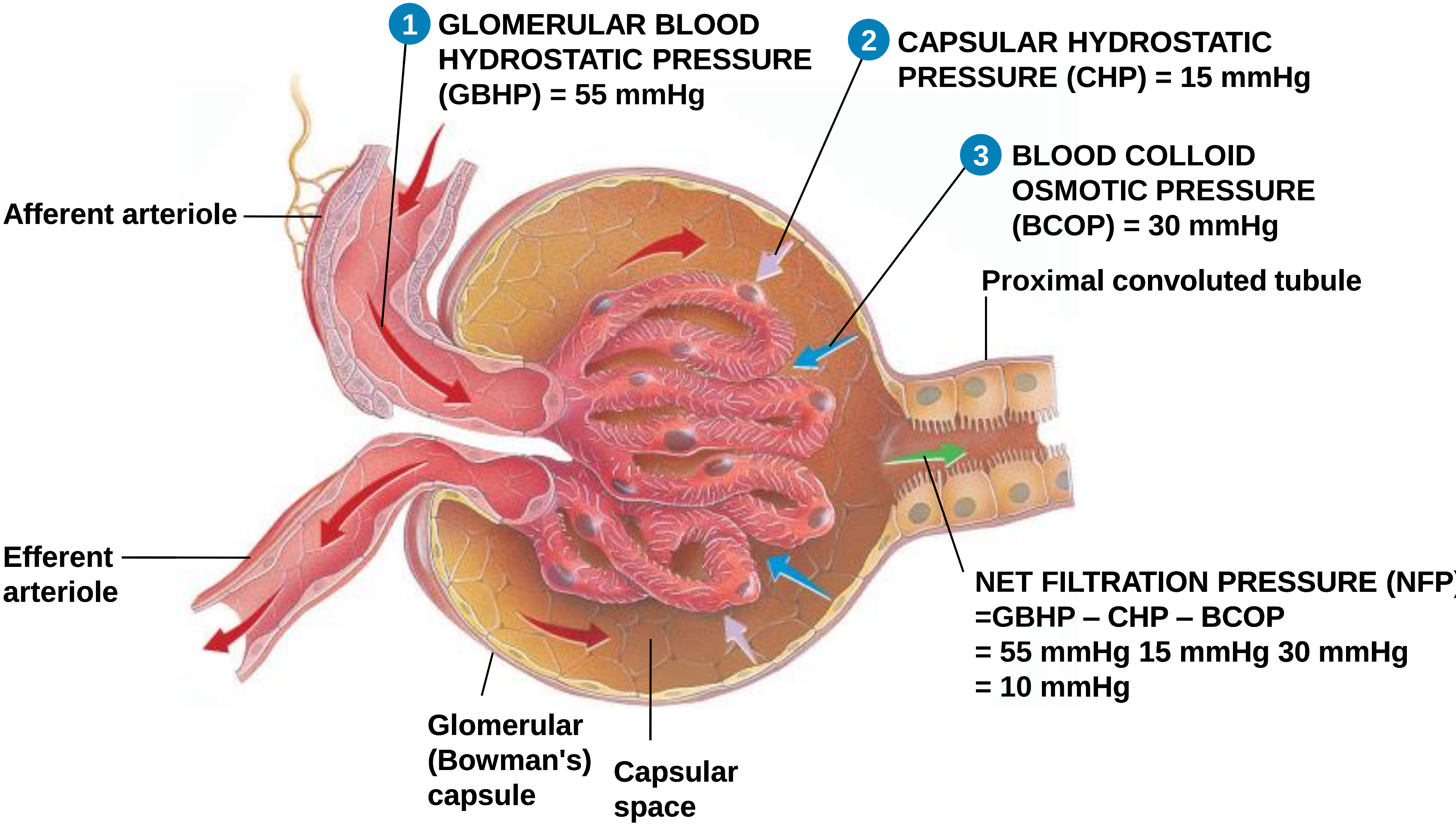
- **Blood hydrostatic pressure (P_H)**
  - Outward filtration pressure of 55 mm Hg
    - Constant across capillaries due to restricted outflow (efferent arteriole is smaller in diameter than the afferent arteriole)
- **Colloid osmotic pressure (π)**
  - Opposes hydrostatic pressure at 30 mm Hg
  - Due to presence of proteins in plasma, but not in glomerular capsule (Bowman's capsule)
- **Capsular hydrostatic pressure (P_{fluid})**
  - Opposes hydrostatic pressure at 15 mm Hg



