Electrolyte quintet

Potassium

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In a logical, stepwise approach to patients presenting with hypokalaemia or hyperkalaemia the clinician must first recognise circumstances in which the dyskalaemia represents a clinical emergency because therapy then takes precedence over diagnosis. If a dyskalaemia has been present for a long time, there is an abnormal renal handling of K^+. The next step to analyse is the rate of excretion of K^+ and, if necessary, its two components (urine flow rate and K^+ concentration in the cortical collecting duct [CCD]) analysed independently. If the K^+ concentration in the CCD is not in the expected range, its basis should be defined at the ion-channel level in the CCD from clinical information that can be used to deduce the relative rates of reabsorption of Na^+ and Cl^- in the CCD. This analysis provides the basis for diagnosis and may indicate where non-emergency therapy should then be directed.

Our approach to the patient who presents with hyperkalaemia or hypokalaemia is illustrated by two clinical cases (a more complete description can be found elsewhere[1–3]). At the outset, only the plasma potassium concentration ($[K^+]$) will be provided (7·4 mmol/L in the first patient and 1·5 mmol/L in the second), relevant information then being revealed step-by-step in a logical progression towards a final diagnosis. However, because hyperkalaemia or hypokalaemia can be life-threatening, therapeutic issues precede diagnostic ones. We will begin by discussing the principles of K^+ homoeostasis,which is the backbone to our clinical approach.

Potassium homoeostasis

K^+ is the most abundant cation in the body. 98% of the total 4000 mmol is in the intracellular fluid (ICF) compartment, only 60 mmol being in the extracellular fluid (ECF) of an adult. The ICF:ECF $[K^+]$ ratio reflects the resting membrane potential (RMP); this potential remains more or less constant in the face of a daily intake of K^+ that approximates the total ECF K^+ content.[2,4]

Acute regulation

The major force that keeps K^+ inside cells is a negative voltage; this is created initially by active transport of cations out of cells by Na^+/K^+-ATPase, which exports three sodium ions (Na^+) in exchange for two K^+ (figure 1).[5] There is thus a nett export of one-third of a positive charge per Na^+ ion transported, providing there is no nett gain of positive charge when Na^+ ions enter cells. Most K^+ ions that enter cells exit by a K^+ channel, carrying one positive charge per K^+, and this contributes most of the RMP. Except in rare conditions such as barium poisoning, dyskalaemia is seldom related to changes in K^+ channel acticity.

The two major hormones promoting a shift of K^+ into cells are insulin and catecholamines. Both result in the export of Na^+ plus positive voltage but the mechanisms differ. With insulin, the Na^+ that is extruded had entered

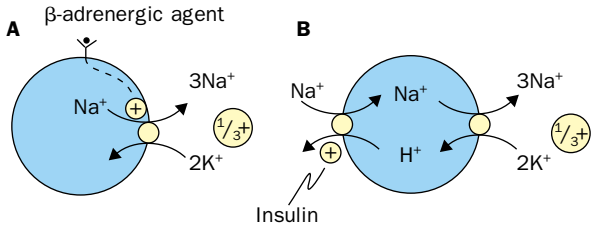

Figure 1: **Hormones shifting K^+ into cells**
Major hormones involved are: (A) insulin and (B) β_2-adrenergic agents.

cells electroneutrally because Na^+ entry accompanies H^+ exit on the electroneutral Na^+/H^+ exchanger.[6] When β_2-agonist agents shift K^+ into cells this is probably due to activation of Na^+/K^+-ATPase,[7] with intracellular Na^+ as the substrate for this ion pump (figure 1).

A similar rationale determines whether K^+ will redistribute across cell membranes when acids are added to the body. Most H^+ ions are buffered in the ICF compartment. A shift of K^+ will only occur if the anion that accompanies added H^+ remains in the ECF. Therefore when H^+ enters cells, Na^+ exits, leaving less Na^+ in the ICF to be exported in an electrogenic fashion[8,9] so the RMP will become less electronegative. The converse could explain the K^+-lowering effect of $NaHCO_3$. As H^+ exits from cells, Na^+ enters electroneutrally; there is now more Na^+ in cells to be transported by Na^+/K^+-ATPase so

