Objectives:

1. **To understand the GFR**
2. **To understand the main functions of the renal tubules and the collecting duct.**

Glomerular Filtration

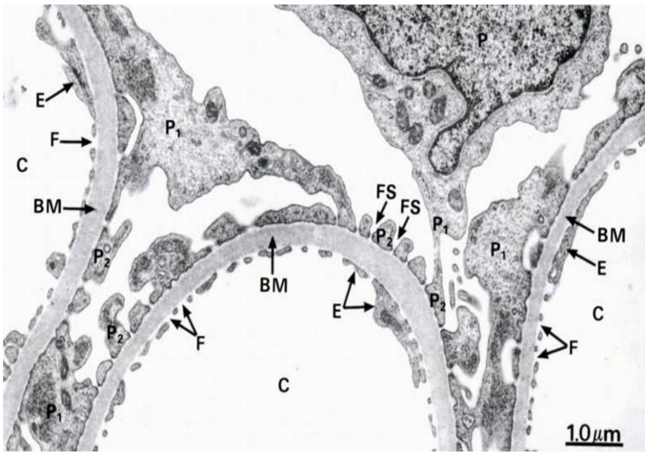
Role: formation of the initial fluid entering the nephron

Composition of Glomerular Filtrate

- ultrafiltrate of plasma, due to size-selective filtration: nonselectively permeable to small particles but not very permeable to larger particles, such as blood cells and plasma proteins
- In other words, all small particles (inorganic ions, glucose, amino acids, etc.) enter Boman's space at exactly the same concentration as in blood plasma

Filtration barriers

- a. capillary endothelium: fenestrated capillaries with relatively large pore size (1000 A); not a major barrier to filtration
- b. basement membrane: negatively charged meshwork of glycoproteins and collagen
- c. epithelial cells with foot processes (podocytes) separated by slits (240 A wide)
- Note: the basement membrane and podocytes are the major filtration barrier, passing particles depending on size and charge

- 

Effect of particle charge:

- because of the negative charge on the membrane pores, the size cutoff is smaller for negative particles (such as plasma proteins) than for neutral or positive particles.
- In kidney inflammation, the membrane charge is reduced or lost, permitting plasma proteins to enter the tubule in larger amounts

Glomerular filtration

- Mechanism: Bulk flow
- Direction of movement : From glomerular capillaries to capsule space
- Driving force: Pressure gradient (net filtration pressure, NFP)
- **Types of pressure:**

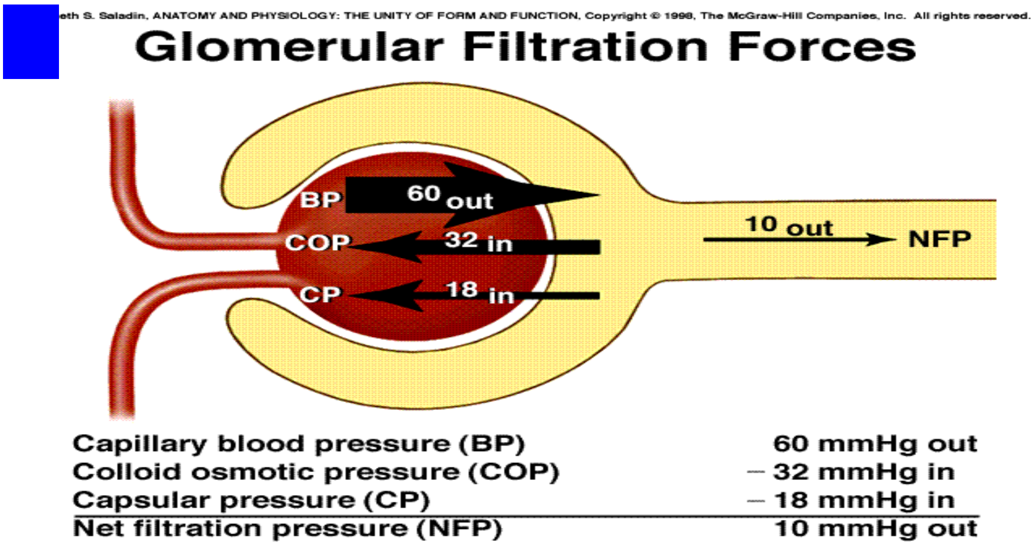
Favoring Force: Capillary Blood Pressure (BP)(hydrostatic pressure),

