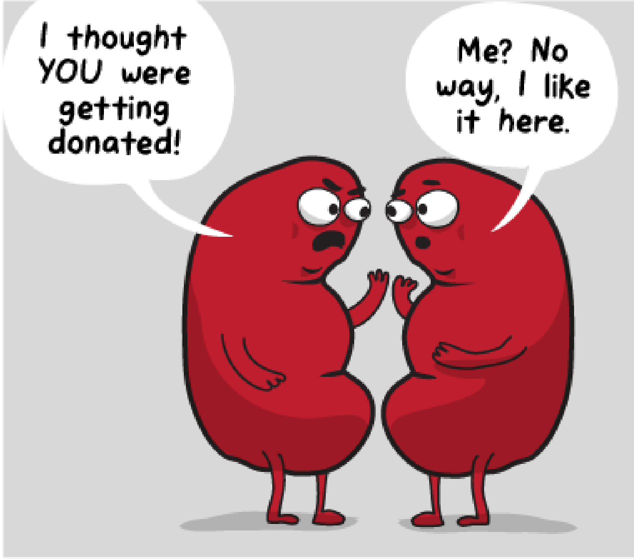

Renal Clearance and Blood Flow Dynamics

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StudyAid Renal Physiology Seminar

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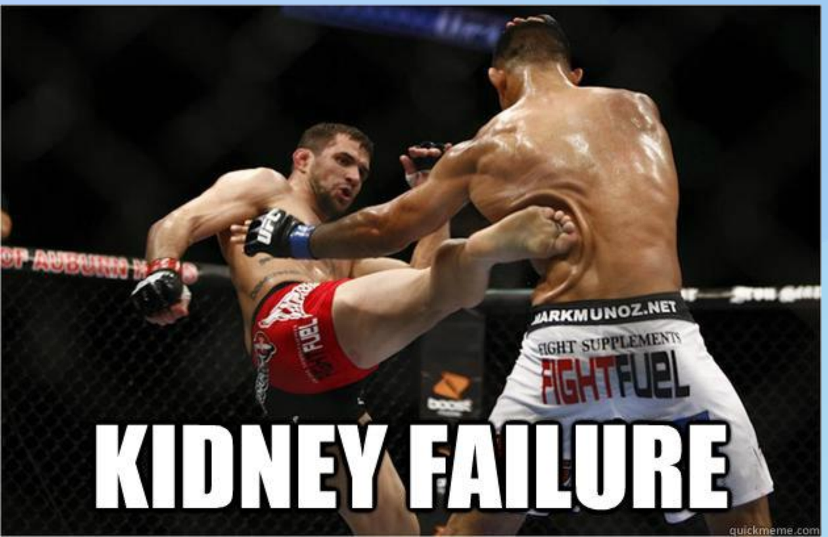

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Memorize – But Understand First

Table 6–4 Commonly Used Equations in Renal Physiology

Name	Equation	Units	Comments
Clearance	$C_x = \frac{[U]_x \dot{V}}{[P]_x}$	mL/min	x is any substance
Clearance ratio	$\text{Clearance ratio} = \frac{C_x}{C_{inulin}}$	None	Also means fractional excretion of x
Renal plasma flow	$RPF = \frac{[U]_{PAH} \dot{V}}{[RA]_{PAH} - [RV]_{PAH}}$	mL/min	
Effective renal plasma flow	$\text{Effective RPF} = \frac{[U]_{PAH} \dot{V}}{[P]_{PAH}}$	mL/min	Underestimates RPF by 10%; equals C_{PAH}
Renal blood flow	$RBF = \frac{RPF}{1 - Hct}$	mL/min	1 minus Hct is fraction of blood volume that is plasma
Glomerular filtration rate	$GFR = \frac{[U]_{inulin} \dot{V}}{[P]_{inulin}}$	mL/min	Equals C_{inulin}
Filtration fraction	$FF = \frac{GFR}{RPF}$	None	
Filtered load	$\text{Filtered load} = GFR \times [P]_x$	mg/min	
Excretion rate	$\text{Excretion} = \dot{V} \times [U]_x$	mg/min	
Reabsorption or secretion rate	Reabsorption or secretion = Filtered load − Excretion	mg/min	If *positive*, net reabsorption If *negative*, net secretion
Free-water clearance	$C_{H_2O} = \dot{V} - C_{osm}$	mL/min	If *positive*, free water is excreted If *negative*, free water is reabsorbed