Panel 1: **Glossary and equations**

Abbreviation	Explanation
ADH	Antidiuretic hormone
AME	Apparent mineralocorticoid excess
CCD	Cortical collecting duct
ECF	Extracellular fluid
ENaC	Epithelial Na^+ channel
11β-HSDH	11β-hydroxysteroid dehydrogenase
ICF	Intracellular fluid
$[K^+]$	Concentration of K^+
N^+/K^+ ATPase	Ion pump in cell membrane (figure 2)
RMP	Resting membrane potential
TBK^+	Total body potassium
TTKG	Transtubular $[K^+]$ gradient

Equations*

K^+ excretion = $U_{vol} \times [K^+]_u$

Flow rate in CCD = $(U_{osm} \times U_{vol}) \div P_{osm}$

TTKG = $([K^+]_u) \div (U_{osm}/P_{osm}) \div [K]^+_p$

*U=urine, P=plasma, vol=volume, osm=osmolality.

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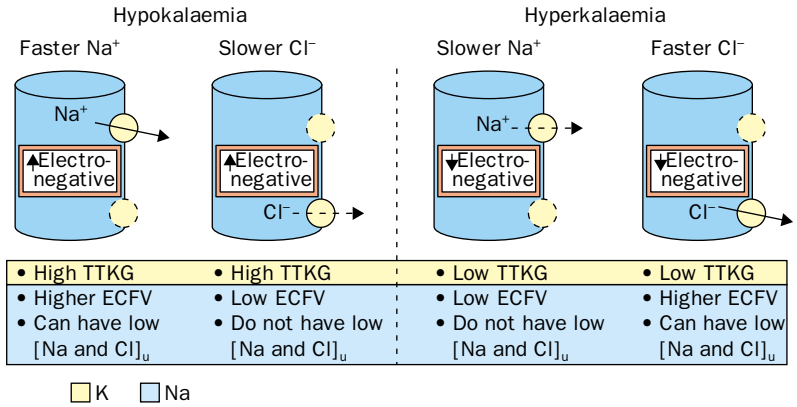

Figure 2: **Components of K^+ excretion in CCD**

Barrel-shaped structures represent CCD. Normal pathways for Na^+ and Cl^- reabsorption shown by rectangles in luminal membrane; slower pathways indicated by smaller open circles with dashed lines and faster ones by open circles with bold arrows. (Reproduced, with permission, from ref 28.)

the RMP will become more electronegative.

Clinical points follow from this analysis. If hyperkalaemia is present in a patient with lactic acidosis or ketoacidosis, its cause will probably be tissue injury and/or an effect related to lack of insulin rather than acidosis as the accompanying lactate or ketoacid anions enter cells along with H^+. Although hyperchloraemic metabolic acidosis causes a shift of K^+ from the ICF,[10] patients with diarrhoea or distal renal tubular acidosis usually present with a normal or low plasma [K^+] because of a loss of K^+.[11] A defect in K^+ excretion should be suspected if hyperkalaemia persists in these patients.[9]

Long-term regulation

Since the kidney regulates long-term balance of K^+, virtually every patient with a chronic dyskalaemia will have a renal (or adrenal) abnormality.[1,2] The rate of excretion of K^+ is the product of urine flow rate multiplied by urinary [K^+], and each factor must be analysed independently. Since the major site of regulation of the excretion of K^+ is the cortical collecting duct (CCD)[12] one should deduce why urine flow rate, urinary [K^+], or both were altered in terms of events in this nephron segment. (Equations relating to K^+ excretion are given in the glossary.)

For there to be a nett secretion of K^+ in the CCD there must be K^+ channels in the luminal membrane of the CCD and an electrical driving force with a lumen-negative voltage. K^+ channels are both abundant and have a high probability of being "open"; they do not seem to be rate-limiting for the excretion of K^+. The generation of a lumen-negative voltage in the CCD requires electrogenic reabsorption of Na^+—ie, reabsorption of Na^+ is faster than reabsorption of its accompanying anion, which is usually Cl^- (figure 2).

