Electrolytes and acid–base: common fluid and electrolyte disorders

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Abstract

Disturbances of fluid and electrolyte balance are common in clinical practice, especially in a hospital setting, and may be iatrogenic or compounded by inappropriate medical or surgical treatment. Their recognition and appropriate management are not necessarily difficult or complex; while specific formulae and standard protocols can be helpful at the bedside, there is no substitute for an understanding, and application, of some basic principles of renal and endocrine physiology, which this article sets out. Some knowledge of basic renal physiology (including transport function along the nephron and its regulation) also makes it easier to understand most clinical disorders of fluid and electrolyte balance. Unfortunately, patients seldom present with a single acid–base or fluid and electrolyte disturbance, so the real challenge is to determine which disorder came first, before rushing in and treating in isolation what might seem to be the major clinical abnormality. The article will start by describing the main homeostatic functions of the kidney and, more specifically, the essential workings of its functional unit, the nephron (glomerulus and renal tubule).

Keywords acid–base; nephron structure; potassium; sodium; water balance

The nephron (Figure 1)

At a normal glomerular filtration rate (GFR) of 125 ml/minute, the volume filtered by the glomerulus is approximately 180 litres/day, which contains about 25,000 mmol of Na^+. The filtrate is so large that the renal tubule is concerned principally with reabsorption, although it is also involved in the secretion of a few ions (H^+ and K^+) and other solutes, such as weak organic acids and bases (including some drugs and metabolites). Most of the reabsorptive (transport) processes, including the transport of glucose, amino acids, bicarbonate, phosphate and calcium, occur in the proximal tubule, which can be divided into three parts (S1, S2, S3), and the loop of Henle (LOH). However, the different parts of the distal tubule and collecting duct (CD) have an important role in determining the final urinary excretion of Na^+, K^+ and H^+, and also of water.[1]

In the distal tubule and along the CD, reabsorption of Na^+ and Cl^- continues, and their final urinary excretion is usually less than 1% of what is filtered (known as the fractional excretion); whereas net secretion of K^+ and H^+ occurs in these nephron segments. Some Ca^{2+} and Mg^{2+} reabsorption also takes place in the distal tubule. Water reabsorption in the distal nephron varies, depending on the concentration of circulating vasopressin (AVP; antidiuretic hormone, ADH), which is determined by plasma osmolality and extracellular fluid volume (ECFV) status.

Most of the transport processes taking place along the renal tubule are coupled directly or indirectly to the reabsorption of Na^+. Sodium ions enter the lining epithelial cells passively from the lumen (filtrate) across the apical cell membrane and down its concentration (strictly, its electrochemical) gradient via a series of transporters (co-transporters and exchangers) or Na^+ channels. Its exit across the basolateral membrane requires the 'sodium pump' (Na^+/K^+-ATPase), which is ultimately responsible for most of the reabsorptive and secretory processes in the renal tubule (except for a few other pumps transporting H^+, Ca^{2+}, and H^+/K^+ exchange that are also energy-requiring ATPases). Indeed, the mechanism of Na^+ reabsorption is essentially the same throughout the tubule; only the route of entry into the cell differs from one segment to another.[1] Sodium is the dominant extracellular cation, and the main determinant of osmolality in the ECFV and of water distribution between extracellular and intracellular fluid compartments. Its balance is critically important in maintaining the circulating blood volume (which is part of the ECFV) and arterial blood pressure (BP). Hence, many of the extrinsic regulators of renal function are intended to alter Na^+ excretion, preserve sodium balance and regulate BP.[1]

The main extra-renal Na^+-controlling mechanisms

Positive or stimulatory

- ***Aldosterone*** is the major regulator of Na^+ reabsorption (and K^+ and H^+ secretion) in the distal nephron; it is secreted by the zona glomerulosa of the adrenal cortex in response to a raised plasma angiotensin II concentration or a high plasma concentration of K^+. Aldosterone stimulates the sodium pump and the apical Na^+ channel (the epithelial sodium channel, ENaC) of *principal cells* in the CD; this increases electrogenic Na^+ reabsorption, which depolarizes the apical membrane and facilitates K^+ secretion by these cells (as well as H^+ secretion by adjacent, acid-secreting *intercalated cells*).
- ***Angiotensin II and sympathetic nerve (noradrenaline) stimulation*** both increase Na^+ reabsorption, mainly in the proximal tubule, but they also reduce GFR by causing efferent and afferent arteriolar vasoconstriction, respectively.
- ***Vasopressin***, in addition to its key role in water handling, increases urea reabsorption in the medullary CD and may also have a minor though significant stimulatory effect on Na^+ reabsorption in this nephron segment.

Negative or inhibitory

- ***Atrial natriuretic peptide*** is released from the cardiac atria in response to stretch; it increases Na^+ excretion by suppressing the renin–angiotensin–aldosterone system and directly inhibiting Na^+ reabsorption in the (medullary) CD.

