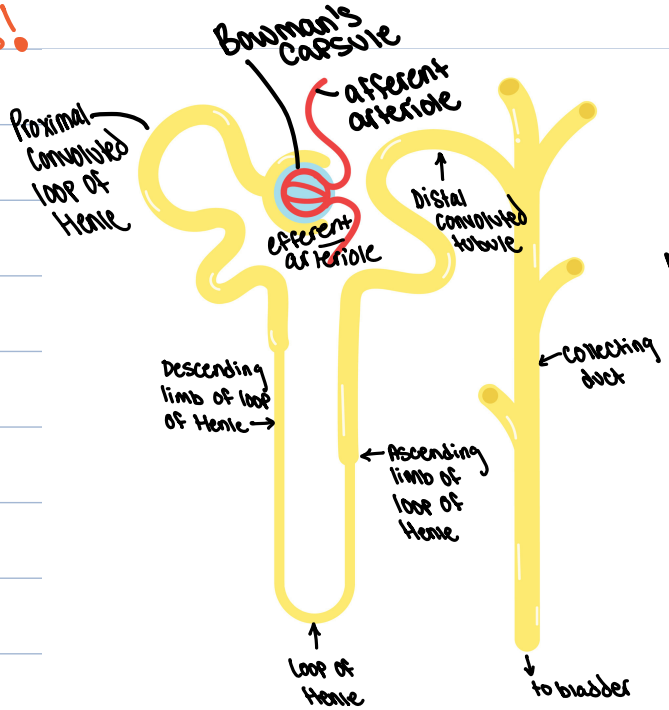
Renal Circulation

Aorta → Renal Artery → Segmental arteries → Interlobar arteries → Arcuate arteries → Afferent arteriole → Glomerulus → efferent arteriole → Peritubular capillaries → vasa recta → Interlobular vein → Arcuate vein → Interlobar vein → Renal vein → Inferior vena cava

Unique things about the glomerular capillary bed

- there is an afferent and efferent arteriole
- two capillary beds in series (peritubular capillary network and vasa recta)

Nephrons!



* 99% of what is filtered is reabsorbed

Location

Nephrons can be cortical or juxtamedullary

- Short nephron loops
  - * most nephrons near peripheral edge of cortex
- Long nephron loops
  - near corticomedullary boarder

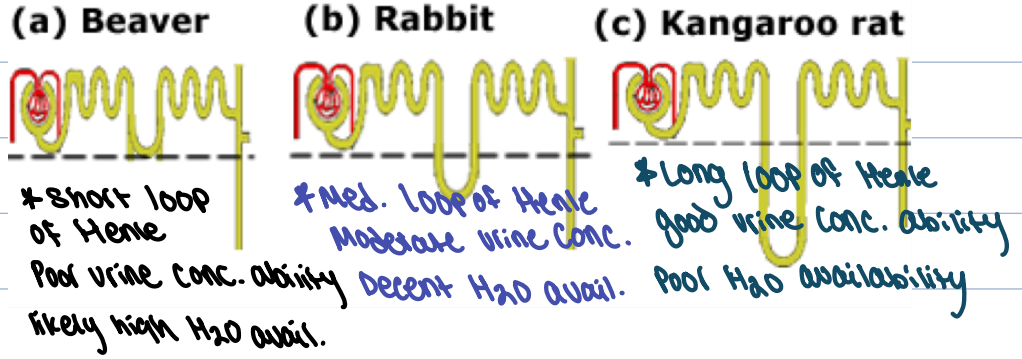
Location determines urine-concentrating ability

↓

more juxtamedullary nephrons, longer loop of Henle

↓

better urine-concentrating ability, likely lower water availability



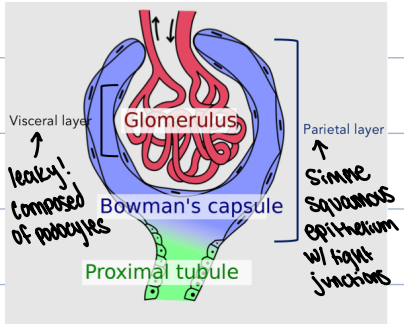
(a) Beaver
- * short loop of Henle
- Poor urine conc. ability
- likely high H_2O avail.