P_H	–	π	–	P_{fluid}	=	net filtration pressure
55	–	30	–	15	=	10mm Hg

KEY

P_H = Hydrostatic pressure (blood pressure)
π = Colloid osmotic pressure gradient due to proteins in plasma but not in Bowman's capsule
P_{fluid} = Fluid pressure created by fluid in Bowman's capsule


1 GLOMERULAR BLOOD HYDROSTATIC PRESSURE (GBHP) = 55 mmHg
2 CAPSULAR HYDROSTATIC PRESSURE (CHP) = 15 mmHg
3 BLOOD COLLOID OSMOTIC PRESSURE (BCOP) = 30 mmHg
Afferent arteriole
Proximal convoluted tubule
Efferent arteriole
NET FILTRATION PRESSURE (NFP)
=GBHP – CHP – BCOP
= 55 mmHg 15 mmHg 30 mmHg
= 10 mmHg
Glomerular (Bowman's) capsule
Capsular space

Nephron
Glomerular Filtration

10 mm Hg of filtration pressure.

Is not high, but has a large surface area and nature of filtration membrane.

Creates a glomerular filtration rate (GFR) of 125 ml/min which equates to a fluid volume of 180L/day entering the glomerular capsule.

- **Plasma volume is filtered 60 times/day or 2 ½ times per hour**
- **Requires that most of the filtrate must be reabsorbed, or we would be out of plasma in 24 minutes!**

Factors affecting GFR

1- Changes in renal blood flow

2- Changes in glomerular capillary hydrostatic pressure
- Changes in systemic blood pressure
- Afferent or efferent arteriolar constriction

3- Changes in hydrostatic pressure in Bowman's capsule:
- Ureteral obstruction
- Edema of kidney inside tight renal capsule

4- Changes in concentration of plasma proteins:
- dehydration, hypoproteinemia, etc (minor factors)

