Renal Physiology

Lecture Outline

- General Functions of the Urinary System
- Quick overview of the functional anatomy of the urinary system
- How the nephron works & is controlled
- Micturition

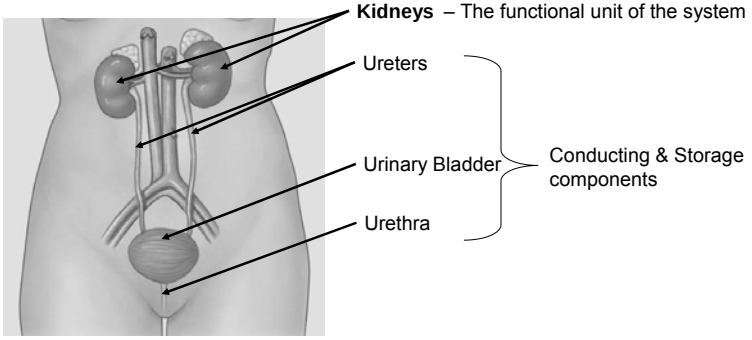
General Functions

- Produce & expel urine
- Regulate the volume and composition of the extracellular fluid
  - Control pH
  - Control blood volume & blood pressure
  - Controls osmolarity
  - Controls ion balance
- Production of hormones
  - Renin
  - EPO

Overview of Function Anatomy

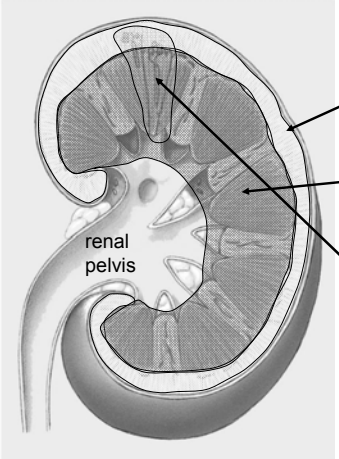
The System

- Urinary system consists of:



Overview of Functional Anatomy

The Kidney

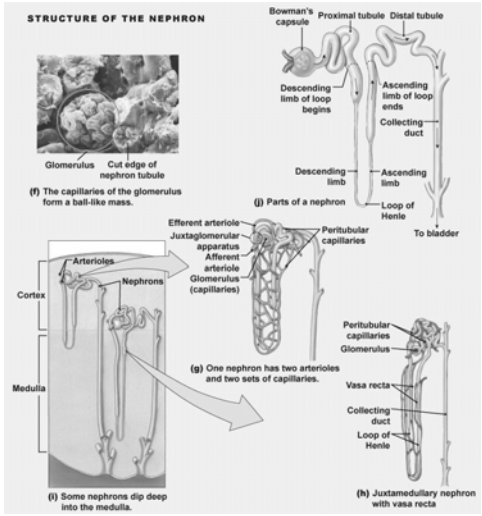


- Divided into an outer cortex
- And an inner medulla
- The functional unit of this kidney is the nephron
  - Which is located in both the cortex and medullary areas

Overview of Functional Anatomy

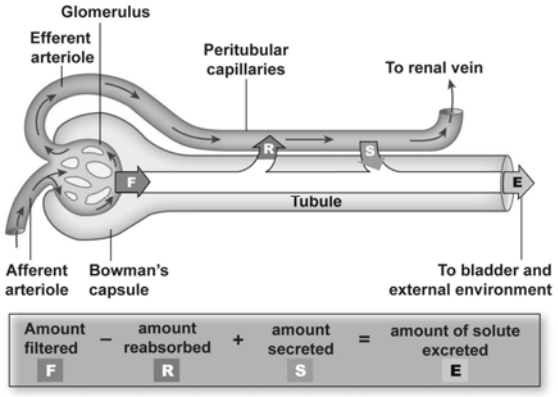
The Kidney

- The nephron consists of:
  - Vascular components
    - Afferent & efferent arterioles
    - Glomerulus
    - Peritubular capillaries
    - Vasa recta
  - Tubular components
    - Proximal convoluted tubule
    - Distal convoluted tubule
    - Nephron loop (loop of Henle)
    - Collecting duct
  - Tubovascular component
    - Juxtaglomerular appartus