Opposing Force: Blood colloid osmotic pressure(COP) and Capsule Pressure (CP)

Glomerular Filtration Rate (GFR)

- 1. Normal value: 120-125 ml/min (for 70 kg human) = 180L/day
- This represents about 20% of the RPF (renal plasma flow). The very high normal GFR is due to the very high permeability of the glomerular barrier

- 2. Measurement: *inulin or creatinine clearance*



Regulation of renal blood flow and GFR

RBF and GFR is regulated using three mechanisms

1. Renal Autoregulation

2. Neural regulation

3. Hormonal regulation

All three mechanism adjust renal blood pressure and resulting blood flow

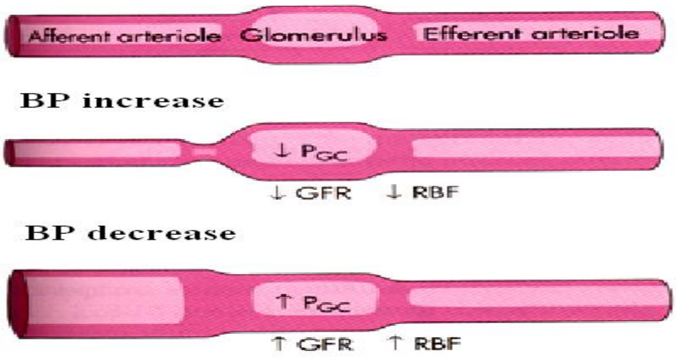
Renal Autoregulation of GFR

- Ability of kidney to maintain a constant GFR under systemic changes.
  - Achieved through effects of locally produced chemicals on the afferent arterioles.
- When MAP (main arterial aterial pressre) drops to 70 mm Hg, afferent arteriole dilates.
- When MAP increases, vasoconstriction of afferent arterioles occurs.
- Tubuloglomerular feedback:
  - upon increased fluid flow or NaCl transport at the macula densa (MD), local vasoconstrictors are released which increase the resistance to blood flow at the afferent arteriole

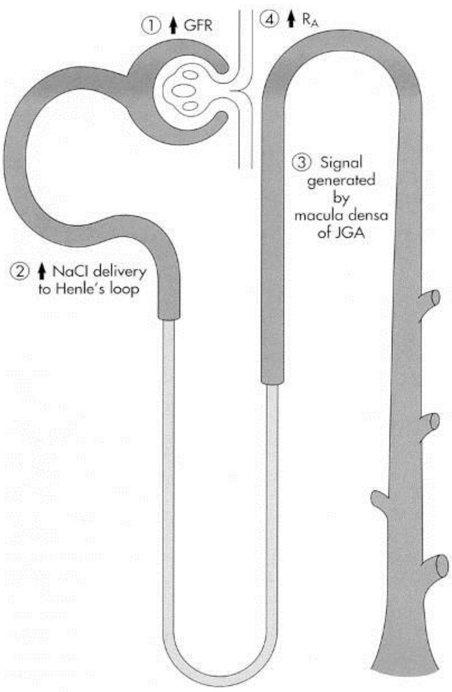
1- Renal autoregulation:

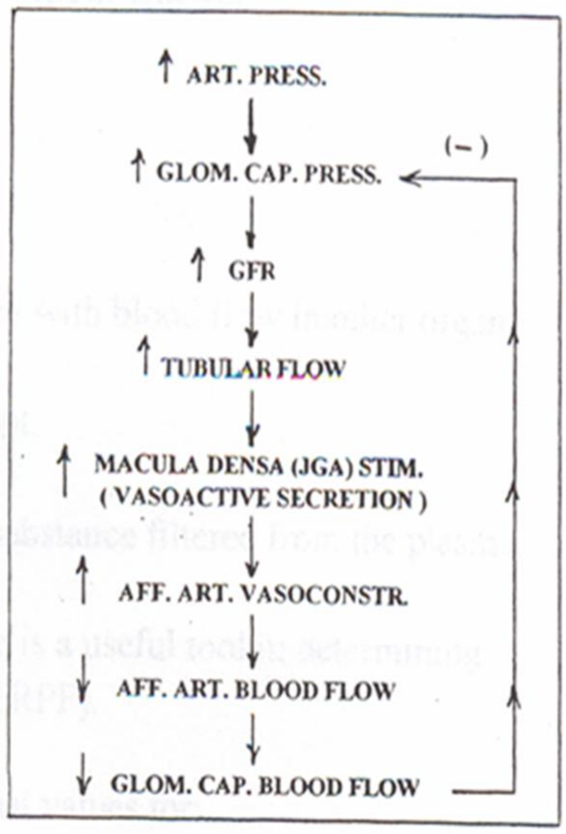
(1)-Myogenic Mechanism of the autoregulation

Blood Flow = Capillary Pressure / Flow resistance



(2)-Tubuloglomerular feedback





2- Neural regulation of GFR

- Sympathetic nerve fibers innervate afferent and efferent arteriole
- Normally sympathetic stimulation is low but can increase during hemorrhage and exercise
- Vasoconstriction occurs as a result which conserves blood volume and permits greater blood flow to other body parts (exercise)

Nerves from the renal plexus (sympathetic nerve) of the autonomic nervous system enter kidney at the hilum→innervate smooth muscle of afferent & efferent arterioles→regulates blood pressure & distribution throughout kidney

Effect:

(1) Reduce the GPF (Glomerular Plasma Flow) and GFR and through contracting the afferent and efferent artery (α receptor)

(2) Increase the Na^+ reabsorption in the proximal tubules (β receptor)

(3) Increase the release of renin (β receptor)

3. Hormonal regulation of GFR

Several hormones contribute to GFR regulation

- Angiotensin II: Produced by Renin, released by JGA cells is a potent vasoconstrictor. Reduces GFR
- ANP: (released by atria when stretched) increases GFR by increasing capillary surface area available for filtration
- Nitric Oxide: regulation of renal haemodynamics
- Endothelin:
- Prostaglandin : Induce renal vasodilatation, Prostaglandins(especially PGE_2 & PGI_2) are probably not of major importance in the regulation of GFR &renal blood flow normally .Prostaglandins,however,may dampen the renal vasoconstrictor effects of sympathetic nerves or angiotensin II ,especially the effect on afferent arterioles. Blockade of prostaglandins (e.g, with aspirin &nonsteroidal anti-inflamatory drugs) may therefore cause significant decrease GFR & RPF

Proximal tubule

- Morphology: epithelium cells have a striate brush border (projections), which enlarge the surface for the reabsorption.
- Function: Reabsorption of the largest volume of solution filtered in glomerular apparatus.

  - 75 - 80 % water
  - Na^+, Cl^-, HCO_3^-, K^+, Ca^{2+}, Mg^{2+}, HPO_4^{2-}
  - Glucose
- Results in ISOOSMOTIC SOLUTION
- Fluid in the filtrate entering the PCT is reabsorbed into the vasa recta, including approximately 2/3 of the filtered salt and water and all filtered organic solutes (primarily glucose and amino acids).

This is driven by sodium transport from the lumen into the blood by the Na+/K+ ATPase in the basolateral M of the epithelial cells .

Much of the mass movement of water and solutes occurs in bt the cells through the tight junctions.

The solutes are absorbed isotonicaly: the osmotic potential of the fluid leaving the proximal tubule is the same as that of the initial glomerular filtrate .

Glucose and amino acids are absorbed actively via cotransport channels driven by the sodium gradient out of the nephron.