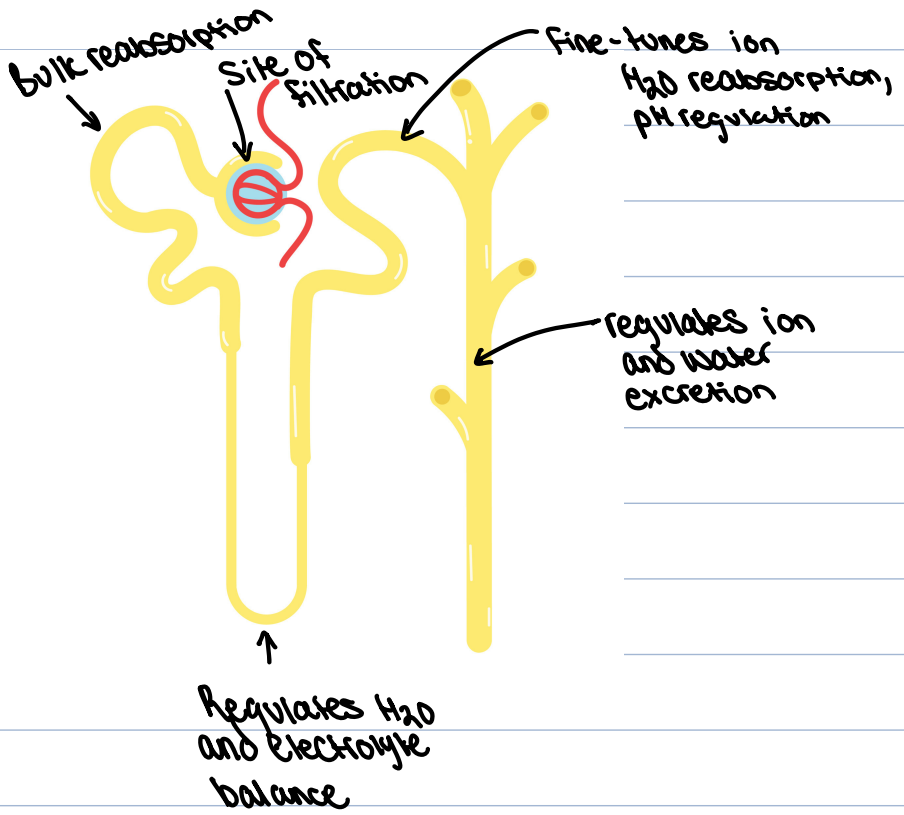
(b) Rabbit
- * Med. loop of Henle
- Moderate urine conc.
- Decent H_2O avail.

(c) Kangaroo rat
- * Long loop of Henle
- good urine conc. ability
- Poor H_2O availability

Urine Formation

Glomerular Filtration → Tubular Reabsorption → Tubular Secretion





Mesangial cells
↳ regulate filtrate flow through glomerulus and phagocytosis

Filtration Barriers

Fenestrated endothelium: glossy filter everything but cells and very large macromolecules

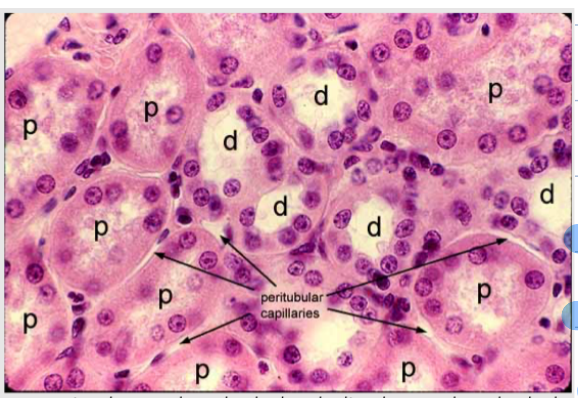
Basement membrane: protein-rich ECM, restricts based on size and charge

Epithelium / Podocytes: negatively-charged filtration slits, small physical filter

Proximal Convoluted Tubule

- Simple cuboidal epithelium
- Extensive brush border
- Metabolically very active
- Eosinophilic
- Reabsorbs most of filtrate