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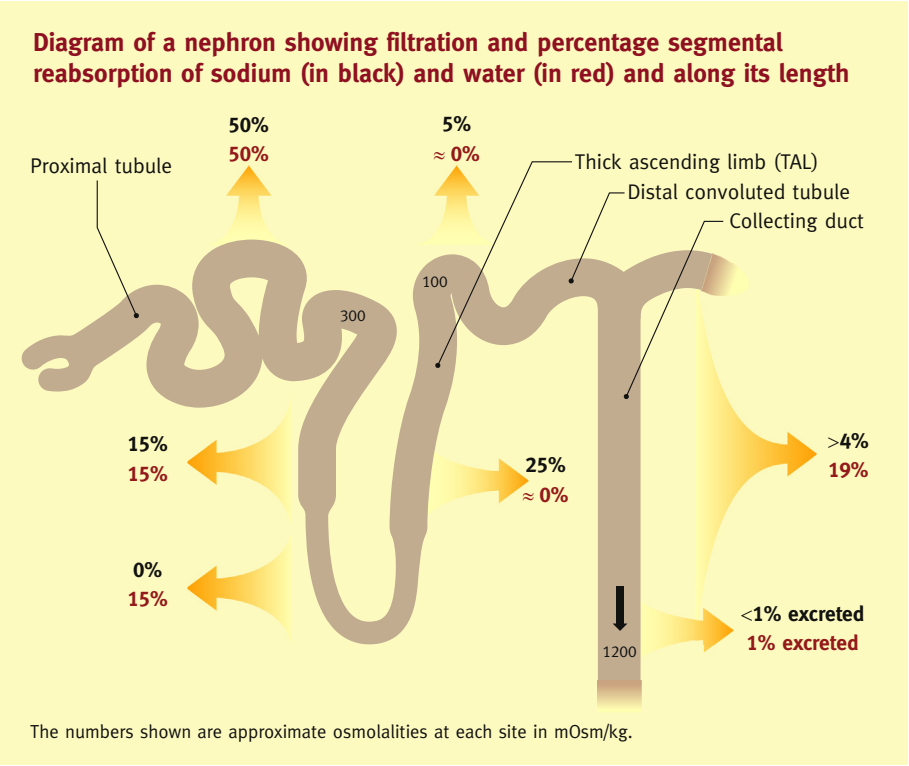

Figure 1

- ***Other factors*** that act locally (paracrine), such as endothelin-1, bradykinin and nitric oxide, all seem to inhibit Na^+ reabsorption along the CD.

Some of the factors listed above also affect vascular tone directly: angiotensin II, vasopressin and endothelin-1 act as vasoconstrictors, whereas atrial natriuretic peptide, bradykinin and nitric oxide act as vasodilators.

Water handling

Vasopressin is the key regulator of water reabsorption along the distal nephron (distal tubule and CD), where it binds to basolateral V2 receptors and stimulates adenylate cyclase, leading to insertion of apical water channels (aquaporin-2, AQP2). However, vasopressin cannot act in the absence of a corticomedullary osmotic gradient that increases progressively from the cortex to medulla (~300–1200 mOsm/kg). This gradient is established and maintained by the active reabsorption of Na^+ (without water) along the thick ascending limb (TAL) of the LOH (the counter-current multiplier system); it also generates the solute-free water (in the so-called 'diluting segment' – about 100 mOsm/kg – Figure 1) that is then concentrated by the action of vasopressin along the CD.

Acid–base excretion

The renal tubule is also the major regulator of acid–base balance; it is the site of bicarbonate (HCO_3^-) reabsorption and H^+ secretion. Bicarbonate reabsorption occurs predominantly in the proximal tubule by Na^+/H^+ exchange, which reclaims the normally filtered HCO_3^- (Figure 2). Net H^+ secretion by an ATPase along the CD determines final urine pH and acid excretion in the urine. To maintain H^+ balance the distal nephron must secrete about 1 mmol H^+/kg body weight per day (net acid excretion). Two important urinary buffer systems aid H^+ excretion: $HPO_4^{2-}/H_2PO_4^-$ and NH_3/NH_4^+. The amount of phosphate available as a buffer depends on its filtered load and is known as *titratable acid* (the H^+ it buffers can be estimated by titrating back to a normal plasma pH of 7.4). NH_3/NH_4^+ is generated in the proximal tubule by the metabolism of glutamine; its production is significantly stimulated by acidosis and hypokalaemia, and inhibited by alkalosis and hyperkalaemia. Figure 2 illustrates the mechanisms of acidification in the proximal tubule and CD.

Effective arterial blood volume (EABV)

EABV is a useful clinical concept that refers to the blood volume on the arterial side of the circulation (remember that most of the blood volume is on the venous side), which is available for organ and tissue perfusion. It may be reduced because of a true fall in circulating volume (as in haemorrhagic shock), an apparent fall due to 'pump' or heart failure (as in cardiogenic shock), or a relative fall (relative to capacity) due to arterial vasodilatation, as in septic shock, liver failure (the hepato-renal syndrome) or the nephrotic syndrome. Hence, EABV is the arterial blood volume judged necessary to maintain adequate tissue perfusion.

The commonest clinical electrolyte and acid–base derangements (see Clinical approach to electrolyte abnormalities on pages 381–388 of this issue for detailed guidance on clinical management)

Hypo- and hypernatraemia

Both are primarily problems of water, rather than sodium balance. Plasma sodium concentration (P_{Na}) represents the ratio of the amount of sodium to water in the ECFV. Hyponatraemia (P_{Na}