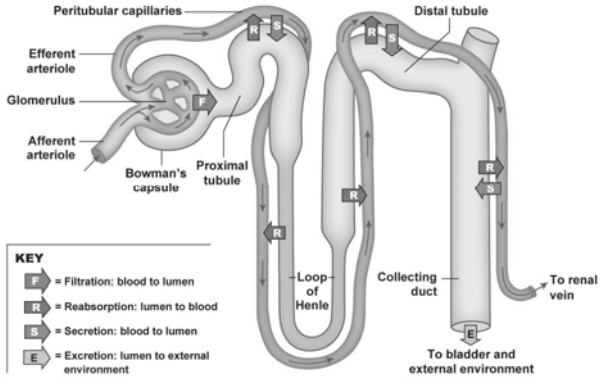
The Nephron

- Simplified view of its functions
  - Glomerular Filtration
  - Tubular Reabsorption
  - Tubular Secretion
  - Excretion



The Nephron

- Locations for filtration, reabsorption, secretion & excretion

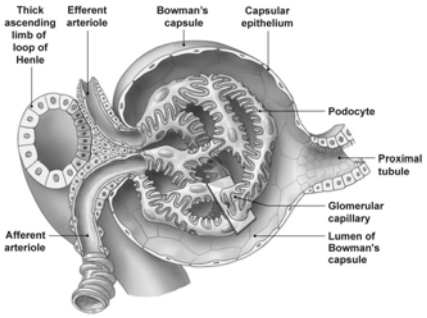


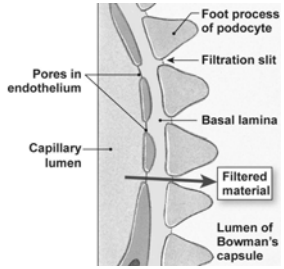
Nephron
Filtration

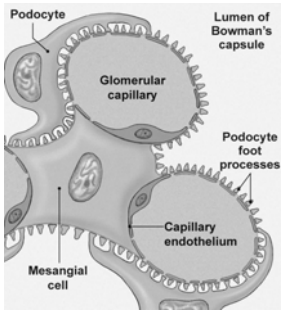
- First step in urine formation
  - No other urinary function would occur without this aspect!
- Occurs in the glomerulus due to
  - Filtration membrane &
    - Capillary hydrostatic pressure
    - Colloid osmotic pressure
    - Capsular hydrostatic pressure

Nephron
Filtration Membrane

- Capillaries are fenestrated
- Overlying podocytes with pedicels form filtration slits
- Basement membrane between the two





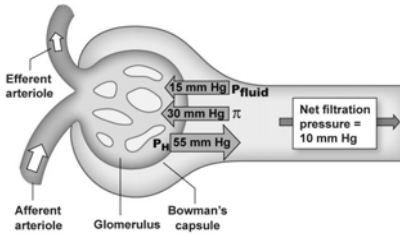


Nephron
Glomerular Filtration

- Barriers
  - Mesanglial cells can alter blood flow through capillaries
  - Basal lamina alters filtration as well by
    - Containing negatively charged glycoproteins
      - Act to repel negatively charged plasma proteins
  - Podocytes form the final barrier to filtration by forming “filtration slits”

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

Nephron
Glomerular Filtration

- 10 mm Hg of filtration pressure
  - 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!
  - Still…. GFR must be under regulation to meet the demands of the body.

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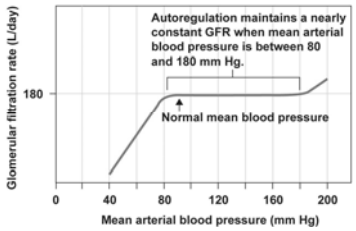
  - GFR maintains itself at the relatively stable rate of 180L/day by
    - Regulation of blood flow through the arterioles
      - Changing afferent and efferent arterioles has different effects on GFR