Renal Clearance

$$C = \frac{[U]_x \times \dot{V}}{[P]_x}$$

where

C = Clearance (mL/min)
$[U]_x$ = Urine concentration of substance X (mg/mL)
$\dot{V}$ = Urine flow rate per minute (mL/min)
$[P]_x$ = Plasma concentration of substance X (mg/mL)

"The rate at which substances are removed from plasma"

High RC = substance intensely filtered & removed by kidneys

- Important concept in physio, pharm, and path
- Can be from 0 to 600 ml/min (physio Renal Plasma Flow)
- Depends on free filtration of substance across glomerular capillaries and reabsorption by nephron

Clearances Used as Standard Parameters

$$C_{PAH} = \text{Effective RPF} = \frac{[U]_{PAH}\dot{V}}{[P]_{PAH}}$$

$$C_{inulin} = \text{GFR} = \frac{[U]_{inulin}\dot{V}}{[P]_{inulin}}$$

- Glucose: RC ~ 0 ml/min since totally filtered & totally reabsorbed
- Albumin: RC ~ 0 ml/min since large molecule, no filtration
- Presence of these substances in urine is always pathological

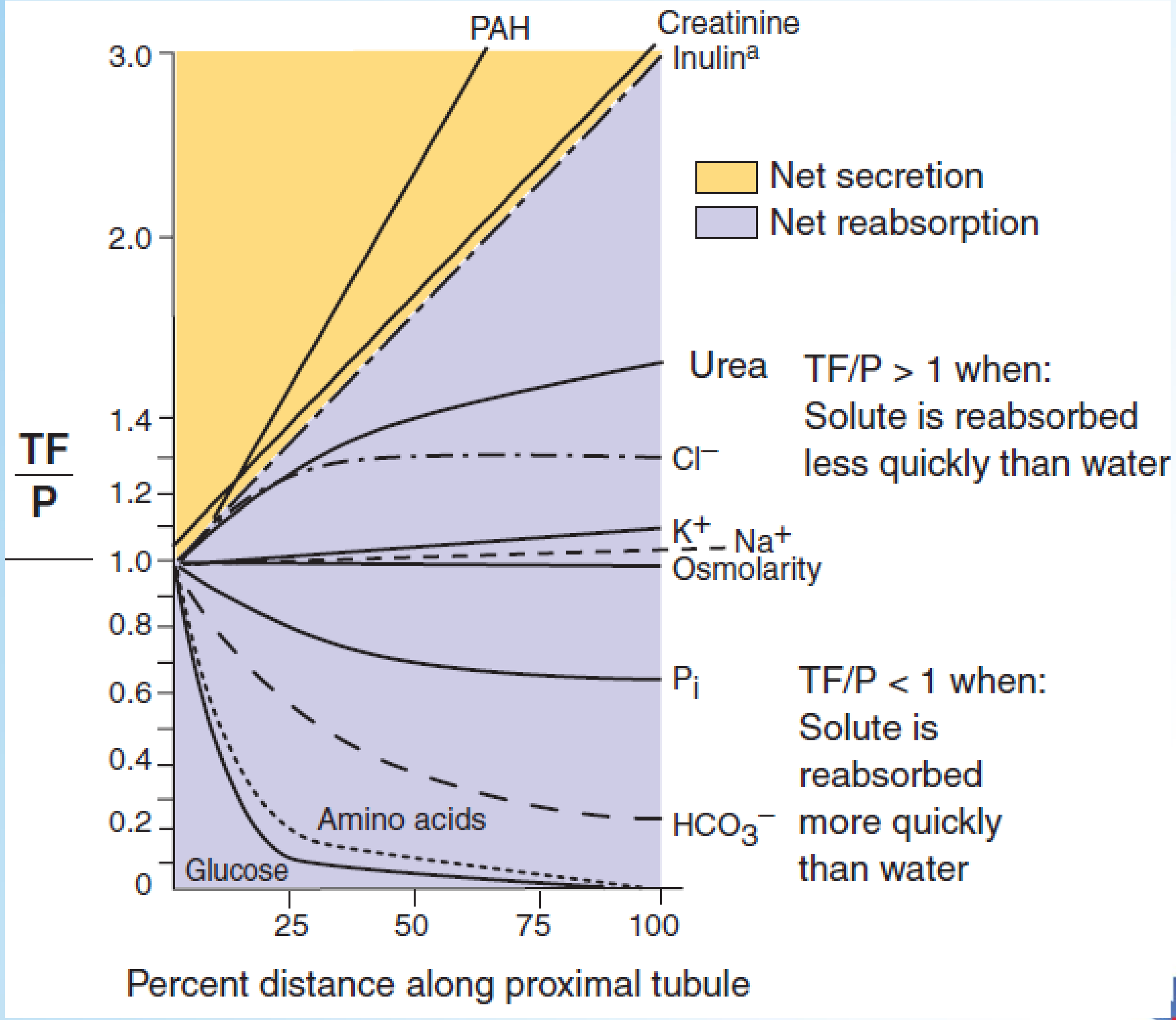
- Inulin: RC = GFR, therefore marker
- Creatinine ~ Inulin ~ GFR
- PAH (*para*-aminohippuric acid):

