



1. total surface area for filtration
2. filtration membrane permeability
3. net filtration pressure

Normal GFR for an adult is 120 - 125 ml/ min. Note a drop in glomerular pressure of 15% will stop filtration altogether.

Note also that GFR is directly proportional to the net filtration rate.

The GFR must be precisely regulated or many substances normally resorbed will be lost in the urine, OR wastes that should be expelled may be resorbed.

There are three mechanisms that help to keep the GFR relatively constant:

1. Renal Autoregulation (intrinsic controls)
2. Neural controls
3. Renin-angiotensin system

**Renal Autoregulation** - the kidney can maintain a relatively constant GFR regardless of fluctuations in systemic blood pressure. This is done by regulating the diameter of the afferent and efferent arterioles. This is done in one of two ways:

1. myogenic mechanisms - responds to changes in the pressure in the renal vessels.
2. tubuloglomerular feedback mechanism - senses changes in the juxtaglomerular apparatus. Using the macula densa cells: these cells release a vasoconstrictor if the GFR is too high or permit vasodilation of afferent arterioles if the filtration rate is too low. This system can work in the range of 80 to 180 mm Hg. It cannot handle low systemic pressures. Below 45 mm Hg filtration stops.

**Neural Control** - Sympathetic control. When the sympathetic nervous system is at rest renal vessels are maximally dilated. Sympathetic stimulation causes constriction of afferent arterioles thus decreasing filtration rate. This stimulation causes release of epinephrine from the adrenal medulla. The epinephrine in turn acts on alpha receptors on vascular smooth muscle. This indirectly starts the renin-angiotensin mechanism by stimulating macula densa cells.

The sympathetic nervous system also directly stimulates the Juxtaglomerular cells (by binding NE to beta adrenergic receptors) to release renin, which begins the renin-angiotensin mechanism.

**Renin-Angiotensin mechanism** - begins when juxtaglomerular cells release renin. Renin acts on angiotensinogen (plasma protein made in the liver) to release angiotensin I which is then converted to angiotensin II by angiotensin converting enzyme.

Resorption in the kidneys is active (requires ATP) or passive depending on the substance to be resorbed.

Sodium ions are the single most abundant cations in the filtrate. Sodium ion resorption is always active.

**Obligatory water reabsorption**: sodium movement establishes a strong osmotic gradient, and water moves by osmosis into the peritubular capillaries. Here the water is “obliged” to follow the salt.

As water leaves the tubules, the relative concentration of the substances still present in the filtrate increases dramatically and, if able, they will begin to follow their concentration gradients into the tubule cell. This is called **Solvent Drag**.

Some substances are not resorbed or are resorbed incompletely. This happens because:

1. they lack carriers
2. they are not lipid soluble
3. they are too large to pass through the plasma membrane pores of the tubule cells.

The most important of these substances are the nitrogenous end products of protein and nucleic acid metabolism: **urea**, **creatinine**, and **uric acid**.

#### Absorptive capabilities of various regions of the renal tubules

Proximal convoluted tubule: is the most active region for reabsorption

All glucose , lactate, and amino acids  
65 - 70% of  $\text{Na}^+$  (linked to cotransport of other solutes or  $\text{Na}^+ - \text{H}^+$  exchange)  
65 - 70% of water  
90% of bicarbonate  
50% of chloride  
>90% of potassium

Almost all uric acid is reabsorbed in the PCT but later is returned to the filtrate.

Of the 125 ml/min of fluid filtered at the glomerulus, only about 40 ml/min remains after the PCT.

#### Nephron Loop (of Henle)

Descending limb: Water moves out freely,  $\text{K}^+$  moves back in.

Ascending limb:  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Cl}^-$  move out, water cannot leave the ascending limb.

#### Distal Convoluted Tubule:

Na<sup>+</sup> and Cl<sup>-</sup> reabsorbed if needed by the body. This is under hormonal control. If needed almost ALL of the water and Na<sup>+</sup> reaching this area can be reclaimed.

Na<sup>+</sup> resorption is under the control of **Aldosterone** from the adrenal cortex. When aldosterone is present almost no Na<sup>+</sup> leaves the body via the urine. In addition the renin-angiotensin mechanism stimulates the release of aldosterone. Aldosterone also promotes water reabsorption because water follows the Na<sup>+</sup>.

**ADH** also plays a role here.

**Atrial Natriuretic Peptide:** (ANP) is a hormone released from the atrial cardiac cells when blood volume and/or blood pressure is elevated. ANP inhibits Na<sup>+</sup> absorption by closing Na<sup>+</sup> channels. This reduces water reabsorption and therefore blood volume.

