POTASSIUM

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<table>
<thead>
<tr>
<th>Compartment</th>
<th>INTRACELLULAR</th>
<th>EXTRACELLULAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrolytes</td>
<td>K, HPO₄, SO₄, Mg, Na, Protein</td>
<td>Na, CL, HCO₃, K, Mg, HCO₃, Protein</td>
</tr>
<tr>
<td>Water</td>
<td>30 Litres</td>
<td>15 Litres</td>
</tr>
</tbody>
</table>

*All figures quoted here apply to the average 70 kg. adult.*

The subject of potassium metabolism, often coloured by forbidding biochemical jargon, has defeated many heroic attempts at comprehension. This article is intended as a clinical translation, both explanatory and descriptive, for the use of the average hospital practitioner seeking to master this difficult field of medicine.

**Distribution**

The distribution of water and electrolytes in the body will be more readily understood when the important concept of the body fluid compartments has been grasped. The skeleton excepted, water is distributed uniformly throughout the body, and of a total body water of 45 litres, 30 litres are *intracellular*, and 15 litres are *extracellular*. The plasma fraction constitutes one quarter of the extracellular compartment (3 1/4 litres).

Electrolytes are not distributed uniformly throughout the body. The intracellular electrolytes are mainly potassium, magnesium and phosphate, whilst the extracellular electrolytes are mainly sodium, chloride and bicarbonate.

Water and electrolytes constitute a finely balanced system, each dependent upon the other. Thus changes in the amounts of body electrolyte result in changes of fluid volume, and most of these changes are reflected by variations in the plasma concentrations.

Having established potassium as but one member of a group of electrolytes, it is necessary to focus upon it in rather more detail. Firstly it must be understood that there is no strict correlation between the concentrations in the intra- and extra-cellular fluids, although one can make the generalization that a sustained low serum level is usually associated with a low cellular level. The average serum potassium is 5 mEq. per litre.

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FIG. 1.—The distribution of water and electrolytes in the two compartments.
also some evidence in favour of an active cell mechanism for expelling sodium. It follows then that the first of the above corollaries does not apply to sodium. Namely:

The serum sodium level, when abnormal, indicates body sodium. (Minor degrees of sodium excess or depletion are, of course, compensated for by changes in volume, the concentration remaining normal.)

**Potassium Balance**

The balance of any substance should always be considered in terms of gain and loss.

**Intake.** Potassium is present in most foods, the average intake from a normal diet varying from 2 to 4 g. daily. Relatively large amounts can be taken by mouth provided that the urine flow is good.

**Loss.** Potassium leaves the body in the urine and in the alimentary secretions. The main loss, under normal circumstances, is via the kidney and conservation occurs only to a limited extent. A profound knowledge of renal physiology is unnecessary for a grasp of the following simple principles:

(a) Decreased glomerular filtration causes potassium retention.

(b) Decreased tubular reabsorption causes potassium depletion.

Loss also occurs from the gastro-intestinal fluid, and in this respect it is worth remembering that the gastric juice contains four times the concentration of potassium to that of plasma. The practical applications of this will be considered later, but it should be apparent already that renal and gastrointestinal disorders are the basis of potassium imbalance.

**Regulation**

Balance and regulation are not synonymous, and therefore the whole story cannot be told merely in terms of input and output. There are a number of factors, both known and unknown, which regulate potassium distribution, and these must now be considered.

1. **Protein Metabolism.** Potassium is the chief cellular electrolyte and therefore tissue breakdown will result in a release of the substance. This mechanism has been postulated to account for some of the manifestations of the crush syndrome. Similarly, raised serum potassium levels have been demonstrated shortly after myocardial infarction (Wilhelm, 1951), and are held responsible for the peaked or deep T waves of the electrocardiogram.