* 65%. H_2O, Na^+, K^+, Cl^-
100%. Glucose, amino acids
85-90%. bicarbonates



p: proximal convoluted tubule; d: distal convoluted tubule

Distal Convoluted Tubule

*Regulates blood pressure

- Senses plasma pressure and NaCl levels

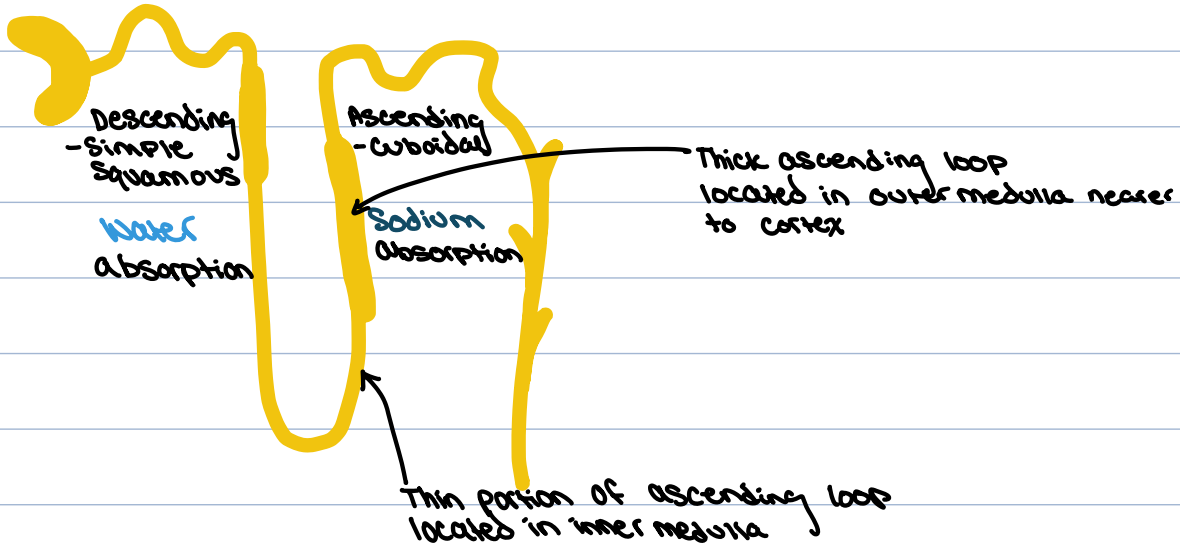
3 cell types

Macula densa cells - sense NaCl levels and flow rate

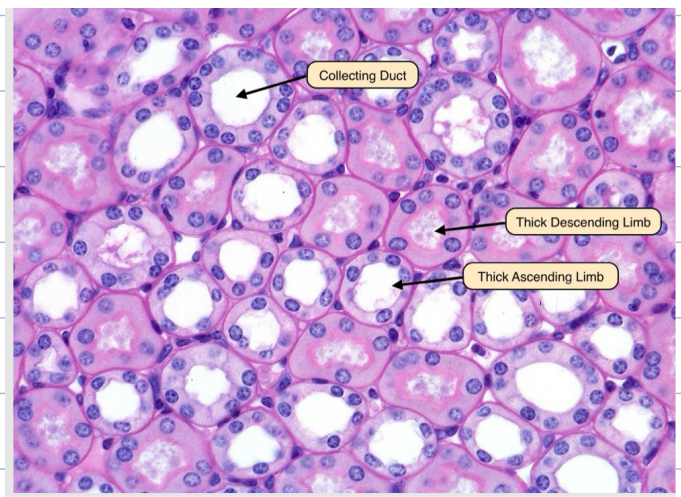
Juxtaglomerular cells - Secrete renin (Sympathetic innervation)