Reabsorption of Na^+ occurs via its specific epithelial Na^+ channel (ENaC) in the apical membrane of principal cells.[13] Aldosterone is the most important factor that causes this ENaC to be in a more open configuration; it also increases the number of ENaC in the luminal membrane of the CCD.[13] Drugs such as some of the K^+-sparing diuretics (amiloride, triamterene) and the antibiotic trimethoprim in its cationic form block the ENaC, decreasing nett secretion of K^+ in the CCD.[14]

The pathways for the reabsorption of Cl^- in the CCD are not well defined. Changes in the "apparent permeability" for Cl^- in the CCD have been postulated in some disorders with hyperkalaemia or hypokalaemia.[2] For example, a decrease in this apparent permeability might be the mechanism by which bicarbonate ions (HCO_3^-) and/or an alkaline pH in luminal fluid augment nett secretion of K^+ in the CCD even when the luminal Cl^- concentration is high.[15] In general, other non-absorbable anions influence nett secretion of K^+ only if the urine is Cl^- poor.[15,16]

It has been suggested that modulation of the delivery of HCO_3^- to the CCD may be important in determining whether NaCl retention or K^+ secretion occur when aldosterone opens the CCD ENaC.[17] Angiotensin II, released in response to contraction of ECF volume, stimulates reabsorption of HCO_3^- in the proximal and distal nephron and thus limits its delivery to the CCD;[18,19] this allows aldosterone to be an NaCl-retaining hormone. On the other hand, hyperkalaemia directly stimulates the release of aldosterone from the adrenal gland and it also increases the delivery of HCO_3^- to the CCD by inhibiting HCO_3^- reabsorption in the proximal tubule; this allows aldosterone to exert its kaliuretic effect (figure 3).

In states where there is a deficit of magnesium, nett secretion of K^+ is often augmented but the mechanism for this is not clear.[20]

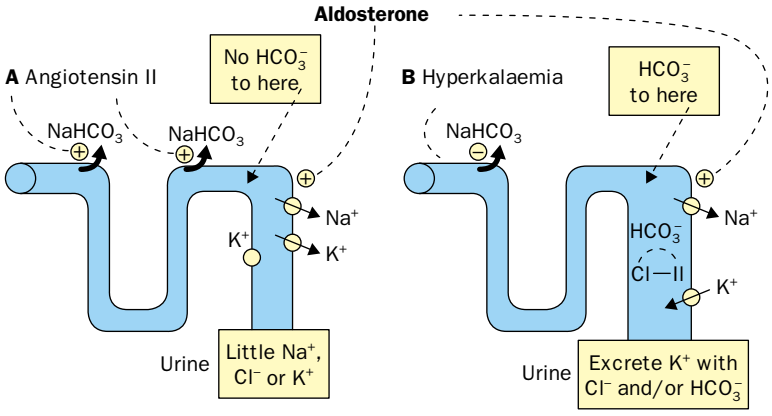

Figure 3: **Role of bicarbonate in modulating effects of aldosterone in CCD**

(A) Secretagogue for release of aldosterone is angiotensin II. Angiotensin II, by stimulating reabsorption of HCO_3^- in proximal and distal convoluted tubules, diminishes delivery of HCO_3^- to CCD and leads to NaCl reabsorption rather than K^+ secretion when aldosterone opens ENaC in CCD.

(B) Secretagogue for release of aldosterone is K^+. Hyperkalaemia, by inhibiting reabsorption of HCO_3^- in proximal convoluted tubule, increases delivery of HCO_3^- to the CCD and kaliuresis is promoted.

(Reproduced, with permission, from ref 28.)

Clinical approach

Since the kidney has such a major role in long-term K^+ homoeostasis the first step in the diagnosis of a patient with a dyskalaemia (figure 4) is examination of the rate of K^+ excretion (panel). If the excretion rate is abnormal, urine flow rate and urinary [K^+] should be examined independently and

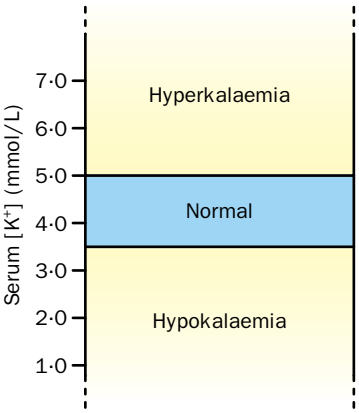

Figure 4: **Normal range for serum [K⁺]**

interpreted in terms of events in the CCD.