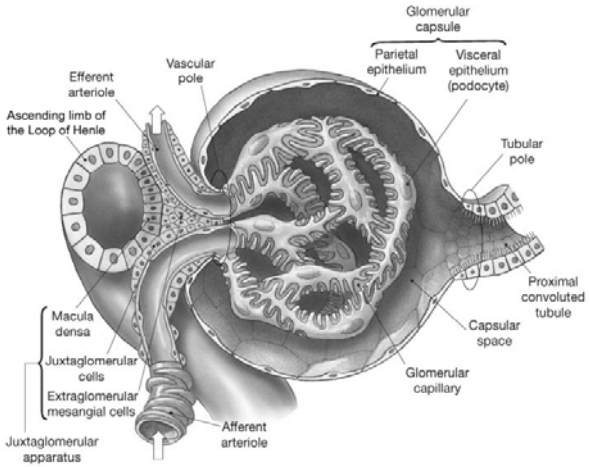
Nephron
Regulation of GFR

- How does GFR remain relatively constant despite changing mean arterial pressure?
  1. Myogenic response
     - Typical response to stretch of arteriolar smooth muscle due to increased blood pressure:
       - increase stretch results in smooth muscle contraction and decreased arteriole diameter
       - Causes a reduction in GFR
     - If arteriole blood pressure decreases slightly, GFR only increases slightly as arterioles dilate
       - Due to the fact that the arterioles are normally close to maximal dilation
       - Further drop in bp (below 80mmHg) reduced GFR and conserves plasma volume
  2. Tubulooglomerular feedback at the JGA
  3. Hormones & ANS

Nephron
Autoregulation of GFR

2. Tubulooglomerular feedback at the JGA
   - Fluid flow is monitored in the tubule where it comes back between the afferent and efferent arterioles
     - Forms the juxtaglomerular apparatus
       - Specialized tubular cells in the JGA form the macula densa
       - Specialized contractile cells in the afferent arteriole in the JGA are called granular cells or juxtaglomerular cells

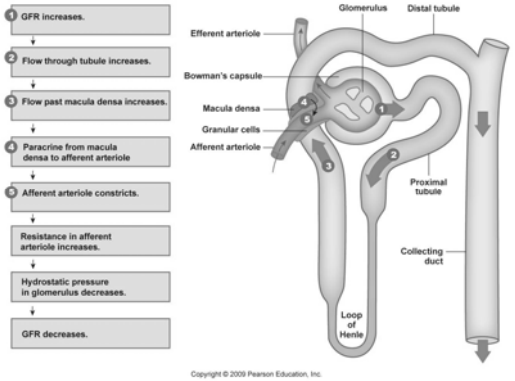
Juxtaglomerular Apparatus



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 (unknown for certain) causing the afferent arteriole to contract, decreasing GFR and NaCl movment



Nephron

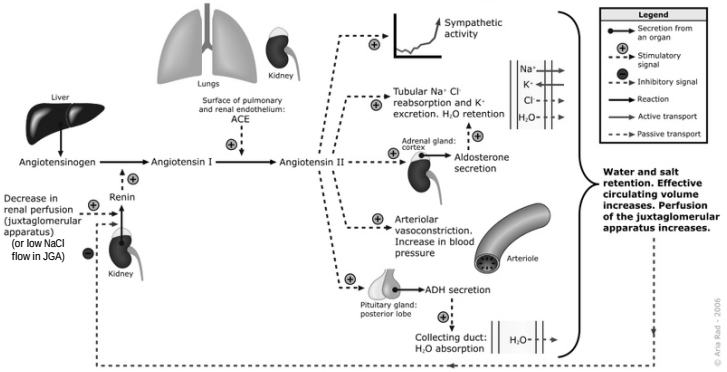
Regulation of GFR

3. Hormones & ANS
   - Autoregulation does a pretty good job, however extrinsic control systems can affect a change by overriding local autoregulation factors by
     - Changing arteriole resistance
       - Sympathetic innervation to both afferent and efferent arterioles
         - » Acts on alpha receptors causing vasoconstriction
         - » Used when bp drops drastically to reduce GFR and conserve fluid volume
     - Changing the filtration coefficient
       - Release of renin from the granular cells (JG cells) of the JGA initiates the renin-angiotensin-aldosterone system (RAAS)
         - » Angiotensin II is a strong vasoconstrictor
       - Prostaglandins
         - » Vasodilators
       - These hormones may also change the configuration of the mesanglial cells and the podocytes, altering the filtration coefficient