Loop of Henle (LH)

- A U-shaped tube that consists of:
  descending limb (thin part)
  ascending limb (thin and thick part) .
- Begins in the cortex, receiving urine from the proximal convoluted tubule, extends into the medulla, and then returns to the cortex to empty into the distal convoluted tubule.
- Function: Its primary role is to concentrate the salt in the interstitium, the tissue surrounding the loop.

Loop of Henle - Descending limb

- Permeable to water and salt, and thus only indirectly contributes to the concentration of the interstitium.
- As the filtrate descends deeper into the hyperotonic interstitium of the renal medulla, water flows freely out of the descending limb by Osmosis until the tonicity of the filtrate and interstitium equilibrate.
- Longer descending limbs allow more time for water to flow out of the filtrate, so longer limbs make the filtrate more hypertonic than shorter limbs.

- Results in hypertonic solution in tubuli.(urine)

Loop of Henle - Ascending limb

- Impermeable to water, permeable for salts.
- Actively pumps sodium out of the filtrate, generating the hypertonic interstitium that drives countercurrent exchange.
- Results in hypotonic solution in tubuli (urine).
- This hypotonic filtrate is passed to the distal convoluted tubule in the renal cortex.

Distal tubule

- Morphology: continuation of the thick Asc limb of the LH in the cortex of kidneys - direct part.
- Convolute part – JGA (the part of distal tubule near the glomerular apparatus) = special cells = MACULA DENSA (thin cells very tight next to each other) Large nucleus, secretion of RENIN
- Reabsorption:
  - Water
  - Na^+
- Results in ISOOSMOTIC SOLUTION
- After traveling the length of the distal convoluted tubule, only 3% of water remains, and the remaining salt content is negligible.
- 97.9% of the water in the glomerular filtrate enters the convoluted tubules and collecting ducts by osmosis.
- The distal convoluted tubule is similar to the proximal convoluted tubule in structure and function. Cells lining the tubule have numerous mitochondria, enabling active transport to take place by the energy supplied by ATP.
- Much of the ion transport taking place in the distal convoluted tubule is regulated by the Endocrine system.
  1. In the presence of parathyroid hormone, the DCT reabsorbs more Ca2+ and excretes more phosphate.
  2. When aldosterone is present, more Na+ is reabsorbed and more K+ excreted.
  3. Atrial natriuretic peptide causes the DCT to excrete more Na+ .
  4. In addition, the tubule also secretes hydrogen and ammonium to regulate pH

Collecting duct

- Collects about 10 distal tubules, continues as medullary pyramides (about 2700 nephrons).
- Final adjustment
- Results in HYPERTONIC SOLUTION
- Each distal convoluted tubule delivers its filtrate to a collecting duct, most of which begin in the renal cortex and extend deep into the medulla.
- As the urine travels down the collecting duct, it passes by the medullary interstitium which has a high sodium concentration as a result of the loop of Henle's.
- The collecting duct is normally impermeable to water, it becomes permeable under the actions of Antidiuretic hormone (ADH).
- As much as 3/4 of the water from urine can be reabsorbed as it leaves the collecting duct by osmosis.
- The levels of ADH determine whether urine will be concentrated or dilute.
- Dehydration results in an increase in ADH, while water sufficiency (excess) results in low ADH allowing for diluted urine.
- Lower portions of the collecting duct are also permeable to urea, allowing some of it to enter the medulla of the kidney, thus maintaining its high ion concentration (which is very important for the nephron).
- Urine leaves the collecting duct through the renal papilla, emptying into the renal calyces, the renal pelvis, and finally into the bladder via the ureter.
- Because it has a different embryonic origin than the rest of the nephron, the collecting duct is usually not considered a part of the nephron proper.

Tubular Transport Maximum [T_m]:

- For many substances transported by carriers (active transport or facilitated diffusion), there exists some maximum rate for their transport; this is termed their tubular transport maximum or T_m
- When the quantity of a substance presented for transport is greater than the T_m for that substance, the excess is not transported and is either excreted (for reabsorbed substances) or returned to the body in the renal venous blood (for secreted stubstances)

  Examples:

  -Glucosuria in diabetes mellitus
  -Albuminurea in nephritis