5- Changes in glomerular capillary permeability

6- Changes in effective filtration surface area

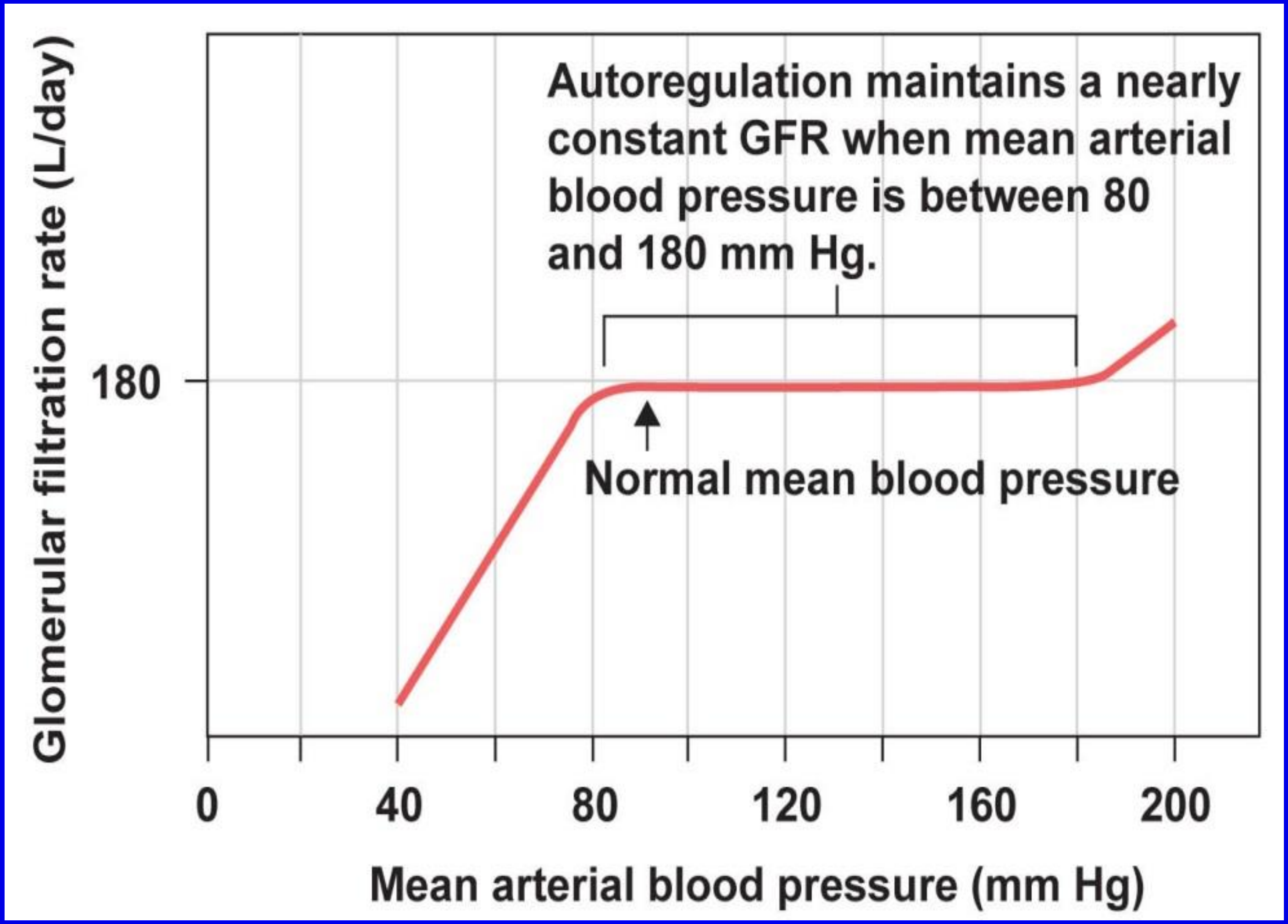
Three processes controlling GFR

- Auto regulation (myogenic)
- Hormonal regulation (tubuloglomerular & renin-angiotensin)
- Autonomic regulation (extrinsic)

Autoregulation of GFR

- Changes diameters of afferent, efferent arteriole, and glomerular capillaries
  - Decrease pressure results in dilation of afferent arteriole, dilation of glomerular capillaries and constriction of efferent arteriole →↑ GFR
  - Increase pressure results in constriction of afferent arteriole → ↓ GFR

Nephron
Glomerular Filtration



Hormonal Regulation of GFR
a) Macula Densa

Involves macula densa cells of juxtaglomerular apparatus.

- **Low filtrate and low osmolality**
  - **Macula densa promotes vasodilation of afferent arteriole, promotes ↑ net filteration pressure and ↑ GFR.**