Flow rate in CCD

The flow rate in the CCD is directly proportional to the rate of excretion of osmoles when anti-diuretic hormone (ADH) acts. Since ADH acts over most of the 24 hours,[21] a minimum estimate of the flow rate in CCD can be obtained by dividing the rate of osmole excretion by the osmolality of fluid in the terminal part of the CCD. The latter is equal to the osmolality of plasma when ADH acts. For example, if the osmolality at the terminal CCD is 300 mosmol/kg H_2O, for every 300 mosmol excreted in the urine there will be 1 litre of fluid in the lumen of the CCD. The major urinary osmole is urea; Na^+ and Cl^- are the other quantitatively important ones.

A low rate of excretion of osmoles can lead to an even lower rate of excretion of K^+; this point is illustrated in patient A (see below). On the other hand, raising the rate of excretion of Na^+ and Cl^- with the administration of a loop diuretic can help augment the excretion of K^+ by increasing the flow rate in the CCD.

[K⁺] in CCD

To obtain a semiquantitative assessment of $[K^+]$ in the CCD, we try to correct the $[K^+]$ in the urine for the amount of water reabsorption in the medullary collecting duct. This can be achieved by dividing the urinary $[K^+]$ by the quotient of U_{osm} and P_{osm} (since osmolality of the fluid in the terminal CCD equals P_{osm} when ADH acts). By dividing this estimate of CCD$[K^+]$ by the plasma $[K^+]$ we obtain the transtubular $[K^+]$ gradient (TTKG).[1,22,23] While many assumptions are made, this calculation does provide a reasonable semiquantitative reflection of K^+ secretion in the CCD. The "expected" values for TTKG in patients with hypokalaemia or hyperkalaemia but with normal K^+ secretion in CCD are provided in the panel.

When the $[K^+]$ in the CCD is not as expected for the patient's plasma $[K^+]$, one should analyse events at an ion-channel level in this nephron segment.[1,2] This involves deriving information about the relative rates of reabsorption of Na^+ and Cl^- in the CCD (figure 2). For example, if a patient with hypokalaemia has a higher than expected $[K^+]$ in the lumen of the CCD, this implies an unusually high lumen-negative voltage. This voltage is the result of faster reabsorption of Na^+ or slower reabsorption of Cl^- in the CCD. The converse is true for hyperkalaemia. Central to the differential diagnosis is an assessment of ECF volume and the ability to conserve Na^+ and Cl^- when the ECF volume is contracted.

As we will now illustrate, this underlying pathophysiology has implications for diagnosis and treatment.

Hyperkalaemia (patient A, 7·4 mmol/L)

Step 1; emergency measures

We began by asking, "Might this patient die as a result of his hyperkalaemia?" Because hyperkalaemia was so severe and because even mild ECG changes can progress rapidly to a dangerous cardiac arrhythmia, we treated this as a medical emergency (figure 5).

Intravenous Ca^{2+} was given to antagonise the cardiac toxicity of hyperkalaemia; the effects of Ca^{2+} should be evident in a few minutes and usually last for 30–60 min. Measures were also taken to shift K^+ into cells. Insulin, with enough glucose to avoid hypoglycaemia, was given, and the plasma $[K^+]$ fell by almost 1·0 mmol/L within 30 min; this effect usually lasts for 1–2 h. Since patient A had a mild metabolic acidosis with his severe hyperkalaemia, $NaHCO_3$ was given. We try to avoid using β_2-adrenergic agonists because large doses can cause arrhythmia; this remains a controversial issue.[24,25] To increase the rate of excretion of K^+, a loop diuretic was given. Lowering the plasma $[K^+]$ from 7 to 6 mmol/L requires very much less K^+ loss than is needed to lower the plasma $[K^+]$ from 6 to 5 mmol/L,[26] and creating a small K^+ loss can be very important when the hyperkalaemia is severe. To re-expand this patient's ECF volume, more NaCl was infused than was being excreted. As we shall discuss below, this patient did not have a large surplus of K^+ in his body—indeed, K^+ supplements were needed later to replace the deficit of K^+ induced by the initial, life-saving therapy.