RC = RPF, gives also RBF

A Closer Look: Inulin & Clearance Ratio

$$\text{Clearance ratio} = \frac{C_x}{C_{inulin}} = \frac{C_x}{GFR}$$

- Clearance ratio: Ratio (%) of substance clearance compared to GFR/inulin standard
- Most substances have ratio less than 1.0, because most are not filtered or filtered & reabsorbed
- Clinical significance: Na clearance ratio (FENa norm: 1-2%)



Bringing it Together: Physological Example

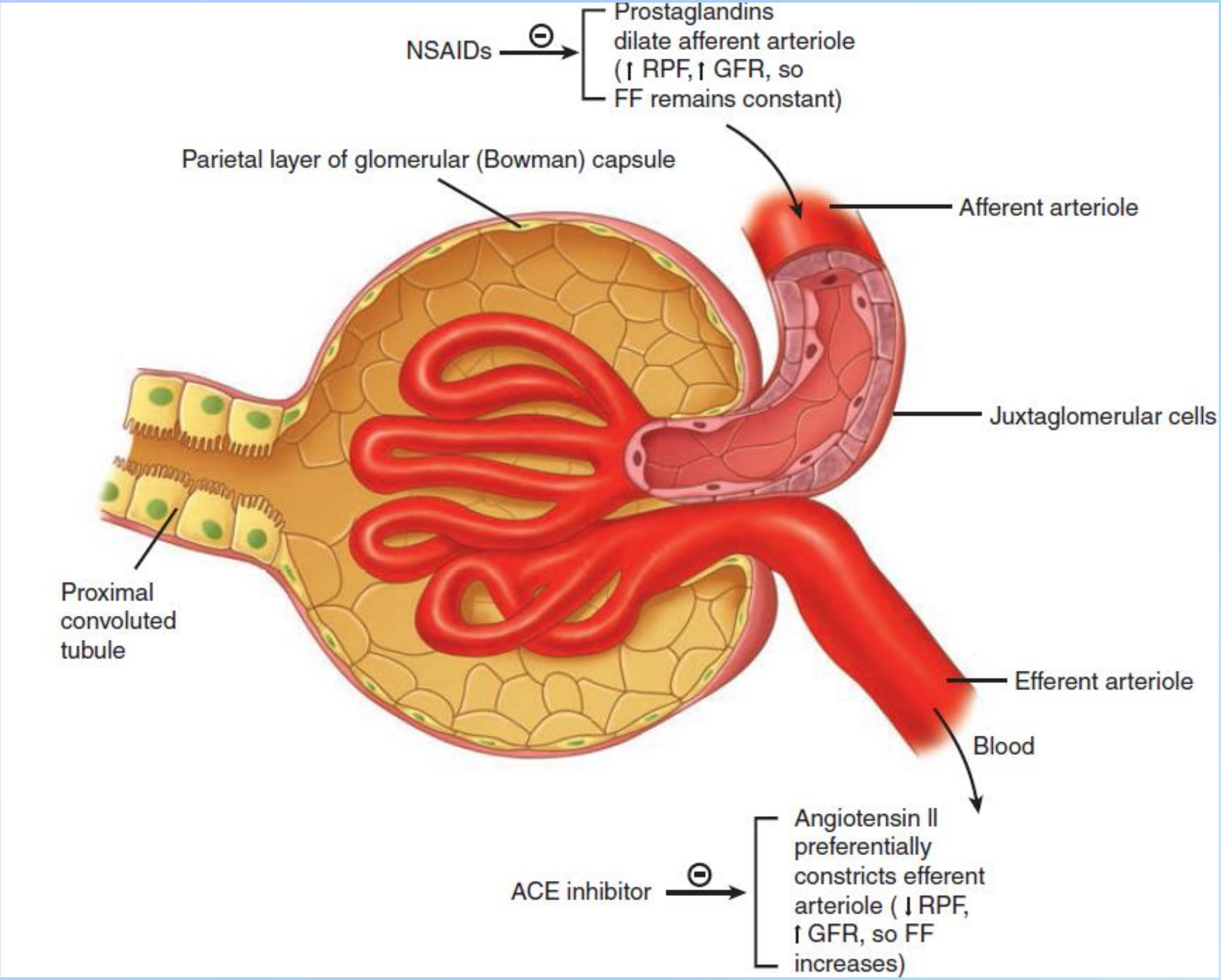
Sodium	Inulin	Creatinine
P_{Na}=150 mEq/L	P_{In}=1 mg/mL	P_{Cr}=
U_{Na}=	U_{In}=150 mg/mL	U_{Cr}=1.25 mg/mL
C_{Na}=5 mL/min	C_{In}=	C_{Cr}=125 mL/min

