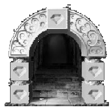
RENAL PHYSIOLOGY
INTRODUCTION



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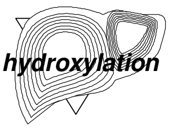
FUNCTIONS OF THE KIDNEY

- **Excretion of wastes (creatinine, urea, benzoate, penicillin, saccharin)**
- **Regulation of water (extracellular fluid volume)**
- **Maintenance of electrolyte balance (Na^+, K^+, HCO_3^-, Ca^{++})**
- **Regulation of arterial pressure**
- **Regulation of blood pH**

FUNCTIONS OF THE KIDNEY
(Cont.)

- **Secretion, metabolism, and excretion of hormones**
  - **Hormone production (Erythropoietin, Renin)**
  - **Activation of Vitmain D**
- **Gluconeogenesis**

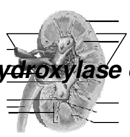
Naturally occurring vitamin D (cholecalciferol)



hydroxylation

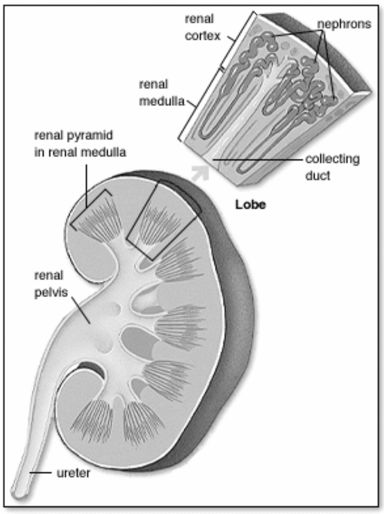
25-hydroxycholecalciferol 25-OHD3)

PTH ⇨ ***1α-hydroxylase enzyme***



1,25-dihydroxycholecalciferol (1,25-(OH)2D3)

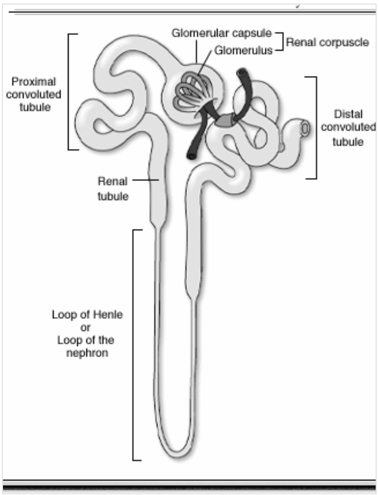
PHYSIOLOGIC ANATOMY OF KIDNEYS



The outer portion of the kidney is the renal cortex. The medulla lies below the cortex; the many parallel tubes within it give it a striped appearance. The innermost portion is the renal pelvis, which collects the urine and passes it to the ureter. Each kidney lobe contains a large number of nephrons.

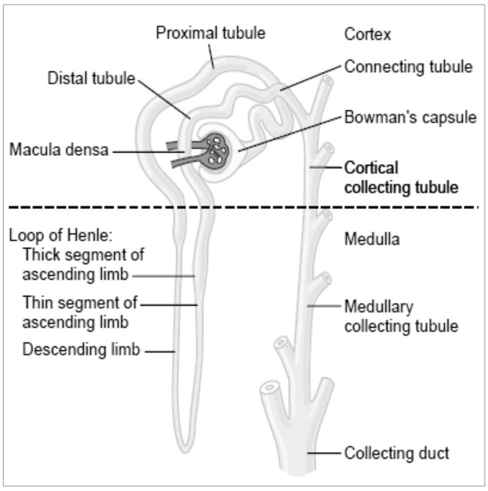
NEPHRON

- **Each kidney in the human contains about 1.3 million nephrons, each capable of forming urine.**
- **The kidney cannot regenerate new nephrons.**
- **After age 40, the number of functioning nephrons usually decreases about 10 per cent every 10 years; thus, at age 80, many people have 40 per cent fewer functioning nephrons than they did at age 40.**

