FLUIDS AND ELECTROLYES 2

Sodium is the principle extracellular cation. It is present in the ECF at a concentration of about 140 mmol/L. There is small increase in amount of sodium on the plasma side compared to the ISF of about 6-7 mmol due to the Gibbs-Donnan effect but the measured levels are usually very similar because the plasma solid effect reduces the measured amount in the PV by about 7%. In ICF the sodium concentration is much lower due to the Na.K.ATPase pump, and the impermiability of the bi-lipid cell wall. It is in the range of 10-20mmol/L depending on specific cell. The total distribution of sodium in the body is ECF = 50%, ICF = 5% and bone 45% and the total amount is approximately 60mmol/Kg. Sodium principlally maintains serum osmolality and ECF volume. Sodium plays a crucial role in the generation of the cell membrane action potential. Disorders of sodium concentration (hyper or hyponatraemia) usually result in from a relative deficit or excess of water respectively. Serum Na^+ concentration and total body Na^+ are closely regulated by renal functions. Sodium is easily filtered by the glomeruli of the kidneys, and most of it reabsorbed by the renal tubules. Several hormones, including aldosterone, ANP, and vasopressin control the reabsorption of sodium and water to maintain the amount of total body Na^+. Aldosterone is responsible for renal Na^+ reabsorption in exchange for for K^+ and H^+ in the distal convoluted tubules and the collecting ducts of the kidneys. Atrial naturetic peptide has an opposing effect by increasing renal excretion of Na^+ it tends to decrease plasma volume. Normally, changes in serum Na^+ and osmolality lead to an appropriate change in vasopressin release by the posterior pituitary which in turn can vary renal free water excretion (urine osmolality 50-1400) in order to maintain Na^+ in the normal range. Daily intake of sodium is approximately 10.5g (457mmol) since (at rest) 11 mmol is lost in faeces and 11 in sweat (nb this is highly variable) the kidneys must excrete the remaining 435 mmol (10g). The end result of these physiological processes is that in situations where there is Na^+ loss, for example diarrhoea or excessive sweating, renal Na^+ conservation is high and urinary Na^+ concentration falls to very low levels. However when Na^+ intake is excessive, decreased tubular reabsorption leads to the loss of increased sodium in the urine.

Potassium is the major intracellular cation and normally has an ICF concentration of 150mmol/L which is about 30 times that of the ECF (normal range 3.5-5). The total amount of potassium in the body is about 40-45 mmol/kg. The distribution of K^+ in the body is ICF = 90%, ECF = 2% and Bone = 8%. It is often said that potassium is 98% ICF and 2% ECF, and whilst this is factually incorrect it is useful from a clinical perspective because the bound potassium in the bone is not physiologically mobile therefore often ignored. Serum potassium is a function of two variables, the total body potassium and the distribution between ICF and ECF. There are numerous major functions of potassium in the body including cell volume regulation (as the major intracellular tonicity component and its role in the Na.K.ATPase pump), intracellular pH regulation, DNA and protien synthesis, growth, enzyme functions, resting membrane potential, cardiac and neuromuscular activity. Total body K^+ and serum K^+ are closely regulated by the renal tubules, so that potassium excretion is usually equal to daily potassium intake (1.5-5g per day). There are several hormones, including aldosterone, adrenaline and insulin that effects on K^+ concentration. Aldosterone facilitates sodium reabsorption in exchange of K^+, resulting in increased renal secretion of K^+ . Adrenaline and insulin alter K^+ by shifting it back into cells. Plasma K^+ is also influenced by the acid-base status this is because in acidaemia H^+ are preferentially excreted instead of K^+ leading to hyperkalaemia and visa versa. The most serious manifestations of hyperkalemia are muscle weakness or paralysis, cardiac conduction abnormalities, and cardiac arrhythmias this is caused by alterations in the generation of action potential. These manifestations usually occur when the serum potassium concentration is ≥7.0 meq/L with chronic hyperkalemia or possibly at lower levels with an acute rise in serum potassium. ECG changes include (progressively) peaked T wave, shortening of the QT interval, prolonged PR interval, p-wave flattening, widening of the QRS and finally a sine wave appearance, VF or asystole. Hyperkalemia also interferes with renal ammonium (NH4+) excretion, thereby limiting acid excretion and possibly leading to the development of metabolic acidosis. The pattern of weakness in hypokalemia is similar to that associated with hyperkalemia. In addition to causing muscle weakness, severe potassium depletion (serum potassium less than 2.5 meq/L) can lead to muscle cramps, rhabdomyolysis, and myoglobinuria. A variety of arrhythmias may be seen in patients with hypokalemia. These include premature atrial and ventricular beats, sinus bradycardia, paroxysmal atrial or junctional tachycardia, atrioventricular block, and ventricular tachycardia or fibrillation. Hypokalemia produces characteristic changes on the ECG although they are not seen in all patients. There is depression of the ST segment, decrease in the amplitude of the T wave, and an increase in the amplitude of U waves which occur at the end of the T wave. Hypokalaemia may also lead to renal abnormalites and gluclose intolerance (through the decreased excretion of insulin).