$$C = \frac{[U]_x \times \dot{V}}{[P]_x}$$

Assume V = 1.44 L/day

<u>Conversion & Units!!</u>

Bonus: What is GFR here?



Kidneys receive 25% of total body blood flow, 1.25 L/min (1800 L/d)!

Renal Blood Flow (RBF)

Regulation

- Highly autoregulated
- Affected by multiple vasoconstrictors/dilators

Dynamic Changes

- Caused by changes in afferent & efferent arteriole contraction
- Balance between RPF and GFR: Ratio expressed as FF

RBF Autoregulation

- Main Idea: RBF will remain constant despite wide variation in systemic blood pressure (80-180 mmHg)
- Two proposed mechanisms
- Tubuloglomerular feedback: Macula densa senses chngs in filtrate and released afferent arteriole vasoconstrictor
- Myogenic mech: Stretch-activated Ca channels in aff art sm musc cause contraction

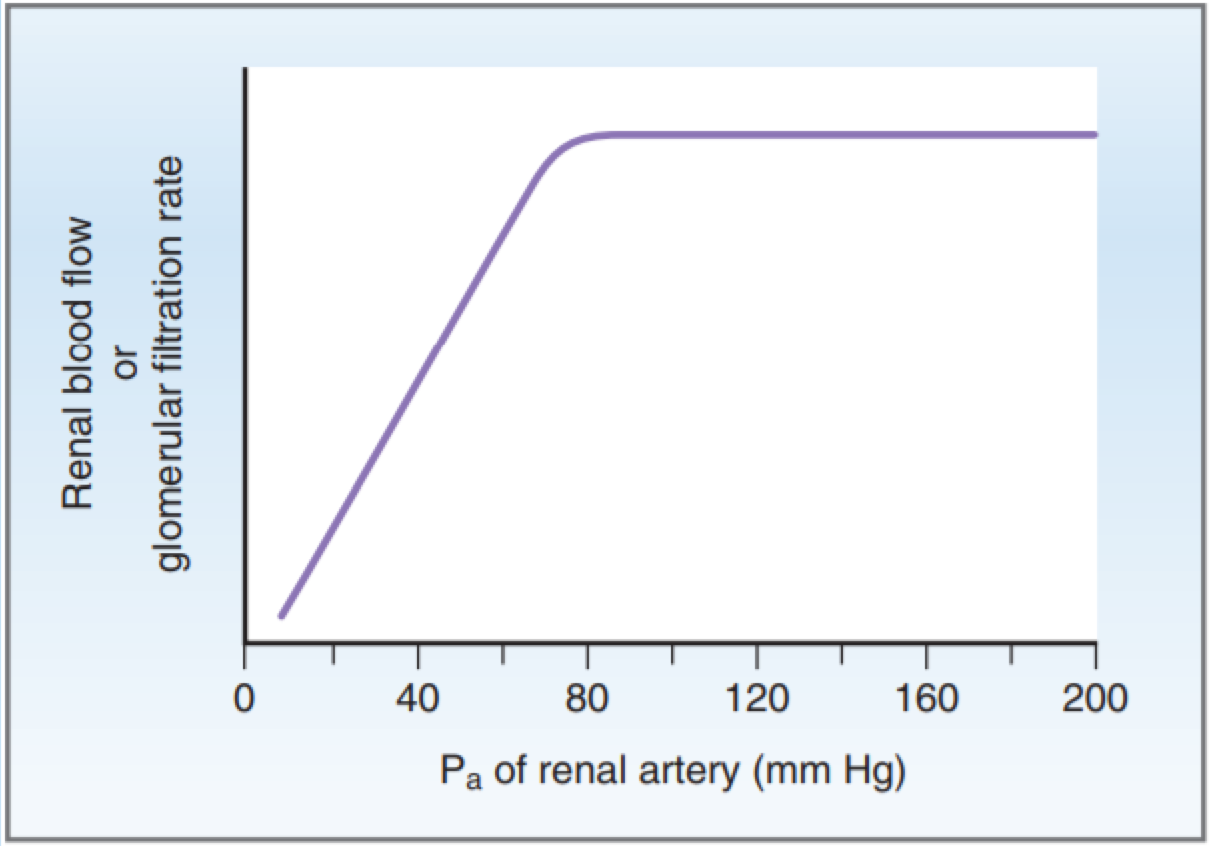
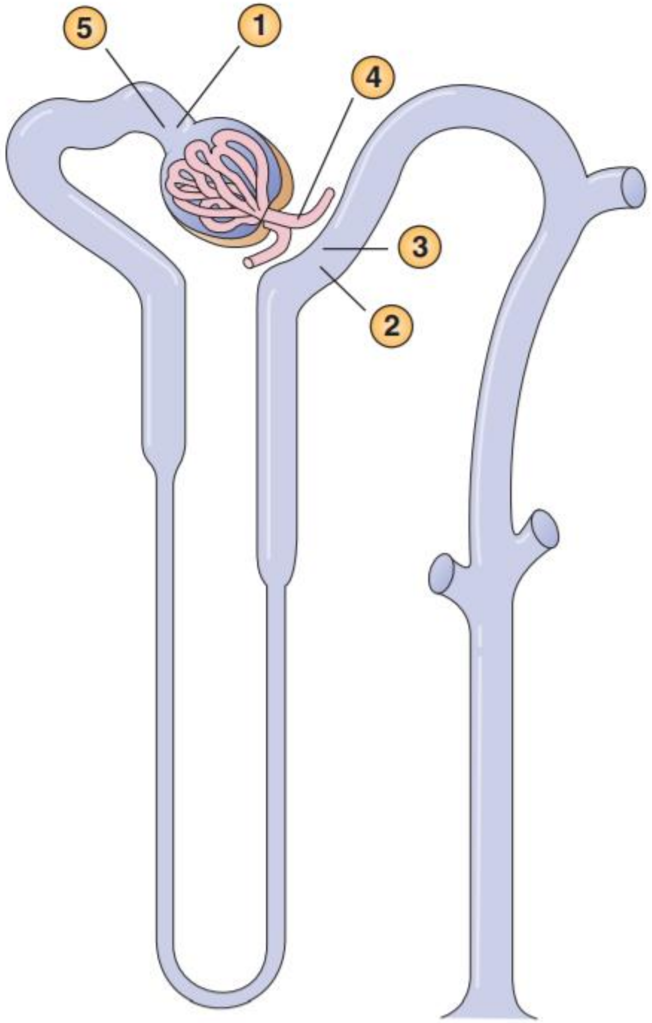


Figure 6–6 Autoregulation of renal blood flow and glomerular filtration rate. P_a, Renal artery pressure.

TUBULOGLOMERULAR FEEDBACK



Step	Event
1	↑ RBF, ↑ GFR
2	↑ Delivery of Na^+ and Cl^- to juxtaglomerular apparatus (sensed by macula densa)
3	Release of vasoactive substance (e.g., adenosine) from macula densa
4	↑ Resistance of afferent arteriole
5	↓ RBF, ↓ GFR

Figure 6–7 Mechanism of tubuloglomerular feedback. GFR, Glomerular filtration rate; RBF, renal blood flow.