2. **Carbohydrate Metabolism.** Potassium moves into the cells whenever carbohydrate metabolism is stimulated. This is dependent upon the
deposition of a cellular potassium-glycogen complex. Thus a fall in the serum potassium can be produced, experimentally and clinically, by the administration of glucose, insulin or adrenaline, and this principle is put to practical use in the treatment of potassium intoxication. Unfortunately it is also a contributing cause of the severe depletion that occurs in a patient who, treated with insulin and intravenous glucose, enters upon the diuretic recovery phase of diabetic ketosis. It has also been suggested that the same factor is operative in the rare condition known as Familial Periodic Paralysis, which is frequently precipitated by a large carbohydrate meal.

3. Acid-Base Disorders. Mention has already been made of the small ion size which renders potassium so freely diffusable across the cell membrane. This exchange is therefore not surprisingly activated by acid-base disturbance. The compensatory rise in serum bicarbonate and fall in sodium and potassium resulting from alkalosis primarily due to loss of chloride is not difficult to follow. (See Fig. 3.) However, the inverse relationship of the serum bicarbonate to intracellular potassium is somewhat more complex. For instance ingestion of lactate or bicarbonate causes an increased excretion of potassium in the urine. Clinically the alkalosis of Cushing's syndrome will not respond to administration of ammonium chloride but will respond to potassium. The fact remains that a rise in serum bicarbonate tends to draw potassium out of the cells. A similar shift takes place in severe dehydration when the osmotic pressure of the body fluids is increased. A low potassium state can also be superimposed upon acidosis when there is a general depletion of base, and it is thought by some that the symptoms of potassium deficiency are then potentiated.

4. Adrenal Cortex. The influence of the 'salt and water' hormone of the adrenal cortex is of course well known. Desoxycorticosterone (DOCA) promotes retention of sodium and excretion of potassium. The patient with Addison's disease has a high serum potassium and a low serum sodium level. In overtreatment with DOCA, ACTH, or cortisone, or in Cushing's syndrome, these levels are reversed. There is much talk at the present time of stress, and it is possible that the post-operative loss of potassium so frequently observed is in part due to adrenal cortical hypersecretion. Evidence in favour of this mechanism is provided by the fall in the number of circulating eosinophils following surgery, when the degree of the response is proportional to the severity of the operation (Coppinger and Goldner, 1950).

Clinical Potassium Depletion

The function of potassium is in some way concerned with nerve and muscle fibre excitability, and this accounts for the clinical features of potassium disturbance.

The symptoms of depletion are listlessness, loss of appetite and muscular weakness. A more advanced state is marked by apathy, breathlessness
and frank flaccid paralysis. The findings include diminished or absent reflexes, rapid shallow respirations and abdominal distension from muscle hypotonia. The latter affects not only voluntary but also smooth muscle. Indeed, paralytic ileus may supervene; it can be caused by, or may be the cause of, a low potassium state. Cardiac changes have also been described and these include elevation of the systemic venous pressure, increased pulse pressure, dilation of the heart, functional systolic murmur and cardiac failure. The diagnosis is supported by typical electrocardiographic changes which are said to appear when the serum potassium level is less than 3.5mEq. per litre (13.6 mg./100 ml.), but serial tracings invariably show a gradual development of these abnormalities at more moderate levels. Final proof is obtained by the estimation of the serum concentration.

Before listing the causes of potassium depletion, emphasis must once again be placed on the physiological principles considered earlier. If one remembers that loss of cell fluid means loss of potassium, and that this loss is either from the urine or in the gastro-intestinal secretions, then a simple classification immediately suggests itself:

<table>
<thead>
<tr>
<th>Cell Fluid Loss</th>
<th>Loss</th>
</tr>
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<tbody>
<tr>
<td>Primary Alimentary</td>
<td>Diarrhoea and vomiting; pyloric stenosis; gastric suction; intestinal obstruction; paralytic ileus; steatorrhoea; ulcerative colitis; ion exchange resins; ?PAS therapy.</td>
</tr>
<tr>
<td>Primary Renal</td>
<td>Diuretic recovery phase of acute tubular necrosis; post-operatively; chronic nephritis (some cases); renal acidosis (nephrocalcinosis); aminoaciduria, e.g. Fanconi's syndrome.</td>
</tr>
<tr>
<td>Metabolic (combined loss)</td>
<td>Diabetic ketosis; alkalosis; water deprivation; familial periodic paralysis; overdosage with DOCA, ACTH or cortisone; Cushing's syndrome; stress.</td>
</tr>
</tbody>
</table>

Perhaps the commonest example, always to be found in every surgical ward, is the post-operative patient on gastric suction and intravenous glucose-saline,—the familiar 'suck and drip.'

