The Medical Importance of Sodium and Potassium

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Abstract
Sodium is the most abundant extracellular cation in the human body and is the main component of the interstitial fluid. Potassium is the major cation in the cytoplasm and contributes about 75% to the cell cations. Sodium plays a critical role in controlling blood pressure and extracellular fluid volume. It plays an essential role in the resting potential of the heart before the initiation of the action potential. sodium is essential for the transmission of nerve impulses and in muscle contractility and ultimately neuromuscular function. Potassium is an important facilitator of nerve impulse conduction. proper hydration and acid-base balances. aldosterone and other hormonal mediators control the final renal adjustments for how much sodium is retained or potassium is secreted. There is an increasing possibility of designing molecules that will rid the body of excess sodium or those that stimulate the retention of potassium.

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1. Introduction

Sodium and Potassium

Sodium and potassium are two electrolytes that are vitally important for proper body function. Sodium is the most abundant extracellular cation in the human body and is the main component of the interstitial fluid. Other small amounts of cations exist in the plasma as well. The total amount of sodium in the human body appears to be about 1225 g, depending on gender and age. Potassium is the major cation in the cytoplasm and contributes about 75% to the cell cations. The total potassium in the human body is estimated to be 225 g, and it has a concentration of approximately 120 mM in the cytoplasm. Both of these cations have been shown to contribute to cell physiology by maintaining the cell potential. (Gao *et al.* 2024) [1] (Mathew & Panonnummal, 2021) [2] (Jomov *et al.* 2022) [3]

Sodium's presence causes a cell to generate an electrical signal, producing an action potential that is conveyed by nerve fibers as an electrochemical signal via sodium and potassium ions' influx. In addition, potassium is released from synaptic vesicles to the synaptic cleft, producing a sharp rise in potassium ions. Moreover, via sodium-potassium ATPase, it pumps the sodium ions out of the cell while potassium ions enter the cell simultaneously in a process that requires energy. Sodium and potassium are also responsible for the contraction of the striated muscle, which is composed mainly of the following three ions, one of which is cation, sodium and potassium. Huge amounts of energy are expended by ATP when cations cross the muscle fiber. The positively correlated predictors of the resting metabolic rate were the concentrations of sodium and potassium in the CSF. For normal physiology, homeostasis of Na+ and K+ is important as it maintains the distinction between the intracellular and extracellular environments in the body. In order to maintain homeostasis, the level of such a maintaining the Na+/K+ ratio is important for health status. (Lindinger & Cairns, 2021) [4] (Senneff & Lowery, 2021) [5] (Glancy & Balaban, 2021) [6]

1.1 Chemical properties and functions

Chemically, both sodium and potassium are alkali metals. They both have atomic numbers below lithium and areherefore reactive. They share a variety of compounds and chemical reactivity with lithium, which in medicine are described as biochemically very different from either sodium or potassium. Almost 99% of the body's potassium is found in the cell, with approximately only 1% extracellular. Physiologically, cellular potassium normally drives a sodium-potassium exchanger pump known as the sodium pump. This drives potassium inside the cell and sodium outside the cell. Under normal conditions, potassium-sodium cotransporters recover a majority of the lost potassium into the cellular compartments. Sodium is largely in the extracellular compartments, and from a homeostatic chemistry point of view, both potassium and sodium constrain the potassium-to-sodium potential. (Fiorentini *et al.*, 2021) [7] (Schlegel *et al.* 2024) [8] (Pairo-Castineira *et al.* 2021) [9]

Physiological interaction between sodium and potassium exists as part of a cellular transmembrane gradient, influencing Na-K-ATPase, a cofactor driving nerve impulses and a mineral, within the sodium salts and potassium salts. As cofactors, they maintain optimal enzymatic activity and regulate a variety of cellular functions. This includes maintaining electrolyte fluid balance and driving osmosis. Excess or deficiency of either element or an increase in one element over the other will significantly contribute as a causative or aggregating mechanism to a major proportion of metabolic and electrolyte-based disorders. They are also key in the metabolic regulatory pathways. (Baj *et al.* 2020) [10] (Yamada & Inaba, 2021) [11] (Iriana *et al.* 2024) [12] (Verzicco *et al.* 2020) [13]