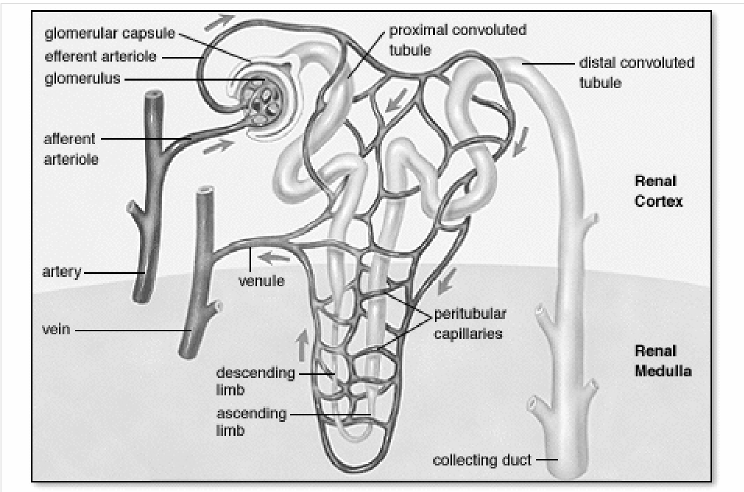


PARTS OF NEPHRON

- **8 to 10 cortical collecting ducts join to form a single larger collecting duct that runs downward into the medulla and becomes the *medullary collecting duct.***
- ***The collecting ducts merge to form larger ducts that eventually empty into the renal pelvis through the tips of the renal papillae.***



RENAL PORTAL SYSTEM

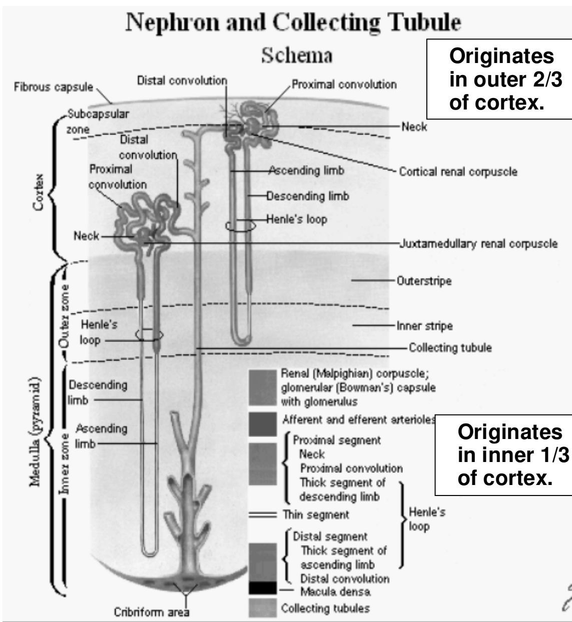


NEPHRON TYPES

- Superficial (cortical) [85 %]
  - Capable of forming dilute urine
- Juxtamedullary [15 %]
  - Capable of forming concentrated (> 300 mOsm/kg) urine

NEPHRON TYPES
Cortical and Juxtamedullary Nephrons

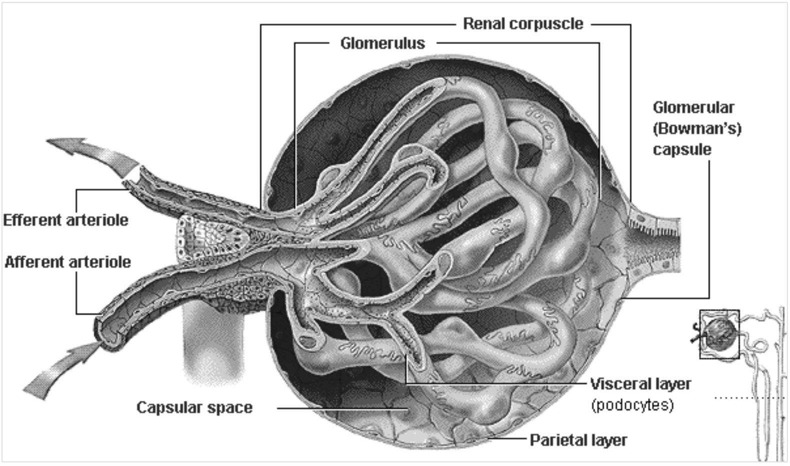
1-2 % Blood Flows Through Juxta Medullary Nephrons



Originates in outer 2/3 of cortex.

Originates in inner 1/3 of cortex.