Step 2; exclude laboratory or technical problems

Despite the ECG changes in this patient, an element of pseudohyperkalaemia could have been present. Haemolysis, megakaryocytosis, and fragile leukaemic white blood cells were excluded. Even if fist-clenching was not excessive during blood sampling pseudohyperkalaemia could still have been present

Tests to examine K⁺ excretion in patients with hypokalaemia or hyperkalaemia*

Test	Advantages	Disadvantages	Expected values
24-h K^+ excretion rate or K^+ per creatinine	Indicates overall renal response in patients with hypokalaemia or hyperkalaemia	Does not indicate mechanism responsible for defect; takes 24 h or measurement of creatinine in urine; collections not always accurate	Normal 60–80 mmol/day (or 6–8 mmol/mmol creatinine); hypokalaemia <10 (or 1–1·5); hyperkalaemia >150 (or 10–15)
Spot urine $[K^+]$	Convenience	Influenced by two independent factors (K^+ secretion and water reabsorption in medulla) so there is a wide gray zone	Hypokalaemia <20 mmol/L if due to renal cause and >20 if due to a renal cause; hyperkalaemia (no "expected" value reported)
TTKG	Corrects for water reabsorption in medullary collecting duct; provides semiquantitative reflection of K^+ secretion in CCD	Assumptions made in calculation	Hypokalaemia due to a non-renal cause <2; hyperkalaemia due to a non-renal cause >10

*Reproduced, with permission, from ref 28.

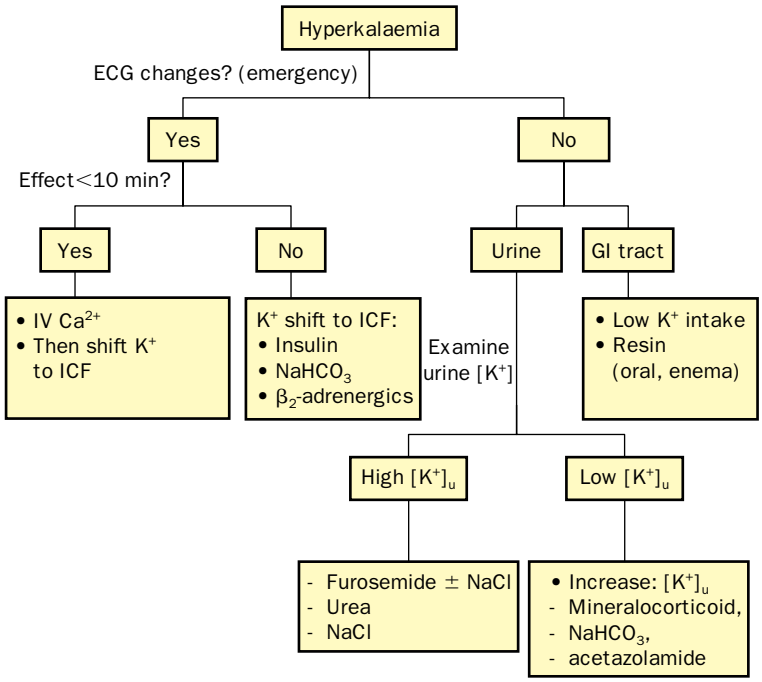

Figure 5: **Treatment of patient with hyperkalaemia**
If an emergency is present (usually cardiac), intravenous Ca^{2+} must be given. This treatment should act promptly. Efforts are also taken to shift K^+ into cells with insulin with or without $NaHCO_3$. Longer term strategies are to limit intake of K^+, prevent its absorption in the gastrointestinal tract, and promote its excretion; the latter includes measuring urine $[K^+]$ and flow rate to decide leverage for therapy. (Reproduced, with permission, from ref 28.)

because the patient was cachectic. Cachexia disturbs the normal T-tubule architecture in skeletal muscle so more K^+ could be released into venous blood with repeated fist clenching during blood sampling. Blood drawn from a femoral vein confirmed a small component of pseudohyperkalaemia; the plasma $[K^+]$ was 1 mmol/L lower than it was in a simultaneously drawn brachial-vein sample.

Step 3; assess renal response to hyperkalaemia

Since this patient's excretion of K^+ was much lower than the expected 200–400 mmol per day (panel) we assessed its two components separately and related them to events in the CCD. Given his urine osmolality (350 mosmol/L) and flow rate (0·0006 L/min), he had a low flow rate in his CCD because the product of these two numbers (0·21) was less than one-half of the usual osmole excretion rate of 0·5 mosmol/min. This low flow rate in the CCD was probably due to a low excretion of urea (low protein intake) and a low ECF volume.