Extraglomerular granular cells

Loop of Henle

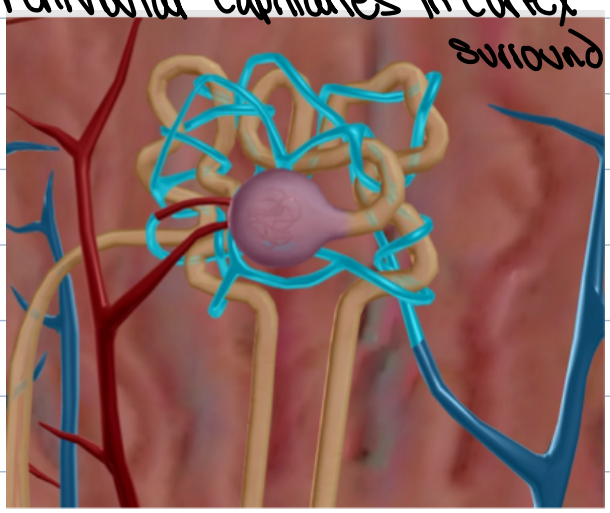


Collecting Ducts



Peritubular Capillaries in Cortex

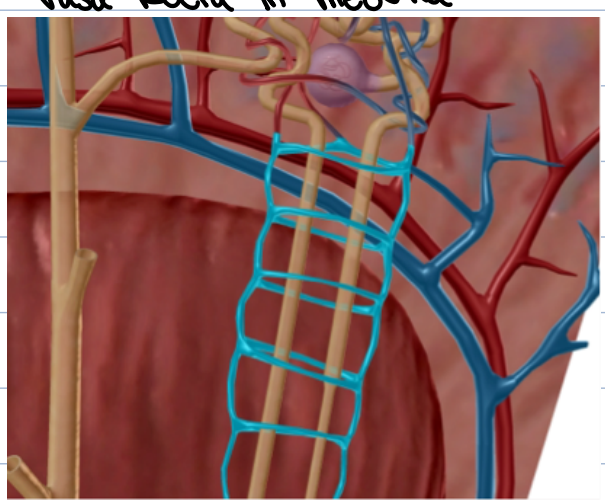
surround PCT and DCT



High blood flow

Important for reabsorbing substances

Vasa Recta in medulla



Surrounds descending + ascending LOH

Slower blood flow enables creation and maintenance of gradients necessary for retaining water

Water, fluid distribution, osmolarity osmolality, and tonicity

60% of weight is water

Total body water distribution

⅔ Intracellular
- Water inside cells

⅓ Extracellular
- Interstitial, plasma and transcellular fluid

*Each compartment has differing ionic composition yet near-equivalent ionic strength

K^+ = major intracellular cation, Na^+ = major extracellular (interstitial) cation

Plasma osmolarity ≈ 300mOsm/L

Iso-osmotic: 270-330 mOsm/L

Hyper-osmotic: >330 mOsm/L

Hypo-osmotic: <270 mOsm/L

Changes >10% define hyper- or hypo- state

*Osmotic pressure depends on number not size or mass of molecules

Effective osmolality: Tonicity

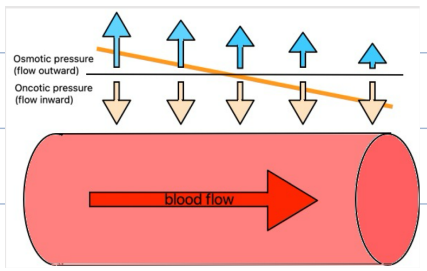
Effective osmoles cannot freely cross a membrane, therefore they exert an osmotic effect
- Na^+, Cl^-, proteins, glucose
- → Water flux from low to high solute concentration

Ineffective osmoles can freely cross a membrane, therefore they do not exert an osmotic effect
- Urea, ethanol, lipid-soluble compounds
- → No net water movement

A fluid's tonicity determines how much H_2O stays in the extracellular space

Osmotic (Hydrostatic) Pressure: "Pushing Pressure" - pushes water and solutes out of the capillaries and into the interstitial space (glomerulus)

Oncotic (colloid) Pressure: "Pulling Pressure" - pulls water back into the capillaries