BOWMAN'S CAPSULE

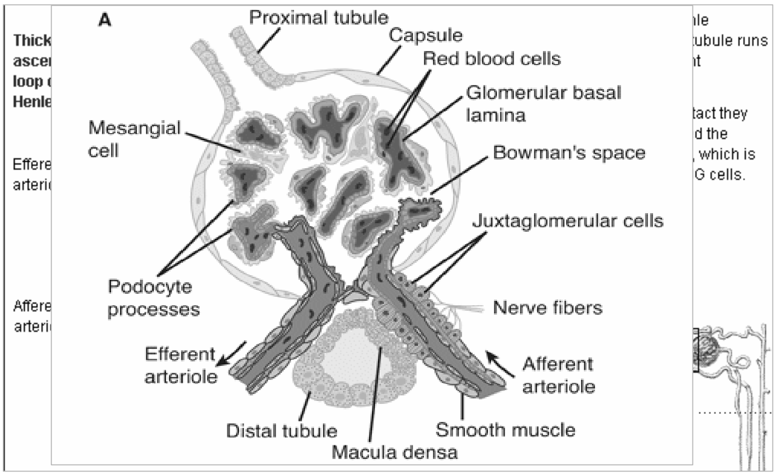


THE RENAL CORPUSCLE COMPRISES FOUR MAIN CELL TYPES

1) Endothelial cells which are fenestrated
2) Visceral epithelial cells (podocytes) which support the delicate glomerular basement membrane by means of foot processes
3) Parietal epithelial cells which cover the Bowman's capsule;
4) Mesangial cells are contractile cells

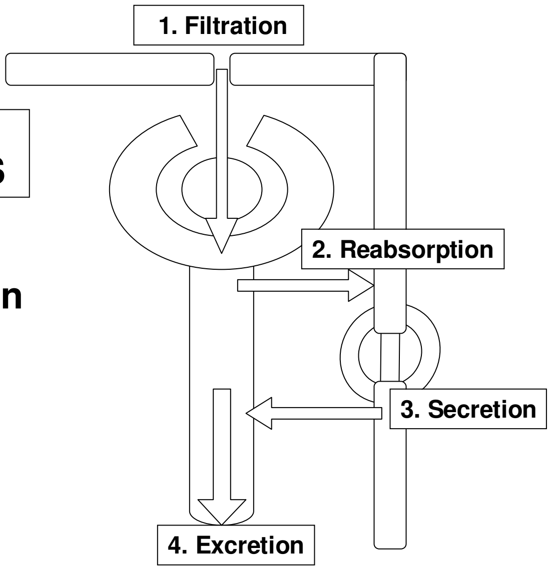
Type I Medullary Interstitial Cells secrete PGE2

JUXTA GLOMERULAR APPARATUS



RENAL PROCESSES

1. Filtration
2. Reabsorption
3. Secretion
4. Excretion



Urinary Excretion Rate = Filtration Rate – Reabsorption Rate + Secretion Rate

RENAL PHYSIOLOGY

GLOMERULAR FILTRATION

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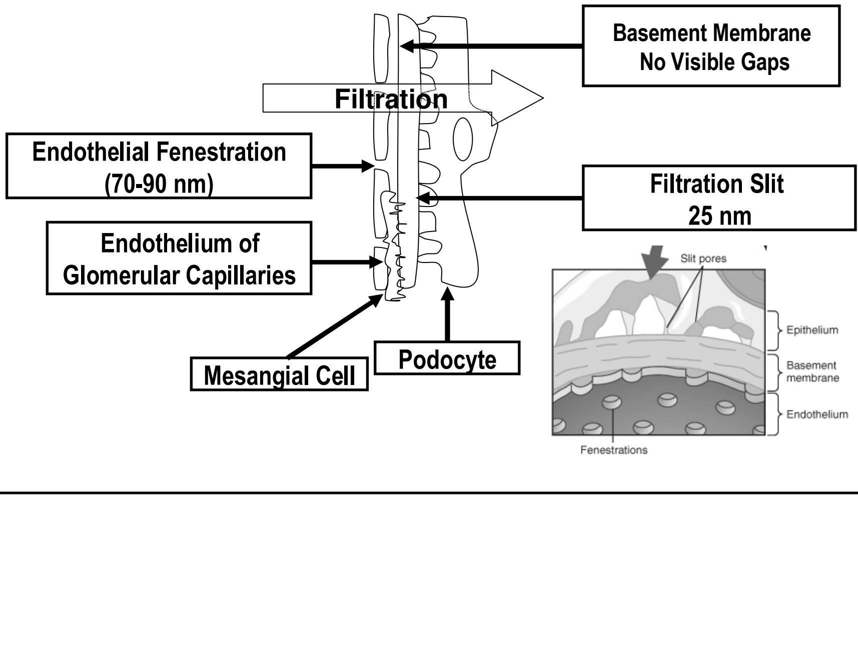
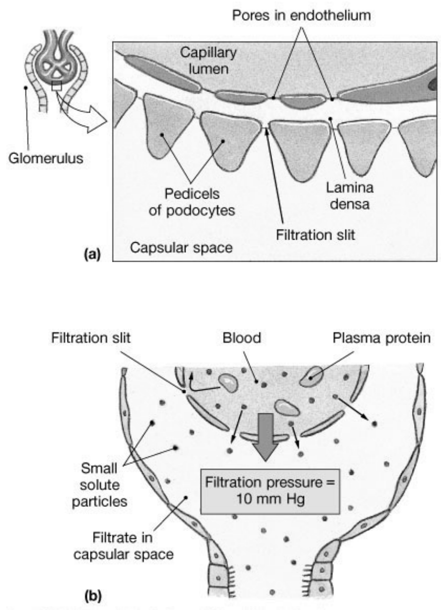
FILTRATION MEMBRANE