It has been shown conclusively that the first post-operative week is marked by retention of sodium chloride and water and by an increased excretion of nitrogen and potassium. The estimation of the urinary chlorides in this period is valueless because it provides an inevitably low result in spite of a normal or raised serum level. These changes are independent of intake and follow any major surgical procedure, including orthopaedic operations and road accidents. The explanation is still not clear, but is likely to be related to compensatory mechanisms consequent upon increased tissue breakdown, or the formation of an inflammatory exudate. (Wilkinson et al., 1949 and 1950.)

Firstly, therefore, some degree of negative potassium balance is inevitable and large volumes of fluid, by raising the urinary output, will aggravate this tendency. Secondly, there is not only a total absence of potassium intake, but, through suction, the electrolyte is being actively removed from the stomach where it is present in four times the plasma concentration. Thirdly, suction has a double disadvantage because it results in alkalaosis which in itself causes a fall in the serum potassium level. Intravenous glucose is a fourth factor for, as already explained, stimulation of carbohydrate metabolism carries potassium out of the extracellular fluid into the cells. Finally, any surgical approach is likely to be attended by a considerable degree of stress and subsequent adrenal cortical hyperactivity.

Illustrative Case History. Mrs. D.M., aged 54, was operated on for the relief of acute intestinal obstruction. A piece of strangulated small bowel had to be freed from an intrapertioneal adhesion, and it was found necessary to employ post-operative suction and intravenous glucose-saline. Her recovery failed to reach expectations, and by the 6th day after operation she was weak, hypotonic, all reflexes were diminished and the ankle jerks were totally absent. Her chart showed an output of 2,000 ml. from suction in the previous 24 hours, alone representing a loss of some 40 mEq. of potassium. The serum potassium was 3.5 mEq./l. and the alkali reserve 35 mEq./l. (78.6 vol. CO₂/100 ml.). The electrocardiogram is shown in Fig. 4. She was given intravenous potassium in the form of Cell Repair Solution (vide infra), 90, 60 and 45 mEq. K⁺ in the first, second and third 24 hour periods respectively. The serum potassium rose to 4.5 mEq./l. on the second day and to 5.2 mEq./l. on the third. Her condition steadily improved and, from then on, she made an uneventful recovery.

The medical counterpart of all this is to be found in the patient recovering from diabetic coma. He too has intravenous glucose and oral starvation, and as a result potassium depletion is a well-recognised complication in the diuretic recovery phase.

By way of interest, mention might be made of the curious relative mildness of tetany in steatorrhea when the serum calcium level is known to be low. This is now believed to be due to an associated hypokalaemia. In such cases tetany has been precipitated by administration of potassium (Engel et al., 1949).
Another important cause of potassium depletion is gastro-enteritis in infants and the pioneer work of Darrow and his associates has contributed largely to our present knowledge in this respect. 

**Illustrative Case History.** A five months old marasmic and dehydrated infant, suffering from diarrhoea and vomiting possibly secondary to a B. proteus urinary infection, was rehydrated with subcutaneous and intravenous glucose and saline infusions. Potassium depletion became evident on the third day of intravenous therapy. His limbs were hypotonic, his cry feeble, his abdomen distended and he could barely take a four drachm feed. An X-ray film of his abdomen showed fluid levels (Fig. 5), the electrocardiogram was abnormal (Fig. 6), and the serum potassium was 2.8 mEq./l. (11.1 mg./100ml.) He was given one litre of Butler's solution (containing 15 mEq. K') intravenously slowly over the next 48 hours, and then oral potassium chloride 0.5 G. b.d. for a further three days. Only four hours after beginning potassium therapy he took a ten drachm feed readily, and by the fourth day was taking five ounce feeds. His ileus had then disappeared and the electrocardiogram returned to normal. He appeared to make a complete recovery, but unfortunately succumbed to a second attack of severe gastro-enteritis two weeks later.