Vasoactive Substance Effects

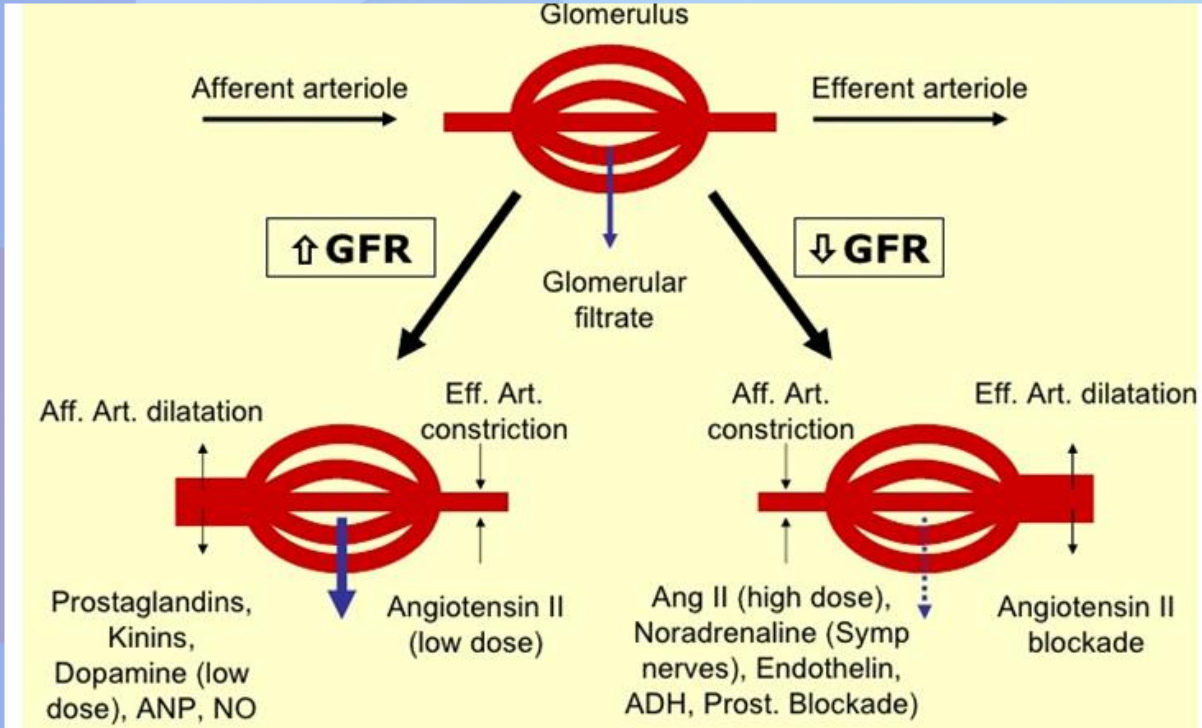


Table 6–5 Renal Vasoconstrictors and Vasodilators

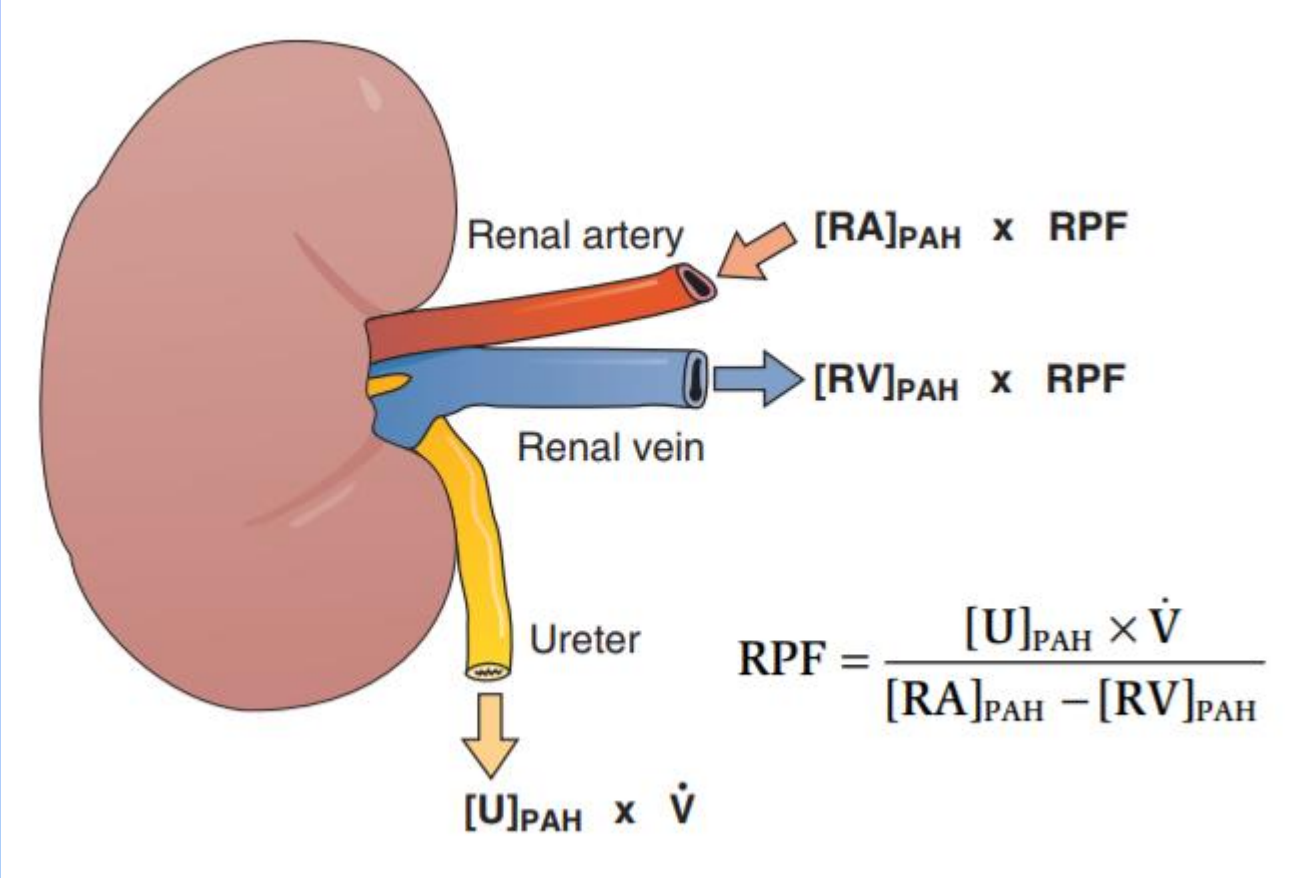
Vasoconstrictors	Vasodilators
Sympathetic nerves (catecholamines)	PGE_2
Angiotensin II	PGI_2
Endothelin	Nitric oxide
	Bradykinin
	Dopamine
	Atrial natriuretic peptide

PG, Prostaglandin.

Changes in glomerular dynamics

Effect	GFR	RPF	FF (GFR/RPF)
Afferent arteriole constriction	↓	↓	—
Efferent arteriole constriction	↑	↓	↑

Calculating RPF



Fick Principle: What goes in (artery) must equal what comes out (vein + urine)

IN		OUT
$[RA]_{PAH} \times RPF$	=	$[RV]_{PAH} \times RPF + [U]_{PAH} \times \dot{V}$

<u>True Renal Plasma Flow</u>

- Impractical to measure
- Assumptions: RVpah ~ 0, RApah = [P]pah

<u>Effective Renal Plasma Flow</u>

- Underestimates true flow by ~10% (extraction ratio is 0.92), but good enough

$$\text{Effective RPF} = \frac{[U]_{PAH} \times \dot{V}}{[P]_{PAH}} = C_{PAH}$$

Filtration Fraction & RBF

$$\text{Filtration fraction} = \frac{\text{GFR}}{\text{RPF}}$$

Filtration Fraction

- Filtration fraction relates GFR with RPF
- FF = % of plasma filtered through capillaries into proximal tubule
- Whatever affects GFR or RPF will affect FF, unless both are affected
- Normally 20%

$$\text{RBF} = \frac{\text{RPF}}{1 - \text{Hct}}$$

RBF = Renal blood flow (mL/min)
RPF = Renal plasma flow (mL/min)
Hct = Hematocrit

Renal Blood Flow

- Actual volume of blood going thru kidney (20-25% of body total of 5 L)
- Blood = Plasma + Hematocrit
- Equation corrects for hematocrit
- Normally 1 – 1.25 L/min