4-8 nm size particles can be filtered easily

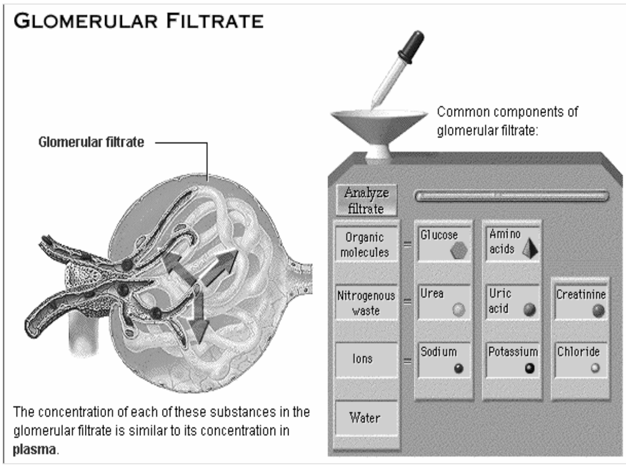




DETERMINANTS OF GFR

Forces Favoring Filtration (mm Hg)	
Glomerular hydrostatic pressure	60
Bowman's capsule colloid osmotic pressure	0
Forces Opposing Filtration (mm Hg)	
Bowman's capsule hydrostatic pressure	18
Glomerular capillary colloid osmotic pressure	32
Net Filtration Pressure = 60 – (18 + 32) = +10 mm Hg	

GLOMERULAR FILTRATE



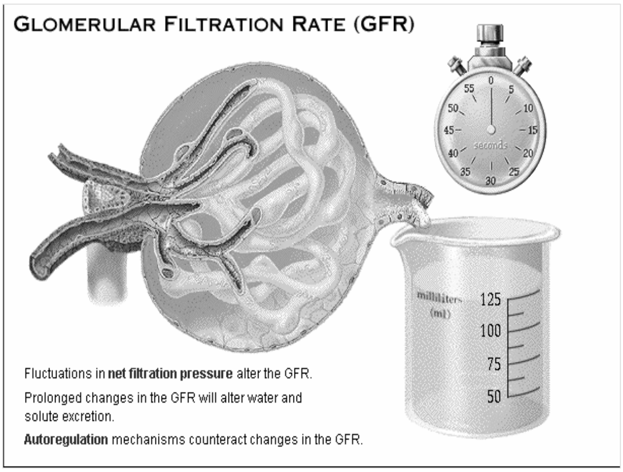
SUBSTANCE	MOLECULAR WEIGHT	MOLECULAR SIZE nm	FILTERABILITY
Water	18	0,15	1.0
Sodium	23	0,1	1.0
Glucose	180	0,33	1.0
Inulin	5,500	1.48	1.0
Myoglobin	17,000	1.88	0.75
Albumin (6 nm)	69,000	3.55	0.005

Filterability of Solutes Is Inversely Related to Their Size

Negatively Charged Large Molecules Are Filtered Less Easily Than Positively Charged Molecules of Equal Molecular Size.

Dextrans are polysaccharides that can be manufactured as neutral molecules or with negative or positive charges.