**Clinical Potassium Intoxication**

Apart from paraesthesiae and irregularities of cardiac rhythm, potassium intoxication is relatively symptomless, but this silence is sinister for it may end in sudden death. Clinical suspicion of the condition is justifiable when a patient with the requisite circumstances for potassium retention develops sudden cold grey pallor with peripheral circulatory collapse, hypotension, indistinct heart sounds and bradycardia or rhythm irregularity. Mental confusion may be evident and numbness and tingling in the limbs are said to be constant features. Patients dying in uraemia may show a terminal rapidly ascending flaccid paralysis.

Since death is due to ventricular standstill it follows that the electrocardiographic changes are of greater clinical significance than the actual serum potassium level. Whilst a fatal issue may be expected when the level exceeds 9 mEq./l. (35 mg./100ml.), the electrocardiogram begins to record changes at about 7.5 mEq./l. (approx. 30mg./100 ml.).

Potassium retention occurs in oliguric or anuric uraemia of renal or pre-renal causation. A raised serum potassium is present in Addison's disease but seldom reaches toxic levels. A dangerous rise is generally due to a combination of circumstances which include defective renal function, increased tissue breakdown in gross infections, and misguided potassium administration.

By now it will have become apparent that the clinical manifestations of potassium disturbance

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**Fig. 4.—Case 1.** The first tracing (serum potassium = 3.5 mEq./l.) shows inversion of the T wave, depression of the ST segment and prominence of the U wave. The subsequent tracings show the gradual reversion to normal with treatment.
Paralytic ileus due to potassium depletion. The first X-ray shows distended bowel with numerous fluid levels. The second film, taken three days later after treatment, shows complete return to normal.

The first tracing shows flat T waves and prominent U waves. The increasing distortion of the tracings from interference as the serum potassium rises is striking testimony of the infant's change from a state of weakness to one of lively resistance.

are due to abnormally high or low extracellular levels. Therefore, even though the serum level is a rather unreliable guide to the state of cellular potassium, it is nevertheless a vital guide in the management of a case. It is perhaps insufficiently realised that the biochemical estimation involves a prolonged series of reactions and precipitations—in fact, almost half a day's work for one technician. Hence, its repeated request inevitably results in considerable ill-feeling between pathologist and clinician. Moreover, the time lag is often too great for the acute emergencies necessitating this investigation. Flame photometry is now superseding biochemical estimation on account of its speed and simple technique, but the apparatus is not generally available as yet.

**Treatment**

1. **Potassium Depletion**

Potassium deserves to be regarded with the same respect as any other dangerous drug. Before it is given to a patient, the practitioner should satisfy himself that its administration is clearly indicated on the clinical evidence already described, and that the urinary output is adequate. Ideally each case should be controlled by estimation of the serum concentration and the electrocardiogram, and in certain patients this is an absolute necessity. The routine treatment recommended is:

1. Control with serum level and/or E.C.G.
2. Correct the causal condition.
3. Replace the depleted electrolyte.
HYPOKALAEMIA

- Flat or inverted T wave.
- Depressed ST segment.
- Large U wave.
- High P wave.
- Prolonged QT interval.
- Ectopic beats.
- A-V block.

FIG. 7.—The electrocardiogram in potassium imbalance. The changes are listed as far as possible in order of appearance. The above tracings have been specially selected for the gross abnormalities which they illustrate, but it is important to appreciate that each person has an individual combination of the various possible abnormalities and that there is no set tracing.

The corresponding serum potassium level of the first tracing, taken from a patient suffering from a carcinoma of the pancreas with obstructive jaundice and profuse vomiting, was 2.9 mEq/l.