2. Physiological roles of sodium and potassium

Sodium and potassium are the main cations found in extracellular and intracellular fluids, respectively, with typically 135–145 and 3.5–5 mmol/L in plasma. Sodium plays a critical role in controlling blood pressure and extracellular fluid volume. It is also essential in generating signals of the nervous system, which involves altering membrane potentials. The concentration of sodium is vital to the regulation of plasma tonicity, a measure of the osmotic pressure of plasma. It tends to attract water and thereby regulates plasma volume and water content of the body. A diet low in sodium activates the renin-angiotensin-aldosterone system in the body, which may increase the potential for hypertension. Potassium homeostasis is crucial for maintaining normal bodily functions and health. It plays an essential role in the resting potential of the heart before the initiation of the action potential. The kidneys are the primary organ that helps maintain potassium homeostasis. (Olde Engberink *et al.*, 2020) [14] (Braam *et al.* 2020) [15] (Zhang *et al.*, 2022) [16] Over 98% of potassium is found in the intracellular space; it is determined by membrane resting potentials and acts as a cofactor for proteins. Potassium is an integral part of resting and active potentials of myocytes, which are needed for the expansion of resting potentials after rapid depolarizations. This replenishment of the potassium gradient is vital for subsequent repolarization of the cell. The extracellular potassium has profound effects on the K+ gradient and resting membrane potential, which directly contributes to the development of cardiac arrhythmias. Mismatch in extracellular and intracellular K+ can, under certain circumstances, cause an efflux of K+ from inside the cell to the extracellular space, resulting in depolarization, which will lead to alterations in the action potential of the heart. This will result in arrhythmias and sudden death. Furthermore, potassium has profound effects on skeletal muscle resting membrane potentials, and any alterations in plasma K+. (Hu *et al.* 2020) [17] (Liu *et al.* 2020) [18] (Pandey & Mahiwal, 2020) [19]

2.1 Sodium

Sodium is the body's major extracellular cation, and it plays a vital role in the body. Fundamental among its many physiological functions is electrolyte and fluid homeostasis. Sodium is the major determinant of extracellular fluid volume and, thus, intravascular volume. It is essential for blood pressure control. Its highly avid reabsorption in the kidneys helps retain water. In addition, sodium is essential for the transmission of nerve impulses and in muscle contractility and ultimately neuromuscular function. Dietary intake of sodium may influence hypertension, cardiovascular health, and some other associated diseases later. (Filippini *et al.* 2021) [20] (Huang *et al.* 2020) [21] (Ellison & Welling, 2021) [22] More than 90% of sodium consumed is excreted in the urine. But when sodium intake exceeds the amount excreted, plasma volume increases. This is followed by the release of the hormones that increase urine sodium excretion, causing a necessary fall in plasma volume. Judgment is on the sodium level and surrounding conditions such as fluid volume and blood pressure. In surgical patients, dehydrated people, and those with a renal salt metabolism disorder may lose excessive sodium. Children may have gastroenteritis and vomiting with subsequent sodium depletion, causing seizures. At the same time, an excess of sodium is harmful to health by elevating one of the most known complications: hypertension. Reducing hypertensive blood pressure and especially its cardiovascular complications is the most important benefit of lowering salt intake. The electrolyte aim is to correct an uneven balance in the body. It focuses less on the sodium level and is more on related electrolytes. It can help prioritize the search for sources of sodium or hypertension-lowering medications that conserve sodium. (Rossitto *et al.* 2021) [23] (Hu *et al.* 2020) [24] (Barnett *et al.* 2022) [25]

2.2 Potassium

Potassium plays a central role in body physiology, not only determining the amount of sodium retention and potassium loss but also influencing the metabolic pathway necessary for the sustained release of sodium. It helps maintain cellular membrane potential and resting potential by modulating the charge difference between intracellular and extracellular compartments, a concept known as repolarization. As a consequence, potassium plays an essential role in the function of excitable cells. In the heart, potassium efflux repolarizes the membrane potential. The time from the end of one action potential to the beginning of the next action potential is known as the refractory period. (Nikitin & Vinogradova, 2021) [26] (Kim *et al.* 2020) [27] (Kumar *et al.* 2020) [28]