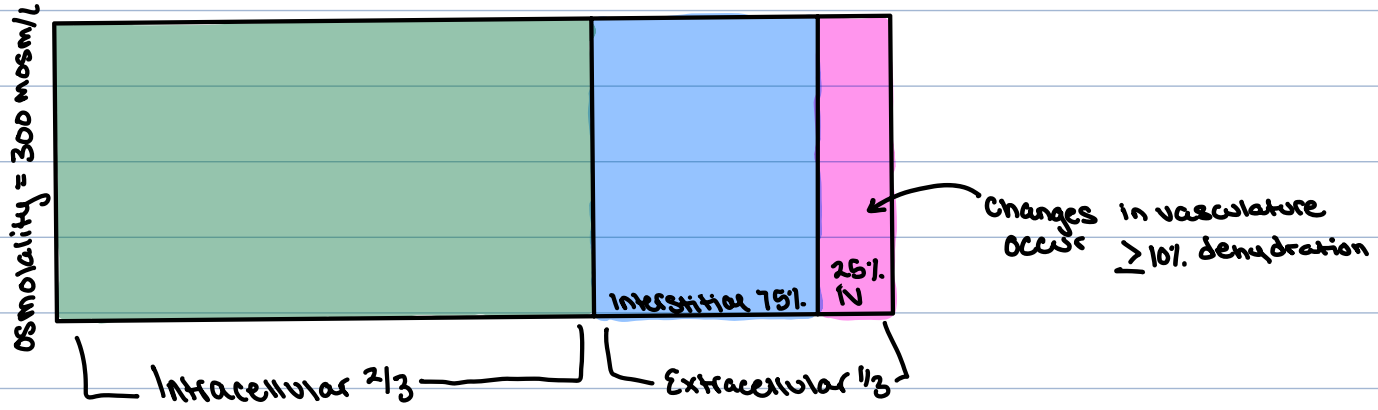
*@ arterial end osmotic pressure > oncotic pressure
- → Net outward movement

*@ venus end, oncotic > osmotic → Net inward movement

Body Fluid movement

Osmolarity = # molecules / L plasma

Total Body water ~60% body weight



Blood volume = Red cell volume + plasma water

Clinical Examples

Isotonic loss → Comes out of extracellular volume → Interstitial and IV

Hypotonic loss → Comes out of interstitial space

Hypertonic loss → Comes out of interstitial space

Hyperglycemia → increases extracellular volume, can make patient hyponatremic

diabetic patients can compensate so the hyponatremia may be artifactual

Azotemia (increased BUN) → hyperosmolar in all compartments → no fluid movement

Isotonic crystalloid infusion (1L 0.9% NaCl) → increases interstitial fluid volume

5% Dextrose (hyperosmotic, hypotonic) → increases intra- 2/3 and extra- 1/3 cellular fluid used for treating hyperosmolality

Assessment of Volumes

Intravascular = Perfusion parameters on physical exam

Mentation, MM color, CRT, Pulse Rate + Quality, Core vs extremity temp

Interstitial = Hydration parameters on physical exam

Skin turgor, dry MM, decreased tear film

Intracellular = measure osmolality

Dehydration is a loss of extracellular fluid volume

* Clinically detectable @ 5% dehydration ↓BW by 5%

Severity	% Dehydration	Clinical Signs	% ECFV Decreased
Mild	5%	Slight loss skin turgor	25%
Mild to Moderate	8%	Obvious loss skin turgor, dry gums	40%
Moderate to Severe	10%	Large loss skin turgor, start to see CV changes	50%
Severe	≥12%	Above + signs of hypovolemic Shock	≥60%

* Vascular changes appear ~10% dehydration

* Hypovolemic Shock @ >12%

Further breakdown of Clinical cases

Isotonic Fluid examples: Saline (0.9% NaCl), LRS, 5% dextrose in H_2O

Equal Loss of Water + Sodium ⟶ Vomiting, diarrhea, sweating, burns, intrinsic kidney disease, hyperglycemia, hypoaldosteronism

* Fluid is drawn completely from the extracellular fluid

- Volume of fluid loss = volume deficit

Dextrose 5% is iso-osmotic but hypotonic so it distributes into all water departments (w/ insulin it is metabolized to water) good for tx hyperosmolality situation

Hypotonic fluid examples: Water, 2.5% dextrose, 0.45% NaCl

More sodium than water loss → high sweat or gastrointestinal water loss

Can also occur when electrolyte deficits are treated w/ water replacement only

- Fluid is drawn from the interstitial space

hypotonic loss is the most common way you become dehydrated

* Osmotic shift of fluid from the intracellular to the extracellular space because H_2O loss causes ECF tonicity to rise. Fluid will then shift from intravascular to interstitial to equilibrate osmolality.