Potassium repletion can be accomplished orally, subcutaneously or intravenously. Oral administration is the method of choice, and the recommended dose is 5-10 g. of the chloride citrate, bicarbonate or phosphate daily, suitably diluted in fruit juice or sweetened water.* The development or pre-existence of paralytic ileus establishes a vicious circle which no amount of oral therapy can break. Thus it sometimes becomes necessary to give potassium intravenously with all the attendant risks of a sudden rise to toxic levels. Therefore strict control of dosage is necessary; in any case not more than 100 mEq. should ever be given in any 24 hours and not more than 10 mEq. in less than any one hour. Solutions should contain 30 mEq./l. or less, and the urinary output should exceed 50 ml./hour.

It only remains now to consider the solution to be employed. Owing to the fact that every worker in this field has concocted his own solution, one is faced with a considerable choice in this respect. Perhaps the most popular misconception is that Hartmann’s solution corrects potassium depletion. Hartmann’s solution is only physiological in the sense that its electrolytes are present in approximately the same concentration as in plasma. Thus, in order to replace the necessary amount of potassium with Hartmann’s solution, vast quantities of saline and water must also be given, and this is clearly undesirable. Butler’s repair solution contains 15 mEq. K’/l.. whilst undiluted Darrow’s solution contains 35 mEq. K’/l., and these are therefore more suitable. However, it is important not to lose sight of one’s purpose in treatment, because these cell repair solutions contain other electrolytes, notably lactate, and are, therefore, best reserved for cases in which acidosis is prominent. Therefore, it is recommended that intravenous potassium salts, when indicated, are given in one of two forms, each solution having the ideal concentration of 30 mEq. K’/l:

(a) For potassium depletion per se: 2.2 G. of KCl in one litre of 5 per cent. glucose.
(b) For cellular depletion in general: Cell Repair Solution. The following cell repair solution was devised by Nabarro et al. (1952) on the basis of metabolic studies of electrolyte retention in recovery from diabetic ketosis, and contains the major cellular electrolytes, potassium, magnesium and phosphate.

<table>
<thead>
<tr>
<th>Electrolyte</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>NaCl</td>
<td>1.17 g.</td>
</tr>
<tr>
<td>K₂HPO₄</td>
<td>0.87 g.</td>
</tr>
<tr>
<td>KCl</td>
<td>1.49 g.</td>
</tr>
<tr>
<td>MgCl</td>
<td>0.24 g.</td>
</tr>
<tr>
<td>Glucose</td>
<td>50 g.</td>
</tr>
<tr>
<td>Water</td>
<td>to 1 l.</td>
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</tbody>
</table>

2. Potassium Intoxication

Potassium intoxication is a medical emergency. Once again the principles of treatment are: 

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*These are adult doses. For the treatment in infants the reader is referred to the Medical Research Council Memorandum No. 26.
1. Control with serum level and E.C.G.
2. Correct the causal condition.
3. Reduce the toxic level.

This last stipulation is achieved by the intravenous infusion of 50 g. of glucose with or without the simultaneous injection of 50 units of insulin. Sodium and calcium are in part physiological antagonists to potassium and the additional use of calcium gluconate or saline is often recommended. When acute renal failure is present, the non-protein electrolyte-free regime devised by Bull and his colleagues should be employed. In special centres more complicated forms of therapy are feasible and these include such measures as the use of ion-exchange resins, peritoneal dialysis and the artificial kidney.

Conclusion

It is a sober reflection when one considers that only a few years ago all that was known of potassium in clinical medicine could be written in a few lines. Now, if anything, the subject is over-emphasised. It is as well to maintain a balanced outlook, for it would be as unwise as it is unnecessary to prescribe potassium indiscriminately to all cases in which depletion is likely to arise. 'The patient is as well as can be expected' is a hospital stock phrase. It is when the patient is not as well as might be expected that the wise practitioner looks for potassium imbalance.

Acknowledgments

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Potassium

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