Potassium is an important facilitator of nerve impulse conduction, as it enhances the amplitude of the action potential and helps in repolarization of the axon membrane. Repolarization of the resting membrane is crucial for proper muscle action, especially in skeletal muscles, and for normal heart muscle repolarization and contractile force. It opens

voltage-gated slow sodium channels inside which sodium flows into the cell, producing an inward current. This depolarization spreads up and down the muscle cell and inward through the transverse tubules, initiating muscle contraction. Potassium also plays a role in the prevention of arrhythmias and in proper hydration and acid-base balances. Chronic kidney disease, heart failure, and some forms of hypertension are associated with deficiencies in dietary potassium. Only diuretic therapy can present symptoms of hypokalemia; its use is associated with the elevation of serum potassium concentration. (Winlow & Johnson, 2021) [29] (Huber *et al.* 2021) [30] (Kaczmarek *et al.* 2022) [31]

Potassium levels are also related to health conditions, such as kidney disease or hypertension. Patients with kidney disease should avoid a diet high in potassium, as the kidneys may not be able to flush more potassium from the blood. However, people with normal kidneys can usually flush away any excess potassium in their urine to maintain a proper potassium balance. Enough potassium is usually obtained through food, such as fruits, vegetables, and dairy. If a patient is experiencing hypokalemia, they should eat more foods rich in potassium, such as bananas, orange juice, avocado, and cantaloupe. A healthy adult should consume 3,500–4,700 mg of potassium per day. Therefore, reliable potassium levels for adults usually range between 3.6 and 5.2 mmol/L. The body regulates potassium levels through renal mechanisms. These include alterations in potassium excretion and reabsorption, intracellular-extracellular shifts, alterations in acid-base balance, and others. For example, a decrease in plasma potassium levels may occur; to stop these levels from dropping any further, extracellular potassium moves into body cells, as do phosphate and magnesium ions. This process is known as transcellular shift, and it helps to maintain potassium homeostasis. (Palmer *et al.*, 2020) [32] (Bhagavathula *et al.* 2021) [33]

3. Regulation of sodium and potassium levels

Sodium and potassium are monitored and regulated by the body to maintain a relatively stable steady state, known as homeostasis. Homeostasis refers to the physiological regulation of the internal environment to maintain a constant, stable internal milieu. The body's primary urinary excretion system, the kidney, adjusts its filtered sodium and potassium load according to the body's needs. Subsequently, the amounts of filtered sodium and potassium that are reabsorbed or secreted will determine net retention or excretion of these electrolytes, as well as overall balance in the body. (Bernal *et al.*, 2023) [34] (McDonough and Fenton2022) [35] (Humalda *et al.* 2020) [36]

Hormonally, aldosterone and other hormonal mediators control the final renal adjustments for how much sodium is retained or potassium is secreted. For example, the kidneys are able to recapture nearly all filtered sodium in response to aldosterone in exchange for potassium secretion. Aldosterone is part of the renin-angiotensin-aldosterone axis, which acts on the juxtaglomerular apparatus in the kidneys. It increases renal sodium reabsorption and leads to potassium excretion by an exchange mechanism in the aldosterone-sensitive distal nephron. Thus, renal and hormonal systems together control the body's total sodium and potassium levels. The finest adjustment of sodium and potassium balance to control their concentration in the extracellular environment is mediated by processes within the nephron, driven by the filtered load. (Yang *et al.* 2020) [37] (Rossi *et al.*, 2020) [38] (Johnston *et al.* 2023) [39]

It is through this dual control of what is excreted as well as not being reabsorbed that the body can maintain relative constancy of sodium and potassium under varying intake conditions. These crucial counterregulatory mechanisms are an inherent part of the homeostatic state, allowing basic maintenance of our internal environment that is required for optimal cell and organ function. Organ systems have feedback systems that respond to the neural and hormonal alterations that normally occur from day to day, as water and electrolyte intake or output varies. These integrative systems secure a relatively stable composition, pH, and electrolyte concentration of the body fluids, even when there are wide daily oscillations in food and water intake. In addition, there is retrograde control in individual organs, where activated organs can also secrete substances that will have an effect on the functions of other organs, including the kidneys, brain, heart, blood vessels, salivary glands, stomach, intestine, and pancreas. Predisposing the system to alterations by food or medications also serves to protect the internal environment but can cause harm or illness in the event of cardiovascular, kidney, or hormonal disease. In the event that a person eats foods high in salt or potassium or suddenly consumes copious amounts of either, the system can still maintain normal internal conditions and excrete the excess, although they were not expected by the feedback systems to occur. However, the body still has control and can determine a normal level of either salt or potassium according to the intake. Stress and increased physical activity are usually associated with decreased consumption of salt, which is consistent with the lower thirst threshold and an appropriate change in body water. (Kumar & Marrapu, 2023) [40] (Oppelaar *et al.* 2021) [41] (Kim *et al.*, 2024) [42]