**Tubular Secretion:** is essentially reabsorption in reverse.

We see tubular secretion in the PCT, DCT and cortical collecting ducts, but not in the nephron loop.

This is important for:

1. disposing of substances that are not already in the filtrate (drugs)
2. eliminating undesirable substances such as urea and uric acid
3. getting rid of excess K<sup>+</sup>
4. controlling blood pH

**Osmolality:** the number of solute particles dissolved in one liter of water. This is reflected in the solutions ability to cause osmosis.

The kidneys have the important job of keeping the body fluids at a constant 300 mosm (milliosmoles). This is done by using a countercurrent exchange system.

Some common terms that apply to urinary physiology:

Acidosis: A condition in which the pH of the blood is below 7.35

Alkalosis: A condition in which the pH of the blood is higher than 7.45

Compensation: the physiological response to an acid/base imbalance that acts to normalize the pH of arterial blood.

Complete compensation: results if the arterial pH is brought to within normal limits

Partial compensation: is only partially corrected but does not fall within the normal range

If a person has an altered blood pH due to metabolic causes, hyper/hypoventilation may bring the pH back into the normal range. This would be known as respiratory compensation.

If a person has an altered blood pH due to respiratory causes then they must use renal compensation to try to return to normal limits. Renal compensation works by changing the secretion of  $H^+$  and reabsorption of  $HCO_3^-$  by the kidneys.

**Metabolic acidosis/alkalosis** results from changes in  $HCO_3^-$  concentrations in the blood.

The normal range for  $HCO_3^-$  is 22 – 26 mEq/liter.

Metabolic acidosis is defined as the arterial blood  $HCO_3^-$  level dropping below 22 mEq/liter. This could result from actual loss of  $HCO_3^-$  as may be seen with severe diarrhea or renal disease, or an accumulation of an acid other than  $HCO_3^-$ , or failure of the kidneys to excrete  $H^+$ . If this problem is not too severe we can use respiratory compensation (through hyperventilation) to bring the blood pH back into the normal range.

Metabolic alkalosis is defined as an arterial blood  $HCO_3^-$  level above 26 mEq/liter. A loss of acid or excessive intake of alkaline drugs can cause the blood pH to rise above 7.45. The most frequent cause is excessive vomiting which results in a substantial loss of HCl. Hypoventilation may provide respiratory compensation.

There are basically 4 steps in diagnosing acid/base imbalances:

1. determine whether the pH is high (alkalosis) or low (acidosis).
2. determine which value ( $PCO_2$  or  $HCO_3^-$ ) is out of range
3. If the cause is a change in  $PCO_2$  the problem is respiratory. If the cause is  $HCO_3^-$ , the problem is metabolic.
4. NOW, look at the value that doesn't correspond with the observed pH change.

If it is within its normal range there is no compensation occurring. If it is outside its normal range compensation is occurring and partially correct the problem.

The partial pressure of carbon dioxide is the single most important indicator of respiratory function.

When respiratory function is normal  $PCO_2$  ranges from 35 - 45 mm Hg.

Respiratory acidosis and alkalosis are both disorders resulting from changes in the partial pressure of  $CO_2$  ( $PCO_2$ )

Values of  $PCO_2$  above 45 mm Hg indicate respiratory acidosis

Values of  $PCO_2$  below 35 mm Hg indicate respiratory alkalosis

Respiratory acidosis is defined as an abnormally high  $\text{PCO}_2$  in arterial blood. Inadequate exhalation of  $\text{CO}_2$  causes the blood pH to drop. Respiratory acidosis can result from slow breathing or hampered gas exchange (pneumonia, cystic fibrosis, emphysema). Here  $\text{CO}_2$  accumulates in the blood. This causes a falling blood pH and rising  $\text{PCO}_2$ . The kidneys may provide renal compensation by increasing the excretion of  $\text{H}^+$  and the reabsorption of  $\text{HCO}_3^-$ .

The goal in treating respiratory acidosis is to increase the blow off (exhalation) of  $\text{CO}_2$ .

Respiratory alkalosis is defined as an abnormally low  $\text{PCO}_2$  in the arterial blood.. The cause of this condition is hyperventilation and  $\text{CO}_2$  is eliminated from the body faster than it is produced.. Hyperventilation may be caused by several factors such as oxygen deficiency due to high altitude, stroke, or severe anxiety. Renal compensation may bring the blood pH into the normal range if the kidneys are able to decrease the excretion of  $\text{H}^+$  and reabsorption of  $\text{HCO}_3^-$ .

Note that, unlike respiratory acidosis, respiratory alkalosis this is rarely caused by pathology.