GLOMERULAR FILTRATION RATE



FILTRATION FRACTION

- **Fraction of renal plasma that becomes Glomerular Filtrate**

Ff = GFR/Renal Plasma Flow

= 125 ml per min/650 ml per min

= 19.2 or approximately 20 %

About 20 per cent of the plasma flowing through the kidney is filtered through the glomerular capillaries

CONTROL OF GFR

$$GFR = Kf \times [(P_G - P_B) - (\pi_G - \pi_B)]$$

GFR = Kf x [(60-18)-(32- 0)]

(1) Hydrostatic pressure inside the glomerular capillaries (glomerular hydrostatic pressure, PG), which promotes filtration
(2) The hydrostatic pressure in bowman's capsule (PB) outside the capillaries, which opposes filtration
(3) The colloid osmotic pressure of the glomerular capillary plasma proteins (πg), which opposes filtration
(4) The colloid osmotic pressure of the proteins in bowman's capsule (πb), which promotes filtration

FILTRATION COEFFICIENT

- Glomerular Filtration Rate in both kidneys per mm Hg Filtration Pressure

Kf = GFR/ Filtration Pressure
= 125 ml per min/ 10 mm Hg
= 12.5 ml/min/mm Hg of filtration Pr

Increased Glomerular Capillary Filtration Coefficient Increases GFR

The Kf is a measure of the product of the Permeability and surface area of the glomerular capillaries. The Kf cannot be measured directly

Kf = GFR / net filtration pressure

increased Kf raises GFR and decreased Kf reduces GFR

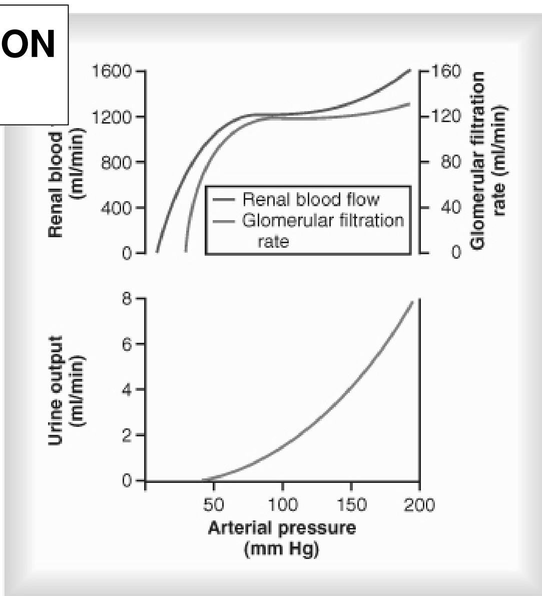
Physical Determinants*	Physiologic/Pathophysiologic Causes
$\downarrow K_f \rightarrow \downarrow$ GFR	Renal disease, diabetes mellitus, hypertension
$\uparrow P_B \rightarrow \downarrow$ GFR	Urinary tract obstruction (e.g., kidney stones)
$\uparrow \pi_G \rightarrow \downarrow$ GFR	↓ Renal blood flow, increased plasma proteins
$\downarrow P_G \rightarrow \downarrow$ GFR	
$\downarrow A_P \rightarrow \downarrow P_G$	↓ Arterial pressure (has only small effect due to autoregulation)
$\downarrow R_E \rightarrow \downarrow P_G$	↓ Angiotensin II (drugs that block angiotensin II formation)
$\uparrow R_A \rightarrow \downarrow P_G$	↑ Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

Kf, glomerular filtration coefficient; PB, Bowman's capsule hydrostatic pressure; πG, glomerular capillary colloid osmotic pressure; PG, glomerular capillary hydrostatic pressure; AP, systemic arterial pressure; RE, efferent arteriolar resistance; RA, afferent arteriolar resistance.

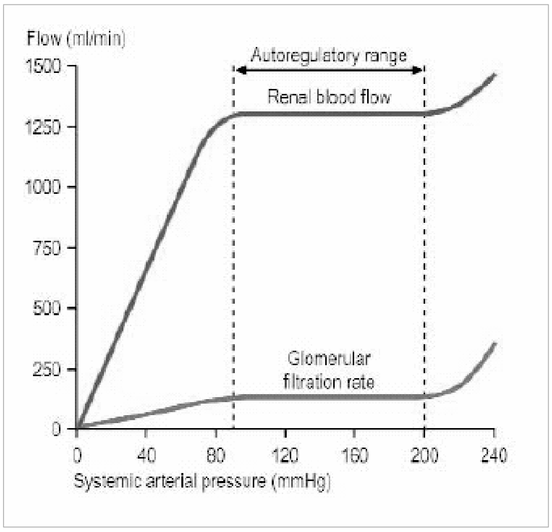
*** Opposite changes in the determinants usually increase GFR.**

