Renal Physiology

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:

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
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

The Nephron

- Simplified view of its functions

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
  – Mesangial 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 ($\pi$)
    • 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 ($P_{\text{fluid}}$)
    • Opposes hydrostatic pressure at 15 mm Hg
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.

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. Tubuloglomerular feedback at the JGA
  3. Hormones & ANS

Nephron
Glomerular Filtration

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    • 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!
  - 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
Autoregulation of GFR

2. Tubuloglomerular 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

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 mesangial cells and the podocytes, altering the filtration coefficient

Nephron Regulation of GFR

• The cells of the macula densa monitor NaCl concentration in the fluid moving into the distal 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 movement

Nephron Regulation of GFR

• Renin-Angiotensin-Aldosterone System

Renin-Angiotensin-Aldosterone System

- Decrease in renal perfusion (normal increase if the GFR falls)
- Angiotensinogen → Angiotensin I → Angiotensin II
- Angiotensin II
  - Increases aldosterone, increases sodium reabsorption
  - Increases atrial natriuretic peptide (ANP), decreases blood pressure
  - Increases aldosterone, increases potassium excretion
  - Causes vasoconstriction
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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
  – Reabsorption
  • Passive and Active Transport Processes
  • Most of the reabsorption takes place in the PCT

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

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Tubular Reabsorption

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

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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

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
Tubular Reabsorption

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

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

<table>
<thead>
<tr>
<th>For any molecule X that is freely filtered at the glomerulus:</th>
<th>Renal handling of X is:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtration is greater than excretion</td>
<td>Net reabsorption of X</td>
</tr>
<tr>
<td>Excretion is greater than filtration</td>
<td>Net secretion of X</td>
</tr>
<tr>
<td>Filtration and excretion are the same</td>
<td>No net reabsorption or secretion</td>
</tr>
<tr>
<td>Clearance of X is less than inulin clearance</td>
<td>Net reabsorption of X</td>
</tr>
<tr>
<td>Clearance of X is equal to inulin clearance</td>
<td>X is neither reabsorbed nor secreted</td>
</tr>
<tr>
<td>Clearance of X is greater than inulin clearance</td>
<td>Net secretion of X</td>
</tr>
</tbody>
</table>

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

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![Diagram of Micturition Reflex Pathway](image-url)