Since his urine $[K^+]$ was 12 mmol/L and his urine osmolality was 350 mosmol/L, the TTKG was <2, which is very low value for a patient with hyperkalaemia (panel).[23] Because he had a low ECF volume and renal salt wasting (urine $[Na^+]$ 62 mmol/L), we suspected that his low CCD $[K^+]$ was due to slow reabsorption of Na^+ in the CCD (figures 2 and 6).

Step 4; differential diagnosis

The differential diagnosis at this point is absence of aldosterone or presence of an agent that inhibits the ENaC in the CCD (amiloride, triamterene, or trimethoprim). He did not have a kaliuretic response to exogenous mineralocorticoid (100 μg 9α-fludrocortisone). The presumptive diagnosis was hyperkalaemia due to an inhibited ENaC by trimethoprim because this drug was being administered for the treatment of *Pneumocystis carinii* pneumonia. When laboratory results became available, both plasma renin and plasma aldosterone concentrations were high, as expected with this diagnosis.

We were unhappy, however, about attributing this severe hyperkalaemia solely to decreased renal excretion of K^+ because this patient's intake of K^+ was very low. We suspected a major shift of K^+ from cells. The likely causes of this would be cell necrosis and/or insulin deficiency; the latter may result from the α-adrenergic effect of adrenaline released in response to the low ECF volume.[27]

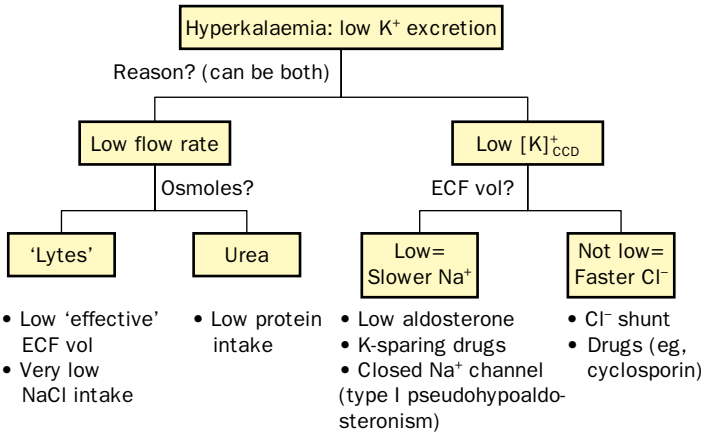

Figure 6: **Approach to patient with hyperkalaemia**
Causes for a low rate of excretion of K^+ (<200 mmol/day) despite hyperkalaemia are too low a flow rate in CCD (left limb) and too low a $[K^+]$ in lumen of CCD (right limb). Both flow rate and CCD $[K^+]$ should be evaluated. Final considerations are shown by bullet symbols. Slower Na^+ reabsorption is suggested by high renin and NaCl wasting despite low ECF volume; converse applies for faster Cl^- reabsorption. In some cases of renal failure, excessive flow rate per nephron limits electrogenic reabsorption of Na^+ and thereby behaves as if there is relatively slower reabsorption of Na^+. (Reproduced with permission from ref 28.)

Clinical outcome

By re-expanding this man's ECF volume, inhibition of the release of insulin should have been diminished, causing a shift of K^+ into cells. The question arose, "Should the trimethoprim be discontinued?" Since this antimicrobial agent was needed for the patient's pneumonia we tried to remove its renal side-effects due to blockage of the ENaC. Increasing urine flow with a loop diuretic plus isotonic saline should not only help excrete K^+ but also dilute the concentration of trimethoprim that blocks the ENaC. Inducing bicarbonaturia could lower the concentration of the cationic form of the drug by decreasing the $[H^+]$ in luminal fluid in the CCD.[14]

Although this patient was taking a drug well known to block the ENaC, it was important to recognise that his severe hyperkalaemia was largely due to a shift of K^+ from cells. This meant that we had to take care not to induce a large loss of K^+. Such a loss would have aggravated his TBK$^+$ deficit and led to very severe hypokalaemia when K^+ shifted back into the cells, via release of insulin due