3.1. Homeostasis Mechanisms

3. Physiology 3.1. Homeostasis Mechanisms Extra- and intracellular Na+ and K+ concentrations are kept constant due to various homeostatic mechanisms irrespective of the intake. One of the main mechanisms of homeostasis has been through the tubuloglomerular feedback system. This feedback system regulates nephron glomerular filtration rate (GFR) and increases the reabsorption of solutes, including water and electrolytes, when the early distal convoluted tubule's (DCT) macula densa (MD) sensors detect a reduction in the distal tubule [NaCl] concentration, lower GFR, and tubular flow. Also, the hormonal regulation of the kidneys modulates electrolyte reabsorption and excretion, as well as the assessment of extracellular volume and osmolality. (McDonough and Fenton2022) [35] (Kumar *et al.* 2020) [28] (Do & Gries, 2021) [43]

Angiotensin II is secreted, via renin secretion, in response to renal juxtaglomerular cells' release of renin in response to β1 adrenergic and ATP release, as a means of increasing its secretion. This response occurs when the body requires an increase in vascular tone and reabsorption of water. Aldosterone is secreted, via the renin-angiotensin-aldosterone system, by the posterior pituitary's antidiuretic hormone and the atria of the heart, via the natriuretic peptide systems. Overall, the main way the body increases Na+ reabsorption is by releasing aldosterone, thus increasing the synthesis of Na+ channels and the Na/K pump function in the kidney—the distal nephron reabsorbs more Na+ and the collecting ducts release more H+ and K+. Decreasing Na+ reabsorption occurs through the atria of the heart, which

increase stretch from the increased extracellular fluid volume, thus releasing the atrial natriuretic peptide, making the DCT and the collecting ducts decrease Na+ reabsorption and increase K+ and H+ removal through the increase in the number of channels. It is the final regulation for natriuresis through GFR. Hydration state and dietary intake are important determinants for properly upregulating feedback mechanisms. The relationship between K+ and Na+ is that K+ secretion and reabsorption follow Na+ concentrations in the collecting duct. Both minerals directly influence one another by controlling their respective K+ and Na+ gradients between the lungs and the capillaries, acting on the cell membrane potential. Via the role of influencing the membrane potential on neurons and muscles, both K+ and Na+ control entire homeostasis in the human body. Thus, disturbances will lead to dysfunctions in these areas of the body. (Rossi *et al.*, 2020) [44] (Rossi *et al.*, 2020) [44] (Tsilosani *et al.*, 2022) [45] (Palmer & Clegg, 2022) [46]

4. Clinical significance of sodium and potassium imbalance

Alterations in sodium and potassium homeostasis could have significant implications for health, and therefore these electrolytes should be closely monitored in disease as well. Essential hypertension and cardiovascular diseases are common disorders. A high dietary intake of sodium has been related to the development of high blood pressure or hypertension. Being hypertensive may increase the risk for heart disease, stroke, degenerative chronic kidney disease, peripheral arterial disease, and death. Those with diabetes, chronic kidney disease, and metabolic syndrome are more vulnerable to these adverse cardiac consequences of a high dietary intake of sodium. (Rusmevichientong *et al.* 2021) [47] (Kurnianto *et al.* 2020) [48]

Sodium concentration can be regulated rapidly and precisely in the short term by the concentration of aldosterone, atrial natriuretic peptide, arginine vasopressin, and the renin-angiotensin-aldosterone system, and in the long term by being regulated by the volume status. On the other hand, an abnormal decrease in the concentration of potassium in the plasma can impair the function of the excitable tissues including myocardium, which may result in hypokalemic periodic paralysis, palpitations, or rhabdomyolysis. By contrast, an abnormal increase in the plasma potassium concentration can be associated with twitching, cramping, or weakness, and has been considered a toxin that impairs neuromuscular function. (Murano *et al.* 2021) [49] (Lindinger & Cairns, 2021) [4] (Jones *et al.*, 2021) [50] (Liu *et al.*, 2024) [51]