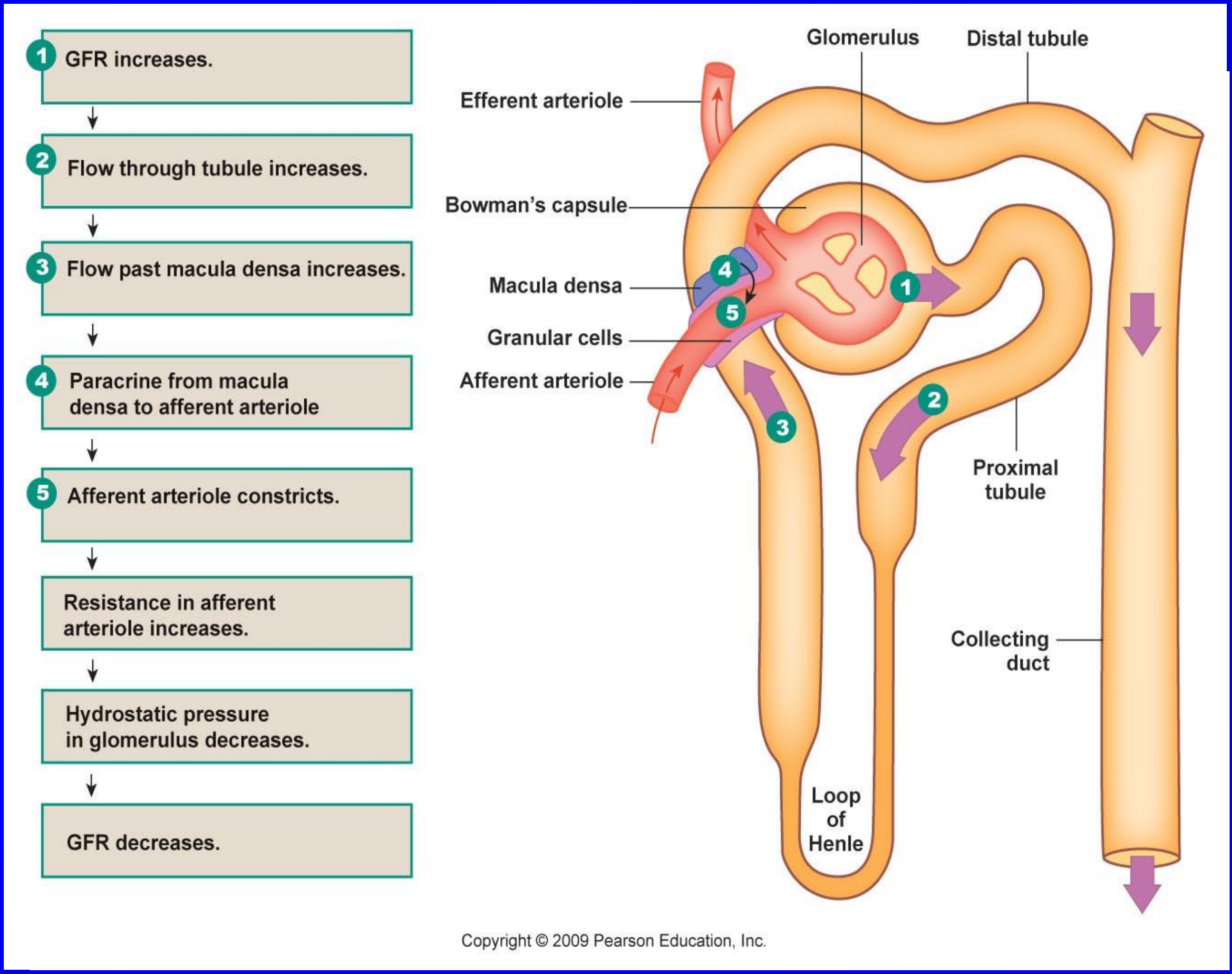
- **High filtrate and high osmolality**
  - **Macula densa promotes vasoconstriction of afferent arteriole, promotes ↓ net filteration pressure and ↓ GFR.**

Nephron
Regulation of GFR

The cells of the macula densa monitor NaCl concentration in the fluid moving into the dital convoluted tubule.

If GFR increases, then NaCl movement also increases as a result.

Macula densa cells send a paracrine message causing the afferent arteriole to contract, decreasing GFR and NaCl movement.



Hormonal Regulation of GFR
b) Renin system

Decrease in blood pressure and decrease in osmolality in the DCT causes release of renin.

The effects of renin include:

- **Vasoconstriction of systemic circulation**
- **Constriction of efferent arteriole**
- **Promote release of aldosterone**

Autonomic Regulation of GFR

Sympathetic nervous system causes **constriction** of afferent arteriole which **decreases** GFR

Agents causing contraction or relaxation of mesangial cells

Contraction	Relaxation
Endothelins	ANP
Angiotensin II	Dopamine
Vasopressin	PGE_2
Norepinephrine	cAMP
Platelet-activating factor	
Platelet-derived growth factor	
Thromboxane A_2	
PGF_2	
Leukotrienes C_4 and D_4	
Histamine	

Measurement of GFR

The substance used should be:

- Freely filtered (not reabsorbed or secreted)
- Not metabolized by the kidney
- Not toxic and stable
- Not bound to plasma proteins
- Does not change renal plasma flow

Inulin is the substance.

Measurement of GFR cont.

Test procedure

- Intravenous loading dose of inulin followed by intravenous infusion of inulin to maintain plasma level constant.

- Urine is collected for 15 or 20 min, to measure inulin concentration in urine and urine volume.

- Blood sample is taken half way of urine collection to measure inulin concentration.

Calculation of GFR

- The amount of inulin excreted = $U_{in} \times U_v$

- The amount of inulin filtered = $P_{in} \times GFR$
- As inulin is not reabsorbed or excreted both quantities are equal
- $P_{in} \times GFR = U_{in} \times U_v$
- $GFR = \frac{U_{in} \times U_v}{P_{in}}$ = ml/min

Filtration fraction

GFR / RPF

125 / 650 = 0.19

= 16-20%