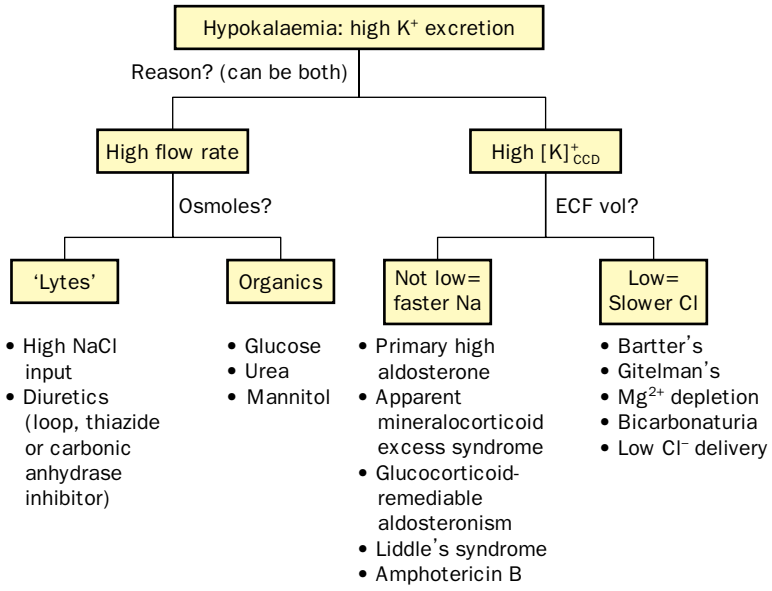

Figure 7: **Approach to the patient with hypokalaemia**
Causes for excessive excretion of K^+ (>15 mmol/day) despite hypokalaemia are too high a flow rate in CCD (left limb) and/or too high a $[K^+]$ in lumen of CCD (right limb). Both flow rate and CCD $[K^+]$ should be evaluated. Final considerations are shown by bullet symbols. A relatively slower Cl^- reabsorption in CCD is suggested by high plasma renin activity and NaCl wasting despite low ECF volume; converse applies for relatively faster Na^+ reabsorption. (Reproduced, with permission, from ref 28.)

to removal of adrenergic inhibition as ECF volume was restored.

Hypokalaemia (patient B, 1·5 mmol/L)

Step 1; emergency measures

We began by asking, "Might this patient die as a result of the hypokalaemia?" Since he had a run of ventricular tachycardia on his ECG, therapy was the first step and K^+ was administered aggressively. Because a large dose and hence a high $[K^+]$ was needed initially, K^+ was given via a central vein while monitoring his ECG.[3] Our plan for therapy was to raise his $[K^+]$ by 2 mmol/L in 1 min. With a blood volume of 5 L (plasma volume 3 L) and a cardiac output of 5 L/min, 6 mmol of K^+ was given over 1 min. Because the interstitial fluid volume is five times the plasma volume, the rise in K^+ concentration in fluid bathing cardiac myocytes would be much less than 2 mmol/L. This procedure could have been repeated if the arrhythmia and severe hypokalaemia had persisted. The rate of infusion of K^+ was then decreased to 1 mmol/min, and plasma $[K^+]$ was monitored very closely. Glucose or HCO_3^- were not infused because either might cause a shift of K^+ into cells and so aggravate the hypokalaemia. The remainder of the K^+ deficit was replaced later, more slowly.

Having dealt with the emergency, we could turn to diagnostic issues and the role of the kidney as a cause of the hypokalaemia.

Step 2; assess renal response to hypokalaemia

In evaluating the rate of excretion of K^+ a note of caution is required; we are looking at the urine of the moment, not at all the urine that had been excreted to develop this deficit of K^+. Nevertheless his rate of K^+ excretion was much greater than expected if the sole cause of his hypokalaemia was K^+ deprivation (panel). The next step was to examine the components of K^+ excretion (figure 7). His osmole excretion rate was 0·45 mosmol/min, which is normal, so a high flow rate in the CCD was not present. However, his urine $[K^+]$ was 40 mmol/L with a urine osmolality of 450 mosmol/L so his TTKG was too high (>10).[23] But which component of the K^+ secretory process was abnormal?

The main clinical characteristics of a patient with hypokalaemia because of excessive secretion of K^+ due to a more open ENaC are ECF volume expansion, low plasma-renin activity, and a tendency to hypertension if the blood pressure is more sensitive to changes in volume than to vasoconstrictors (figure 2). When ECF volume contraction is induced, the urine should be free of Na^+ and Cl^-.