4.1 Hypertension and cardiovascular disease

Hypertension is a widespread issue associated with increased cardiovascular disease risk and mortality. The classic study showed that every rise of 20 mmHg in systolic blood pressure increased the risk of developing cardiovascular disease by two times. It was also calculated that moderating sodium intake by 50 mmol/day could lower the blood pressure of hypertensive patients by an average of 2.5 mmHg diastolic, thus significantly diminishing cardiovascular disease risk. In different communities around the globe, some of which were in industrialized countries, coronary heart disease and stroke were directly correlated with the amount of sodium consumed. A recent analysis of different clinical studies showed a positive correlation of sodium intake with blood pressure, even in people of normal blood pressure, as well as between urine sodium and cardiovascular disease. Low sodium levels have been shown to be associated with a higher cardiovascular disease risk because undernourishment leads to plasma volume depletion, activating the renin-angiotensin system that in turn increases the reabsorption of sodium. (He *et al.* 2021) [52] (Gholizadeh-Moghaddam *et al.* 2023) [53] (Filippini *et al.* 2022) [54]

Moderate cardiac myocyte necrosis is often seen after the ingestion of a high sodium chloride meal due to the accumulation of arginine vasopressin and the sympathetic nervous system, eventually leading to renin-angiotensin-aldosterone system activation. Observed in older subjects, the elevation of ambulatory blood pressure caused by the addition of salt can be countered by lowering or changing a person's sodium intake. Eating an assortment of diets where more potassium than sodium is consumed has been shown to diminish individual and countrywide blood pressure levels. These changes also have been shown to minimize an individual's long-term risk for developing high blood pressure. Public health interventions, like the installation of national programs to support these dietary lifestyle changes, could have a substantial impact on the prevalence of hypertension worldwide. Excessive sodium, primarily through the effects of volume expansion, causes a frequent rise in blood pressure. (Nkosi) [55] (Felemban and Hamouda 2024) [56] (Vallinoto *et al.*, 2022) [57]

4.2 Hypokalemia and hyperkalemia

Hypokalemia, commonly defined as serum potassium levels of less than 3.5 mEq/L, should be approached cautiously because the severity of the presenting clinical condition depends on the velocity at which the disturbance occurred. The clinical manifestation of hypokalemia depends on the rate at which potassium is lost or translocated into cells. The symptoms are possibly related to the severe intracellular potassium deficiency. The most frequent disorders associated with hypokalemia and elevated 24-hour urinary potassium excretion are diarrhea and vomiting, causing significant potassium loss. Malabsorption of potassium may happen in celiac disease, surgery, or inflammatory bowel disease. The most common cause of hypokalemia in patients with essential hypertension is diuretic treatment. (Alfano *et al.* 2021) [58] (Abensur *et al.* 2020) [59] (Virojanawat *et al.* 2021) [60]

The potassium level of six patients with colonic adenomas was significantly lower than that of sex- and age-matched controls. The magnitude of risk for colonic adenomas was similar with the gender, age, and localization of colonic adenomas matched controls and was significantly higher in hypokalemic patients. The most frequently occurring clinical complication behind these fractures was vertebral compression fracture, which accounted for over 60% of all osteoporosis fractures observed in hypokalemic patients. (Zhang *et al.* 2021) [61] (Rizzello *et al.* 2023) [62] (Virmani *et al.* undefined) [63]

Hyperkalemia of its association with life-threatening heart rhythm abnormalities. It can be caused by the kidney being unable to excrete potassium or from the release of potassium from the cells. The symptoms of hyperkalemia can be vague, but some serious warning symptoms to look for are chest pain, shortness of breath, or weakness. Early clinical features of hyperkalemia are nonspecific and include fatigue, malaise, and irritability. The above case discusses hypokalemia and hyperkalemia symptoms, diagnosis, and treatment. The

routine testing for potassium is the serum potassium concentration. The normal serum potassium level is usually considered to be between 3.5 and 5.0 milliequivalents per liter (mEq/L). However, arousing concern are tissues such as the heart, muscles, and nerves. Functionality tests can be performed to measure the activity of the muscles, the nerve function, and the acid-base balance. Such tests include electrocardiography and electromyography of muscles. Serum potassium level is one of the few blood tests available to diagnose hypokalemic paralysis. (Rauf and Naim2021) [64] (Tinawi, 2020) [65] (John & Pasha, 2024) [66]