Nephron

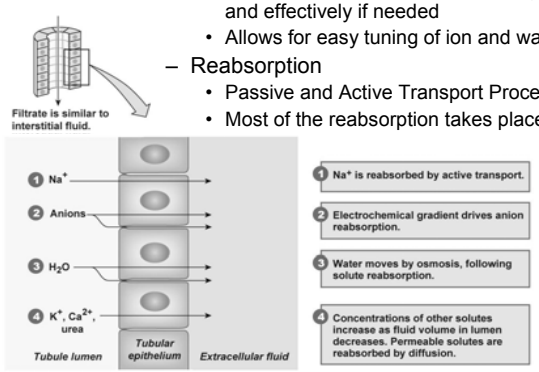
Regulation of GFR

- Renin-Angiotensin-Aldosterone System



Nephron
Tubular Reabsorption

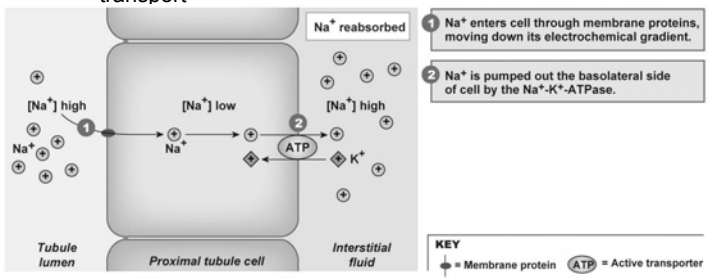
- GFR = 180 L/day, >99% is reabsorbed
  - Why so high on both ends?
    - Allows material to be cleared from plasma quickly and effectively if needed
    - Allows for easy tuning of ion and water balance
  - Reabsorption
    - Passive and Active Transport Processes
    - Most of the reabsorption takes place in the PCT



Movement may be via epithelial transport (through the cells) or by paracellular pathways (between the epithelial cells)

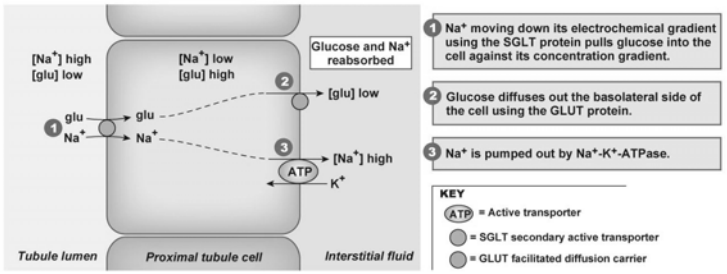
Nephron
Tubular Reabsorption

- Na^+ reabsorption
  - An active process
    - Occurs on the basolateral membrane (Na^+/K^+ ATPase)
      - Na^+ is pumped into the interstitial fluid
      - K^+ is pumped into the tubular cell
    - Creates a Na+ gradient that can be utilized for 2º active transport



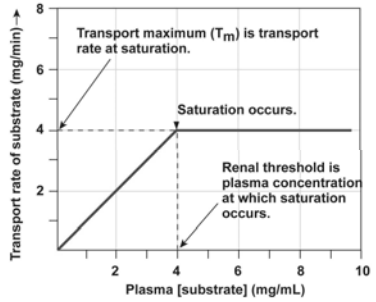
Nephron
Tubular Reabsorption

- Secondary Active Transport utilizing Na^+ gradient (Sodium Symport)
  - Used for transporting
    - Glucose, amino acids, ions, metabolites



Nephron
Tubular Reabsorption

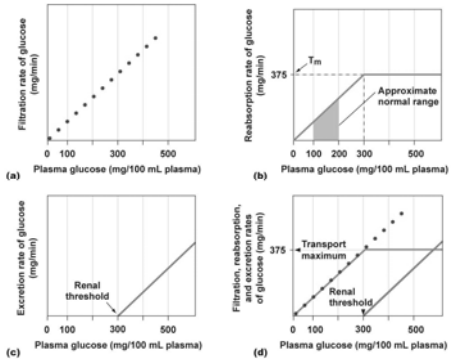
- The transport membrane proteins
  - Will reach a saturation point
    - They have a maximum transport rate = transport maximum (T_m)
      - The maximum number of molecules that can be transported per unit of time
      - Related to the plasma concentration called the renal threshold…
        - » The point at which saturation occurs and T_m is exceeded



Nephron
Tubular Reabsorption

- Glucose Reabsorption
  - Glucose is filtered and reabsorbed hopefully 100%
    - Glucose excreted = glucose filtered – glucose reabsorbed

Implication of no glucose transports past the PCT?