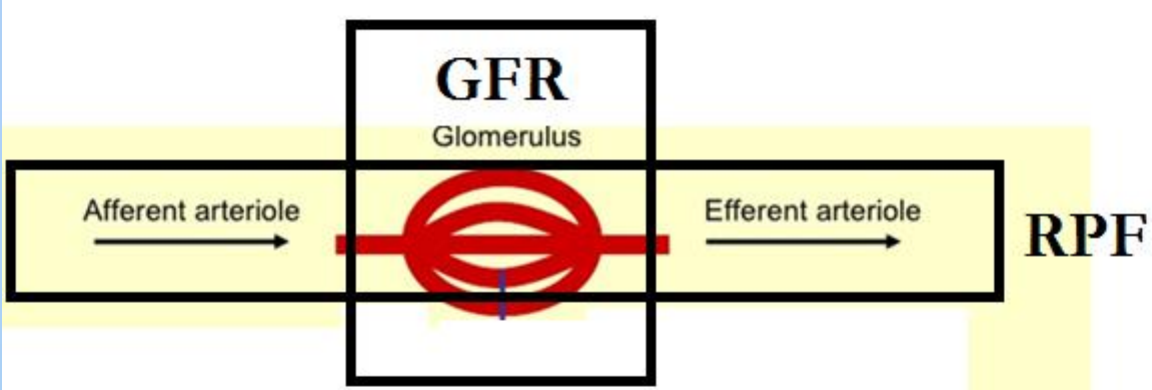
Bringing it Together: Physological Example

Parameter	Value
renal blood flow	RBF=
hematocrit	HCT=40%
glomerular filtration rate	GFR=120 ml/min
renal plasma flow	RPF=
filtration fraction	FF=20%
urine flow rate	V=1 mL/min

$$\text{Filtration fraction} = \frac{\text{GFR}}{\text{RPF}}$$

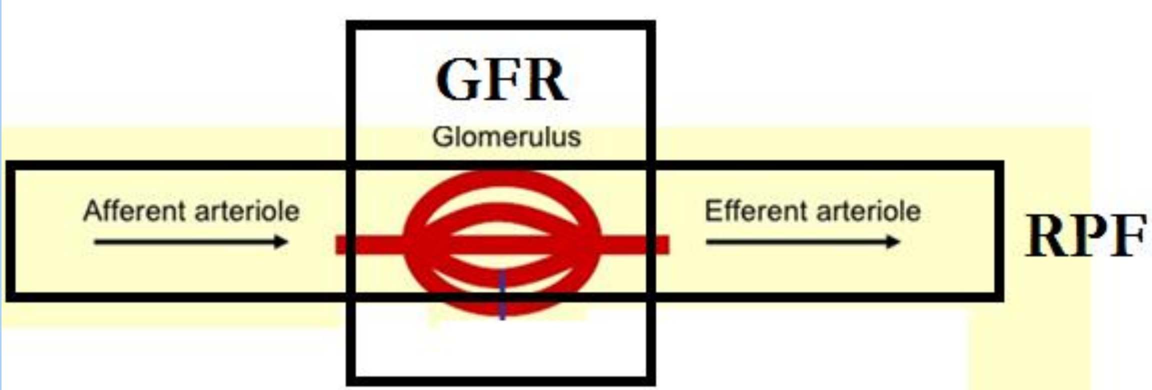
$$\text{RBF} = \frac{\text{RPF}}{1 - \text{Hct}}$$

Dynamic Effects



	GFR	RPF	FF (GFR/RPF)
Constriction of afferent arteriole			
Constriction of efferent arteriole			
Dilation of afferent arteriole			
Dilation of efferent arteriole			
Increase in serum protein			
Ureter stone obstruction			
ACE inhibitors (Vasodilate efferent)			
NSAIDs (Vasoconstrict afferent)			

Dynamic Effects



	GFR	RPF	FF (GFR/RPF)
Constriction of afferent arteriole	↓	↓	NO CHANGE
Constriction of efferent arteriole	↑	↓	↑
Dilation of afferent arteriole	↑	↑	NO CHANGE
Dilation of efferent arteriole	↓	↑	↓
Increase in serum protein	↓	NO CHG	↓
Ureter stone obstruction	↓	NO CHG	↓
ACE inhibitors (Vasodilate efferent)	↓	↑	↓
NSAIDs (Vasoconstrict afferent)	↓	↓	NO CHANGE