5. Diagnostic methods for assessing sodium and potassium levels

INTRODUCTION: Accurate measurements are essential in order to establish whether a person's sodium or potassium level has reached a quantifiable level of the opposite condition, no matter if it is hyper or hyponatremia, as this could be due to the normal compensatory mechanism of osmotic regulation. The measurement of osmolarity could help identify it. In the case of decreased sodium, potassium level quantification is necessary in order to differentially diagnose and establish aetiology. BLOOD TESTS: The blood test that is used to measure plasma or serum sodium measures the sodium content in the blood vessels. Four types of analyses are used for sodium measurement: direct potentiometry, indirect ion-selective potentiometry, flame photometry, and photometric test. By using this test, further information can be found, such as the sodium/potassium ratio expressed as a fraction, which could be useful for diagnosis and treatment, and the osmolarity, which should be established especially in subjects with CNS symptoms and initially normal sodium. The potassium blood test normal value reflects the amount of serum potassium concentration with a small addition due to the potassium present inside platelets and white blood cells, which is released by hemolysis. The majority of laboratories have the possibility to test potassium serum or plasma concentration, with further distinction between direct potentiometry and indirect ion-selective potentiometry. URINE TESTS: Urine tests are complementary and allow assessment of the pathologic loss or retention of these electrolytes, to confirm the origin of hyponatremia or hyperkalemia, and to measure their concentration in selected types of specimens. Twenty-four-hour urine volume and concentration may be performed in some pathologic conditions; in general, testing pH or biochemical electrolytes in twenty-four-hour urine seems more appropriate for identifying other acid-base abnormalities. Some of the above-mentioned difficulties can be overcome using the urinary Na concentration. Even if a four-hour collection might be optimal, a random Na test is practically useful: it is obtained by sending a random urine sample to the laboratory in the late morning, obtained after three to four hours of fasting. Even if the patient may provide a split specimen directly in the laboratory, Na from a random morning urine is also well correlated with true twenty-four-hour creatinine clearance. If the value is <20 mmol/L, it represents some doubts and needs to be confirmed with a twenty-four-hour collection. However, if it is >30 mmol/L, a loop diuretic use, pseudohyponatremia, or inappropriate therapeutic management should be investigated. (Kalra *et al.* 2024) [67] (Merrill & Chambliss, 2020) [68] (Bennet *et al.* 2021) [69]

5.1. Blood Tests

Blood tests are the most common method used to measure the concentrations of sodium and potassium in the body. The "serum electrolytes" test is a blood test that is often ordered as part of a test panel or "chemistry panel" to evaluate one's general state of health or to assess a specific medical problem. "Serum" means that the fluid part of the blood is tested from which cells and proteins are residing. The weight/30 volume concentration of salt within these fluids' changes in chronic cardiorenoal-cerebral disease and states of chronic disorder as it does in acute volume-depleted subjects. Reference ranges are derived from patient results and suggestions of mean, standard deviations, or percentiles. Pathological data can be used to determine the percentage of patients suffering from the condition at the time of the measurement. If an electrolyte test is requested, the chance of the measuring value being within the reference range for 95% of "normal" individuals can be over 90%. But each illness changes the reference range of the electrolytes. The blood samples most frequently requested for the concentrations of Na+ and K+ can be collected from any vein. (Rasheed *et al.* 2023) [70] (Zaitsev *et al.*, 2020) [71] (Mulatero *et al.* 2020) [72] One type of blood test often used to evaluate the electrolyte composition of the body is called a "comprehensive metabolic panel." This panel provides more information about the body than a "basic chemistry panel." With an electronic blood pressure meter, the heart rate is also measured. Another type of basic blood test commonly used to evaluate the general state of health or to assess a person with a specific medical problem is called a "basic metabolic panel." The medical caretaker may want to rule out tetany. There are several things that can affect this test, including hydration status and various medications. There is a major advantage and significant limitation with the reference range. The reference range answers the question of what the ordered test has been developed to measure. If a physician suspects a problem and orders the test, the result is interpreted within the clinical setting. It is important to be hydrated, while not singularly stemming salt or water intake, as it will "dilute" the data for subsequent measurements as the Na+ or K+ more quickly shift in blood or electrolyte fluid volumes. (Gava *et al.* 2021) [73] (Carobene *et al.* 2022) [74] (Pan *et al.* 2021) [75]