Nephron
Tubular Reabsorption

- Where does filtered material go?
  - Into peritubular capillaries because in the capillaries there exists
    - Low hydrostatic pressure
    - Higher colloid osmotic pressure

Nephron
Tubular Secretion

- Tubular secretion is the movement of material from the peritubular capillaries and interstitial space into the nephron tubules
  - Depends mainly on transport systems
  - Enables further removal of unwanted substances
  - Occurs mostly by secondary active transport

  - If something is filtered, not reabsorbed, and secreted… the clearance rate from plasma is greater than GFR!
    - Ex. penicillin – filtered and secreted, not reabsorbed
      - 80% of penicillin is gone within 4 hours after administration

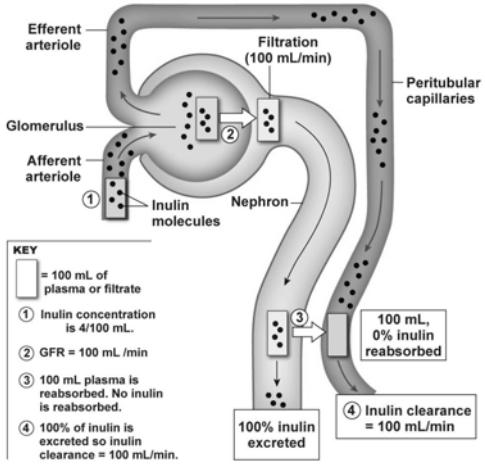
Nephron
Excretion & Clearance

Filtration – reabsorption + secretion = Excretion

- The excretion rate then of a substance (x) depends on
  - the filtration rate of x
  - if x is reabsorbed, secreted or both
- This just tells us excretion, but not much about how the nephron is working in someone
  - This is done by testing a known substance that should be filtered, but neither reabsorbed or secreted
    - 100% of the filtered substance is excreted and by monitoring plasma levels of the substance, a clearance rate can be determined

Nephron
Excretion & Clearance

- Inulin
  - A plant product that is filtered but not reabsorbed or secreted
  - Used to determine clearance rate and therefore nephron function



Nephron
Excretion & Clearance

- The relationship between clearance and excretion using a few examples

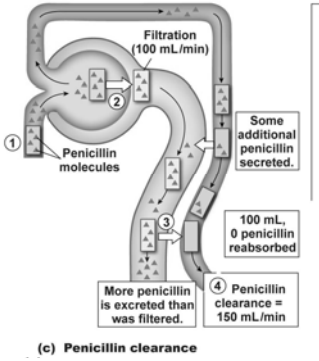


Table 19-2 Renal Handling of Solutes

For any molecule *X* that is freely filtered at the glomerulus:	Renal handling of *X* is:
Filtration is greater than excretion	Net reabsorption of *X*
Excretion is greater than filtration	Net secretion of *X*
Filtration and excretion are the same	No net reabsorption or secretion
Clearance of *X* is less than inulin clearance	Net reabsorption of *X*
Clearance of *X* is equal to inulin clearance	*X* is neither reabsorbed nor secreted.
Clearance of *X* is greater than inulin clearance	Net secretion of *X*

Nephron
Excretion & Clearance

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Clearance of *X* is greater than inulin clearance	Net secretion of *X*

Nephron
Urine Concentration & Dilution

- Urine normally exits the nephron in a dilute state, however under hormonal controls, water reabsorption occurs and can create an extremely concentrated urine.
  - Aldosterone & ADH are the two main hormones that drive this water reabsorption
    - Aldosterone creates an obligatory response
      - Aldosterone increases Na+/K+ ATPase activity and therefore reabsorption of Na+… where Na+ goes, water is obliged to follow
    - ADH creates a facultative response
      - Opens up water channels in the collecting duct, allowing for the reabsorption of water via osmosis

Micturition

- Once excreted, urine travels via the paired ureters to the urinary bladder where it is held (about ½ L)
- Sphincters control movement out of the bladder
  - Internal sphincter – smooth muscle (invol.)
  - External sphincter – skeletal muscle (vol.)

Micturition

- Reflex Pathway