Relatively slow reabsorption of Cl^- in CCD may occur for two major reasons. The first requires a large delivery of Na^+ and Cl^- to the CCD and a stimulus to reabsorb these ions (ECF volume contraction) together with a capacity to reabsorb Na^+ faster than Cl^- in the CCD. In the second, the apparent permeability of the luminal membrane for Cl^- decreases. In both types of lesion there will be ECF volume contraction and hyperreninaemia; patients will not conserve Na^+ and Cl^- appropriately despite ECF volume contraction. Because of the hypovolaemia, blood pressure is not usually high despite a high level of the vasoconstrictor angiotensin II.

Since patient B's ECF volume was expanded, a relatively faster reabsorption of Na^+ in the CCD is presumed (figure 7). His plasma renin and aldosterone were both very low (figure 8). Disorders such as apparent mineralocorticoid excess syndrome or Liddle's syndrome may be present but inherited disorders are unlikely in a patient presenting in his late 50s. The patient was not taking substances that inhibit 11β-hydroxysteroid dehydrogenase (11β-HSDH) (eg, liquorice or chewing tobacco). An ACTH-producing tumour was suspected even though the clinical signs of Cushing's syndrome were not evident. The eventual diagnosis was oat-cell carcinoma of the lung. It is our clinical impression that hypokalaemia is often very severe in patients with an ACTH-producing tumour.

Step 3; assessment of factors that could shift K^+ across cell membranes

Other than a degree of metabolic alkalosis, there were no other obvious causes of a shift of K^+ into cells because respiratory alkalosis does not cause an important shift of K^+ into cells.[8,9]

Step 4; assess contribution of K^+ intake

A low intake of K^+ in this patient could have contributed to the severity of the hypokalaemia.

The strategy outlined allowed us to characterise the abnormality causing patient's B hypokalaemia—it was a relatively fast Na^+ reabsorption in the CCD. Since plasma renin and aldosterone concentrations were suppressed, an ACTH-producing tumour was suspected. Besides the obvious therapeutic implications for the treatment of the

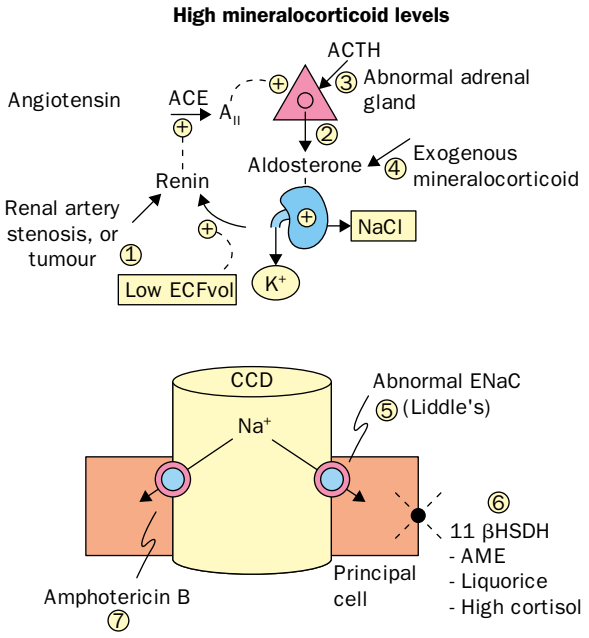

Figure 8: **Differential diagnosis of renal causes of hypokalaemia**
Seven causes for high mineralocorticoid action are identified. Those with high levels of aldosterone in plasma are: (1) group associated with high renin levels (eg, renal artery stenosis, renin-producing tumours); (2) those with adenoma or hyperplasia of adrenal cortex producing excessive aldosterone or a compound with mineralocorticoid bioactivity; and (3) a genetic lesion in which ACTH drives synthesis of a compound with mineralocorticoid bioactivity; suppressing ACTH with glucocorticoids decreases their production.

There might be low or absent levels of aldosterone in plasma. Examples are (4) exogenous compounds that mimic actions of aldosterone, such as fludrocortisone; (5) an ENaC in luminal membrane of CCD which is permanently in open conformation due to mutation (Liddle's syndrome); (6) decreased destruction of cortisol in principal cells by a relatively low activity of 11β-HSDH; and (7) insertion of artificial Na^+ channel in luminal membrane of CCD (eg, amphotericin B).

underlying malignancy, the use of an ENaC blocker (amiloride) would provide specific therapy for both the hypokalaemia and the hypertension.

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