Accurate measurements of the fluids require the collection of the specimen with approved and validated vacutainers and sufficient recommended mixing, decanting, filling, and handling protocols accompanied by corrosion-inhibited instrumentation. The reflection of blood test results is used in the fields of surgery, anesthesiology in the intraoperative and postoperative period, in traumatology, neurology, internal medicine associated with coexisting medical conditions or prior modalities of medical evaluation, and so on. The technicalities or interpretation given by statistical medicine to the electrophysiological and echocardiographic measurement requirements are also evaluated for their ability to measure severely low values of salt and water in children. Estimation of Na+ and K+ loss is a joint clinical criterion on the scale for electrolyte measurement spectrum to ensure the sufficiency for their respective test interpretation. If there is a suspicion of an electrolyte problem in a poorly functioning patient, urgent blood tests to evaluate the concentrations of Na+ and/or K+ may be needed. (Ing *et al.* 2020) [76] (Song *et al.* 2023) [77] (Lippi *et al.* 2020) [78]

5.2 Urine Tests

Urine concentration of sodium and potassium may be of value to distinguish disorders of renal tubular handling from errors in total body sodium and potassium balance. While serum levels of electrolytes reflect the state of body metabolism and intake, the concentrations in the urine are a direct result of the kidneys' handling of sodium and potassium. Most importantly, measuring the urine concentration of electrolytes can be used to distinguish whether the patient has a renal disease, a systemic disease, or an inappropriate intake of those electrolytes. A 24-hour urine collection can be used to measure the excretion of electrolytes over an entire day. A spot urine collection can be used to roughly determine the electrolyte excretion and urinary concentration within a smaller time frame of around 1 hour. However, both tests can only be used to obtain a rough idea of the excretion of the electrolytes and metabolism of the body. (Gounden *et al.*, 2024) [79] (Oh *et al.* 2021) [80] (Umbrello *et al.*, 2020) [81]

If a 24-hour urine collection cannot be done, a spot urine collection can be used to obtain a rough idea of how much electrolytes are being excreted by the body. Urine sodium levels can range from 20 to 140 mmol/day, and urine potassium levels can range from 20 to 100 mmol/day. Urine results should always be compared alongside the serum results. The renal tubular handling of sodium and potassium can be accessed via the 24-hour urine collection. Urine osmolality, sodium concentration, and potassium concentration can be used to determine inappropriate diuresis. Only one urine test that is used to measure the concentration of the electrolytes has an effect, and that is the urine specific gravity result. The concentration of urine has almost the same information as urine osmolality, as it measures the level of dilution of urine carried out by the kidney. The specific gravity urine level should, therefore, be considered in conjunction with the osmotic urine level. A random urine can often be diluted due to the variations in fluid intake throughout the day. The hydration status of the patient should be taken into account to interpret these results. Often, the first urine that is produced in the morning by the patient is concentrated due to the patient's reduced intake of fluids. This can also be seen in the dehydration state. After drinking, the kidneys reabsorb excess fluid, and this can cause the urine to dilute. For this reason, it is important to check the time in which the urine sample was taken. Often, a high output of urine is seen in diabetic patients who have too high blood sugar levels. Therefore, whether the patient is diabetic or not needs to be taken into account. (Sonuch *et al.* 2021) [82] (Jaques *et al.* 2023) [83] (Islam *et al.* 2023) [84]

6. Treatment and management of sodium and potassium disorders

Management of sodium and potassium disorders depends on their etiology and severity. The key to managing these disorders is a systematic and focused approach, as their prevalence continues to increase in clinical settings and populations. Recognizing the impact of particular electrolyte disorders is essential to reduce the rate of associated complications, which are expected to increase due to the aging population and changes in dietary habits. Salt intake or prescription of potassium-sparing drugs should be limited in disorders of increased sodium. The intake of sodium should be restricted in the treatment of edema or ascites caused by water retention. Eating high-potassium foods is essential, and the restriction of potassium-containing ingredients is not usually required except in patients with kidney failure. It is important to have targeted plans that can be tailored to the desires and possibilities of each patient. It is also essential to allow individualization of treatment or nutritional recommendations based on the patient's lifestyle and dietary possibilities. (Adrogué *et al.*, 2022) [85] (Yamada & Inaba, 2021) [11] (Seay *et al.* 2020) [86]