Calcium is found predominantly in the bone (99%) and the ICF (1%). Serum calcium is approximately 40% protien bound (mostly albumin), 10% chelated to serum anions and 50% in free ionised form. It is the latter which has an ECF concentration of 1-1.5 mmol/L which is the physiological active component. Ionised calcium (Ca^{2+}) in the ICF is at a concetration of approximately 50 mmol/L. Ca^{2+} performs many important functions including neuromuscular transmission, excitation-contraction coupling in muscles, release of hormones and neurotransmitters, enzyme activation, blood coagulation, and bone structure. It is also an important intreacelllular second messenger. Calcium is regulated by two primary hormones, parathyroid hormone (PTH) and 1,25 dihyroxy-vitamin D (activated vitamin D). Both of these are secreted in response to a decrease in serum ionised Ca^{2+}, and stimulate Ca^{2+} release from bone, reabsorption from the renal tubules and absorption from the intestines. They are able to maintain a tight calcium control even in the setting of decreased intake. Patients with mild hypercalcemia (calcium [3 mmol/L]) may be asymptomatic, or they may report nonspecific symptoms, such as constipation, fatigue, and depression. A serum calcium of (3 to 3.5 mmol/L) may be well-tolerated chronically, while an acute rise to these concentrations may cause marked symptoms, including polyuria, polydipsia, dehydration, anorexia, nausea, muscle weakness, and changes in sensorium. As calcium is an inotrope the cardiovascular symptoms/signs are shortening of the QT interval, bradycardia, hypertension. Hypocalcemia may be associated with a spectrum of clinical manifestations), ranging from few if any symptoms if the hypocalcemia is mild, to life-threatening seizures, refractory heart failure or tetany (initally perioral tingling, then sensorium changes and cramps progressing to laryngospasm) if it is severe. In addition to severity, the rate of development of hypocalcemia and chronicity determine the clinical manifestations.

Magnesium is the fourth most common cation in the body and is found mostly in the ICF and in the bone. Of total body Mg^{2+} , 99% is intracellular and only 1% is extracellular. Of the normal serum, Mg^{2+} (normal range 0.8-1.2mmol/L) free 'ionised' Mg^{2+} represents approximately 50% this amount and is the physiologically active component. Serum Mg^{2+} is regulated by renal excretion. Free Mg^{2+} is an essential co-factor for ATP requiring enzymes such as the cell membrane Na.K.ATPase pump and more than 300 enzymes involved in energy metabolism. Mode of action: Many processes are dependent on magnesium (Mg^{2+}) including the production and functioning of ATP (to which it is chelated) and the biosynthesis of DNA and RNA. It has an essential role in the regulation of most cellular functions. It acts as a natural calcium (Ca^{2+}) antagonist. High extracellular Mg^{2+} leads to an increase in intracellular Mg^{2+}, which in turn inhibits Ca^{2+} influx through Ca^{2+} channels. It is this non-competitive inhibition that appears to mediate many of its effects. It also competes with calcium for binding sites on sarcoplasmic reticulum thereby inhibiting its release. High concentrations inhibit both the pre-synaptic release of ACh and as well as post-junctional potentials. Mg^{2+} also has an antiadrenergic action: release at all synaptic junctions is decreased, and it inhibits the release of catecholamines. Central and peripheral nervous systems : Magnesium penetrates the blood–brain barrier poorly, but it nevertheless depresses the CNS and is sedating. It acts as a cerebral vasodilator, and it interferes with the release of neurotransmitters at all synaptic junctions. Cardiovascular: It mediates a reduction of vascular tone via direct vasodilatation. It also causes sympathetic block and the inhibition of catecholamine release. Magnesium decreases cardiac conduction and diminishes myocardial contractile force. This intrinsic slowing is opposed partly by vagolytic action. Respiratory: Magnesium has no effect on respiratory drive, but it may weaken respiratory muscles. It has some bronchodilatory effects hence its use in asthma. Uterus It is a powerful tocolytic, which has implications for mothers who are being treated with the drug to control hypertensive disease of pregnancy prior to delivery. Normal adult requirements are 0.4 mmol/L/kg/day orally or a quarter this parentally. Magnesium replacement has been shown to reduce arrythmias in post MI patients even when initially magnesium replete although the mechanism for this is not clear. It is also used in pre-eclampsia and acute severe asthma. Hypomagnesaemia is common in critically ill patients and many drugs, including catecholamines, aminoglycosides and diuretics will lower this further. The symptoms of low magnesium are variable, the most concerning is the increased risk of arrhythmias. Hypermagnesaemia is more clearly defined. Initial symptoms include nausea, vomitting and drowsiness. ECG changes occur from the range of 2.5-5, and are characterised by increased PQ and widened QRS. At roughly 5.0 loss of the patellar reflex In the range of 6-8 there is a respiratory paralysis, 7.5 complete heart block and finally at greater than 12 asystole.

Phosphate is found mostly inside the cell. Bone accounts for 85%. The normal serum phosphate level ranges from 0.8 to 1.3 mmol./L in adults. Serum phosphate is regulated by renal excretion. It follows that the most common cause of hyperphosphotaemia is renal failure (others include tumour lysis syndrome, rhabdomyolysis and lactic acid ketoacidosis). Phosphate plays a vital role in oxidative phosphorylation of carbohydrate, fat and protein metabolism. Phosphate is a structural component of nucleic acids, phopholipids and the cell membrane. It is also essential for intracellular second messenger systems including cAMP and IP3. As part of 2,3 DPG it assists in the offloading of oxygen from Hb to tissue. Hyperphosphotaemia is symptomatic when the increased binding of calcium leads to hypocalcaemia (seizures, heart failure and eventually tetany). Hypophosphotaemia is common in intensive care patients and may cause muscle weakness. It is often used as a marker of refeeding syndrome.

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