AUTOREGULATION OF GFR

- GFR remains constant over a large range of values 75-160
- Autoregulation largely occurs by the regulation of renal vascular resistance



AUTOREGULATION OF RBF AND GFR



GFR REGULATION: *INTRINSIC*

1) **MYOGENIC:**
   - o **Intrinsic property of mesangial (smooth muscle) cells and in afferent arteriole**
   - o **Reflex contraction induced by increased blood pressure reduces filtration**

2) **TUBULOGLOMERULAR FEEDBACK:**
   - o **Flow rate sensed by macula densa (part of juxtaglomerluar apparatus), sends chemical signal to alter afferent arteriole resistance**

GFR REGULATION: *EXTRINSIC*

- **SYMPATHETIC INNERVATION**
  - o **Sympathetic stimulation/ epinephrine released from adrenal medulla cause arteriole vasoconstriction and reduced GFR**
- **ANGIOTENSIN II**
  - o **Produced as a result of renin release from kidney**
  - o **Constricts efferent ↑ arteriole; prevent decrease in GFR**

GFR REGULATION: *EXTRINSIC*

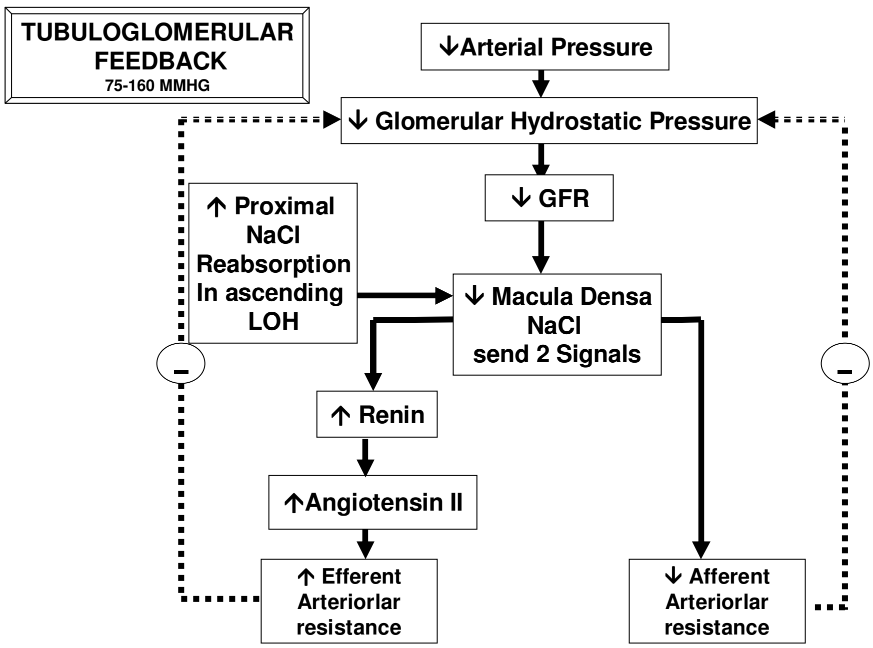
(Cont.)

- NITRIC OXIDE (NO)
  - o Causes arteriolar vasodilation
  - o Elevated NO may result in hyperfiltration of early Diabetes Mellitus
  - o Reduced NO after salt intake may lead to hypertension

GFR REGULATION BY HORMONES OR AUTACOIDS

Hormone or Autacoid	Effect on GFR
Norepinephrine	↓
Epinephrine	↓
Endothelin	↓
Angiotensin II	↔ (prevents ↓)
Endothelial-derived nitric oxide	↑
Prostaglandins	↑

TUBULOGLOMERULAR FEEDBACK



GLOMERULOTUBULAR BALANCE

An increase in GFR causes an increase in the reabsorption of solutes to keep the percentage of the solute reabsorbed constant

When the GFR is high, there is a relatively large increase in the oncotic pressure of the plasma leaving the glomeruli via the efferent arterioles and hence in their capillary branches

Increase in arterial pressure theoretically would increase GFR but we know it exerts much less of an effect on urine volume for two reasons:

(1) renal autoregulation prevents large changes in GFR that would otherwise occur