Hypertonic fluid examples: Saline solutions >0.9%, Dextrose solutions >10%.

Dextrose 5% in 0.9% NaCl, Dextrose 5% in 0.45% NaCl, Dextrose 5% in LRS

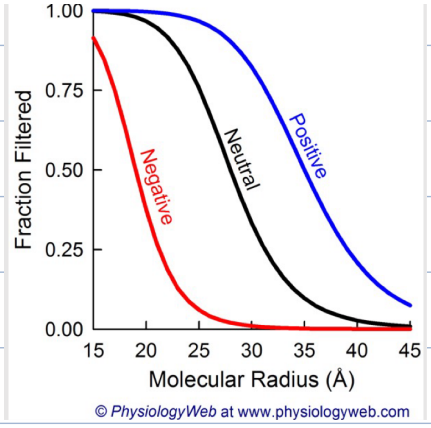
More water than sodium loss → Sweating, Fever, Osmotic diuresis (→ glycosuria), diuretic drugs, diabetes insipidus, inadequate intake

- Comes out of interstitial space

The Glomerulus

Path for filtering: Fenestrations in glomerular capillary endothelial layer
↓
Basement membrane
↓
Slit-diaphragms between podocyte foot processes

Effective pore: 8.5nm diameter w/ negative charge (prevents movement of large molecules or protein-bound solutes)



Glomerular filtration rate is based on

- Hydraulic permeability
- SA of glomerular pores
- Net filtration pressure

} constants in healthy animals so we use K_f

$GFR = K_f \times NFP$

What forces favor filtration?

Hydrostatic pressure in capillary (P_{GC}) "pushing"

Oncotic pressure in Bowman's capsule (π_{BC}) "pulling"

What forces oppose filtration?

Oncotic pressure in the capillary (π_{GC}) "pulling"

Hydrostatic pressure in Bowman's capsule (P_{BC}) "pushing"

If NFP > 0 filtration occurs

If NFP < 0 reabsorption occurs

Renal clearance: volume of plasma that is completely cleared of a substance in a unit of time

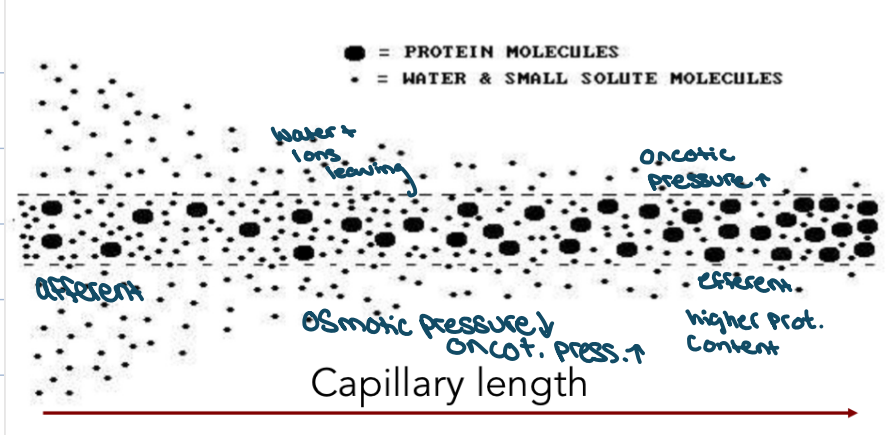
C_x = GFR (only filtered)

C_x > GFR (filtered and secreted)

C_x < GFR (reabsorbed)

Net filtration pressure changes across the length of the capillary

↓ It decreases



"Pulling" pressure increases as you move towards the efferent end of the capillary

Filtration Fraction: How much fluid reaching the kidneys is filtered into renal tubules

