

Potassium

Potassium is the major intracellular cation. Total body potassium content is approximately 50 mEq per kilogram body weight. Therefore, a 70 kilogram person has about 3500 mEq total body potassium, 98% of which is in the intracellular compartment. The sodium potassium ATPase is the major cellular enzyme responsible for maintaining very low intracellular Na concentration and increased potassium intracellular concentration.

Although only 2% of total body potassium (70-100meq) remains in the extracellular compartment, the extracellular potassium concentration plays a critical role in maintaining cell membrane resting potential. This is particularly important for electrically excitable cells, (muscle and nervous system activity). The Nernst equation, which can be used to calculate resting membrane potential, shows that resting membrane potential is a function of the ratio of extracellular over intracellular potassium concentrations. Since extracellular potassium is approximately 4 mEq/l and intracellular potassium concentration is greater than 100 mEq/l, it can be seen that relatively small changes in extracellular potassium concentration can significantly alter resting membrane potential. Alterations in resting membrane potential alter the functional activity of electrically excitable cells, muscle and nerve. Furthermore, since only a small quantity of potassium is normally present in extracellular fluid, the removal or addition of small numbers of potassium ions to this space can significantly alter extracellular potassium concentration with subsequent adverse effects on neuromuscular function.

The extracellular potassium concentration, therefore, must be kept within a very narrow range. This must occur in the face of alterations in dietary potassium intake. The average daily dietary intake is 70 to 100 mEq of potassium. In order to maintain homeostasis (maintaining total body potassium content at a constant and normal level), the same quantity, 70 to 100 mEq of potassium, must be removed from the body daily. This is primarily done by renal excretion. During conditions of neutral potassium balance, the daily intake of potassium is equal to the daily excretion rate, primarily in the urine. Only a small amount of potassium is excreted through the gut.

Potassium balance includes two major features: 1) external balance, which involves matching daily intake of potassium to the amount excreted into the urine, and 2) internal balance, which refers to getting potassium into the intracellular space. External potassium balance is a relatively slow process, such that the daily intake is excreted by the kidneys over approximately 24 hour time frame. In contrast, since meals are typically eaten in bolus fashion, there is significant abrupt potassium entry into the body. If this potassium were allowed to remain in the extracellular space, hyperkalemia and its adverse effects on neuromuscular function would occur. The process of delivering potassium into the intracellular space is referred to as internal balance. This process of the internal balance prevents meal related hyperkalemia. The major regulator for potassium entry into the intracellular space, after dietary potassium intake, is insulin. Food ingestion, which includes potassium, leads to insulin release. Other factors involved in internal balance include a) osmolality: increased osmolality in extracellular space leads to water movement from the intracellular compartment. Potassium will exit the cell through solvent drag effect. b) pH changes: metabolic acidosis with normal plasma anion gap results in hydrogen ions entering intracellular compartment for buffering by intracellular buffers, in exchange for potassium exiting from the intracellular compartment. This typically is a relatively small effect, which changes extracellular potassium concentration < 1 mEq/l. Metabolic acidosis with increased plasma anion gap has minimal effects on internal potassium balance. In these disorders, hydrogen ions enter the intracellular compartment for buffering accompanied by the acid anion, such that no hydrogen ion potassium ion exchange occurs. Respiratory acid base disorders have trivial effects on internal potassium balance. c) aldosterone has a modest effect to promote potassium entry into the cell d) beta 1 receptor activation promotes potassium entry to the intracellular space.

Renal handling of potassium (the primary regulator of the external balance of potassium):

Plasma potassium is freely filtered at the glomerular membrane. Potassium is initially reabsorbed in the proximal tubule and loop of Henle. Potassium ultimately enters the urine through the process of active tubular secretion. The cortical collecting duct is the major renal tubular site for potassium secretion. The major factors which influence potassium secretion at the cortical collecting duct include 1) distal delivery of sodium and tubular fluid 2) aldosterone 3) presence of nonabsorbable anions in the tubular fluid perfusing this segment.

Abnormalities in the external balance of potassium are primarily caused by abnormalities in renal tubular potassium secretion. The major factors which could lead to impaired potassium secretion include:

1) decreased GFR. Typically, compensatory changes occur with decreasing GFR, which allow the maintenance of normal external potassium balance until the GFR is severely reduced to < 20 ml per minute. Thus, potassium is the last electrolyte for which homeostasis is lost with chronic kidney diseases.

2) Decreased renal blood flow or decreased renal perfusion pressure: when these processes occur, the glomerulus must begin the process of autoregulation to maintain a stable glomerular filtration rate. When GFR is maintained at normal levels during conditions of decreased renal blood flow, a greater percentage of plasma reaching the glomerulus is becoming glomerular filtrate. This is described as an increased filtration fraction. Filtration fraction equals GFR/renal plasma flow. Since normal glomerular filtration rate is 120 ml per minute and normal renal plasma flow is approximately 600 ml per minute, the normal filtration fraction is 0.2, or 20%. Filtration fraction increases during the process of glomerular autoregulation. During autoregulation, the plasma leaving the glomerulus at the efferent arteriole has decreased hydrostatic pressure and increased oncotic pressure. The efferent arteriole subsequently becomes the peritubular capillaries surrounding the proximal tubule. The Starling forces within these capillaries, decreased hydrostatic pressure and increased oncotic pressure, lead to greatly augmented proximal tubular reabsorption. Conclusion: proximal tubular reabsorption is enhanced during conditions of glomerular autoregulation. The net result of enhanced proximal tubular reabsorption is decreased delivery of sodium and tubular fluid to the distal nephron, including the cortical collecting duct. This significantly impairs the potassium secretory process.

3) Aldosterone deficiency or resistance to the effects of aldosterone at the tubular level: Adrenal insufficiency would lead to both decreased cortisol and aldosterone production. Hyporeninemic hypoaldosteronism leads to decreased aldosterone because of decreased renin and, therefore, decreased production of angiotensin II, which is a primary stimulus for aldosterone secretion from the zona glomerulosa of the adrenal gland.

Aldosterone resistance is typically seen in conditions which lead to direct tubular damage to the cortical collecting duct. The most common example would be obstructive uropathy. Kidney diseases leading to chronic interstitial damage with tubular damage could also lead to aldosterone resistance: analgesic nephropathy, allergic interstitial nephritis, polycystic kidney disease, etc.

Drug effects: Aldosterone can be inhibited by the competitive antagonist, spironolactone. It can also be inhibited by drugs which block the sodium channel in the luminal membrane of the cortical collecting duct (amiloride and trimterene). Angiotensin converting enzyme inhibitors and angiotensin II receptor antagonist may also lead to impaired aldosterone production.

Trimethoprim and cyclosporine may also directly impair potassium secretion. Potassium secretion by the cortical collecting duct will be impaired aldosterone deficiency, aldosterone deficiency, or the drug related inhibition of the effects of aldosterone.

Prolonged heparin usage can directly impair adrenal aldosterone production. Beta 1 receptor antagonists may have a mild effect to impair the renin angiotensin aldosterone system. Severe digoxin toxicity may impair the sodium potassium ATPase.

Potassium secretion by the cortical collecting duct will be impaired by aldosterone deficiency, tubular resistance to the effects of aldosterone, or to drug related inhibition of the effects of aldosterone.