Potassium levels could be corrected according to the cause only in hypokalemia in all cases. Drug treatment with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers that contribute to potassium retention may be started after resolution of hypokalemia. It is also prevented by eating potassium-rich foods. Dietary recommendations should also be implemented during periods of hypokalemia. Moreover, the need to implement lifestyle modifications is increasing to correct electrolyte disorders. Among the lifestyle recommendations are the need to practice exercise, reduce weight, and drink enough water. Health professionals such as the primary care physician and dietitian should make the final recommendations. The presence of a dietitian can also help adjust nutritional guidelines for fluid intake, sodium, protein, and potassium intake according to the patient's condition and ability to follow dietary guidelines. In addition, it is essential to determine a system of follow-up and evaluation after nutritional treatment or recommendations. (Schlüter and Cadamuro2023) [87] (Alfano *et al.* 2021) [58] (Chen *et al.* 2020) [88]

6.1 Pharmacological Interventions

There are numerous classes of medications that may influence sodium and potassium levels. Arguably the most clinically relevant in regard to electrolyte balance are the diuretic substances, which promote urinary excretion of sodium and water and raise potassium retention. The effect of diuretics results in decreased fluid load with the loss of sodium that draws more fluid into the urine from the body. The net effect is reduced plasma volume, which has outcomes in blood pressure control and reduced edema. However, chronic use of diuretics can lead to imbalances of sodium and potassium, which can further lead to blood pressure disorders of hypotension and muscle weakness. (Guo *et al.*, 2023) [89] (Patel *et al.*, 2022) [90] (Vern, 2023) [91]

There are other classes of antihypertensive medications that can directly modulate renal handling of sodium and indirectly influence potassium excretion. Angiotensin-converting enzyme inhibitors can modulate glomerular filtration rates with an effect of lowering sodium and water retention. This effect on GFR can lead to a compensatory retention of potassium, and potassium-sparing antihypertensive medications are used when high dosage ACE inhibitors or angiotensin type 1 receptor antagonists are used. This kidney-modulating potassium-sparing antihypertensive effect is also used to counteract the potassium-wasting effects of diuretics. Prerenal hypoxic kidney disease can have lower sodium resorbing ability by the kidney, which leads to systemic sodium loss. As a result, symptomatic hyponatremia requires attention, and antihypertensive medications that lower urine sodium excretion need dosage adjustment to prevent accumulation. An inability to excrete combined sodium and water leading to hypertension and secondary heart failure can be treated with a necessary combination of antihypertensive diuretic medications. Monitoring and documenting adverse effects of medications are important in identifying cases of

electrolyte imbalance. (Capolongo *et al.* 2022) [92] (Wilcox, 2020) [93] (McArdle *et al.* 2023) [94]

7. Future research and developments

The study of electrolytes in health and disease is far from over, and future research studies will further increase our understanding of these biochemical entities, both in terms of physiology and their clinical importance. Some of the future directions of research and developments in sodium and potassium include the following: Ongoing studies have now reversed our long-held belief that potassium is the good guy and sodium is the bad guy. It is the study of the complex roles of these two electrolytes in making up their protective virtues. There is an increasing possibility of designing molecules that will rid the body of excess sodium or those that stimulate the retention of potassium. Novel targets include the aldosterone-mineralocorticoid pathway with the development of nonsteroidal and selective mineralocorticoid receptor antagonists, as well as aldosterone antisera. More analytical advances are probably in the development of selective sodium and potassium electrodes for point-of-care—easy-to-use clinical diagnostic equipment. The knowledge of the physiological and pathophysiological intestinal and renal regulating factors and mechanisms for sodium and potassium should connect the fields of physiology and clinical pharmacology. There is a pressing need to understand the clinical impact of changing potassium and sodium foods on public health and disease outcomes. (Bu *et al.* 2024) [95] (Bruen *et al.* 2022) [96] (Walker, 2024) [97]

Future studies investigating some of the aforementioned potential therapeutic approaches to lowering blood pressure include blockade of the sodium entry pathways, endothelin antagonism, angiotensinergic therapies that do not cause hyperkalemia and thus reduce aldosterone levels, and the central action of inhibitors of sodium location. An understanding of the altered sodium/potassium biochemical set point for patients with congenital and acquired channelopathies could theoretically help in the design of future therapeutic advances in ongoing cooperation between research and clinical pharmacology into the underlying molecular mechanisms. (Puljko *et al.* 2022) [98] (Warren *et al.* 2023) [99] (Mendes *et al.* 2024) [100]

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