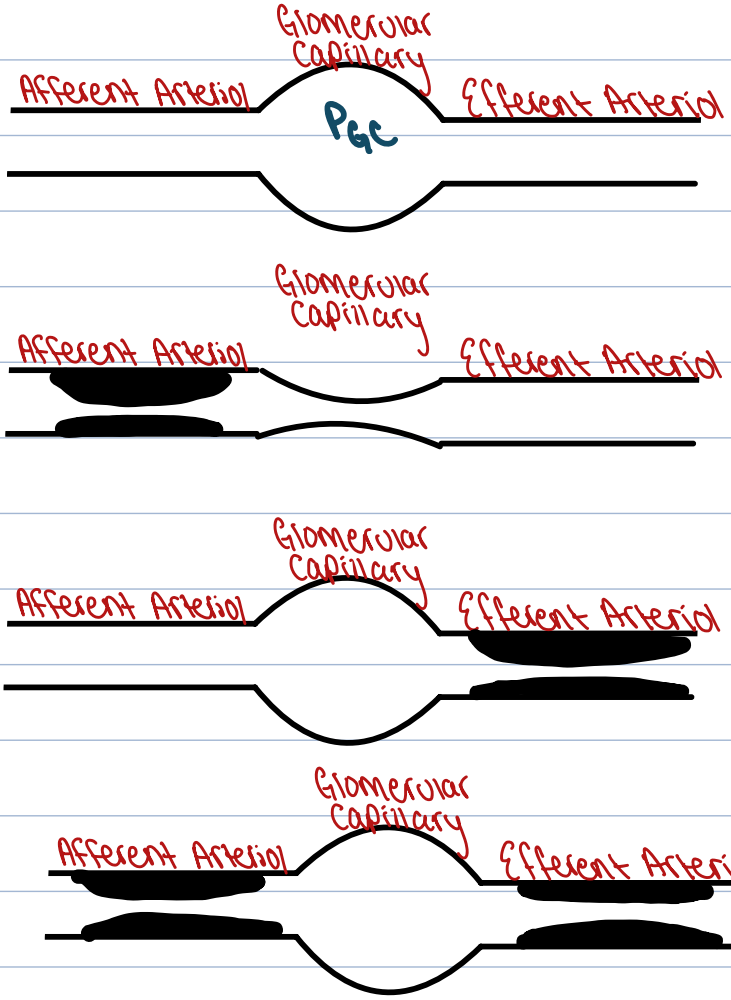
FF = GFR / Renal plasma flow
RPF = Renal blood flow x (1 - HCT)
Normal FF ~ 0.2

* Measures kidney efficiency + function Normally ~20%.

Typically ↑RBF ↓FF (less contact time)
↓RBF ↑FF (more contact time)

Renal plasma flow depends on capillary resistance

* The sites of blood flow resistance in the kidney are primarily the afferent and efferent arterioles



↓ Because less blood comes in

↓RBF ↓P_{GC} ↓GFR

↓ Bottle-neck
↓ Blood spends longer in the glomer. capillary

↓RBF ↑P_{GC} ↑GFR

not much change, slight decrease?

RBF↓↓ P_{GC}↓ GFR↓

Determinants of Renal Blood Flow

Intrinsic (autoregulatory)

Extrinsic

Help maintain net filtration pressure

Intrinsic regulation of GFR and RBF

* occurs primarily @ the afferent arteriole

2 mechanisms of intrinsic regulation

Myogenic

- Smooth muscle walls of afferent arterioles respond to changes in blood pressure
- ↑ Hydrostatic pressure causes arterioles to stretch
- Entry of extracellular calcium causes smooth muscle contraction → vasoconstriction

* Maintains steady bloodflow by causing arteriolar smooth muscle constriction when blood pressure increases and causing relaxation when blood pressure decreases

Tubuloglomerular feedback

Involves communication originating in the Juxtaglomerular Apparatus

Involves paracrine signaling @ JGA to cause vasoconstriction or vasodilation to maintain a steady rate of blood flow

Neural Hormonal Reg. of RBF

Increase Arteriolar Resistance ↓RBF

Adrenaline → binds to α_1 adrenergic receptors on afferent > efferent

Angiotensin II

Renin from JGA cells becomes Angiotensin I in response to low BP

Converted to angiotensin II by ACE in lungs

Binds to efferent smooth muscle to maintain GFR, later afferent to reduce GFR

You can measure GFR with inulin or creatinine

or

Para-aminohippurate ↑ its clearance = RPF

Pathology of Glomerular Disease