THE TOTAL EXCHANGEABLE POTASSIUM IN PATIENTS WITH HYPOKALAEMIA

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THE original concept underlying the determination of total body spaces with radioactive isotopes was outlined by Moore in 1946 and the basis of the present determination of the total exchangeable potassium (Ke) was published by Corsa, Olney, Steenburg, Ball and Moore in 1950. The methods have assisted in the great advances in the understanding of electrolyte abnormalities during the last 15 years but unfortunately their role in the daily clinical field has proved to be rather limited. Numerous papers have been published giving the results of Ke in normals and in various chronic diseases but these have been mainly in patients in a steady state and even then the interpretation of the results has been difficult. In contrast little has been published in patients with manifest hypokalaemia.

In this paper the values of Ke are reported in seven patients with hypokalaemia from different causes before and after the administration of potassium supplements. The patients were seen and investigated in hospital and with the exception of Case 6 the original determination of Ke was made before any potassium supplements were given. Only cases with a serum potassium less than 3.0 mEq/l., have been studied. Ke was determined by the method of Corsa and his co-workers (1950), two spot samples of urine being collected for the determination of the specific activity after equilibration between 23 to 24 and 24 to 25 hours as described elsewhere (Staffurth, 1961). Serum potassium was measured with an EEL flame photometer and other biochemical measurements were determined by standard methods.

Case Reports

Case 1. M.H., a female aged 55, has been described fully elsewhere (Staffurth and Allott, 1962). Briefly, she was admitted to hospital with hypokalaemic paralysis, hypocalcaemia and a metabolic acidosis with azotaemia due to chronic pyelonephritis. The hypokalaemia was shown to be due to the combined effect of chronic purgation and an inadequate diet, for full investigations showed that it was not caused by excessive renal loss.

On admission when the serum potassium was 2 mEq/l., Ke was 780 mEq. Three weeks later, after

supplemental potassium (88 mEq daily for 10 days), the serum potassium was 5.5 mEq/l. and Ke had risen to 1,465 mEq. No further potassium supplements were given until eight months later, when she presented with a mild relapse, serum potassium being 2.5 mEq/l. and the Ke had fallen to 1,180 mEq. After further potassium supplements Ke rose to 1,630 mEq, which was 185 mEq higher than the comparable value on the first admission. Ke/(kg. body-weight) was 42 mEq on each occasion and the higher value was considered to be due to an increase in muscle bulk, which was clinically evident and which was explained by the fact that long-standing potassium deficiency had led to a loss of muscle mass (Flear, 1960).

Case 2. E.P., a female aged 62, was admitted to hospital for investigation of un-united fractures of the left radius and ulna following an injury seven months previously. There was general lassitude and muscular weakness, but no true paralysis. There was a history of recurrent attacks of muscular weakness which had first occurred at age 16 and which had been shown to be due to hypokalaemia in 1952.

On admission serum potassium was 2.3 mEq/l. and serum bicarbonate 24 mEq/l., but in the next two weeks the serum potassium rose spontaneously to 4.1 mEq/l. before the administration of potassium supplements. She was ultimately discharged on potassium supplements, but three months later she was readmitted, at which time the serum potassium had fallen to 2.1 mEq/l. and Ke was found to be 650 mEq. After two weeks on the ward diet only serum potassium had risen to 4.1 mEq/l. and Ke to 825 mEq. Supplemental potassium (60 mEq daily for 12 days) was then given and after two weeks Ke had risen to 1,240 mEq.

Her history was long and complicated, but the relevant facts were that she was a case of anorexia nervosa with a life-long history of severe constipation due to a megacolon. She took numerous purgatives and gave herself frequent rectal washouts, which, in association with the inadequate diet, were considered to be the cause of the recurrent hypokalaemia. The un-united fractures were shown to be due to osteomalacia, which was probably caused by a dietary deficiency of vitamin D.

Case 3. W.W., a male aged 35, was admitted to hospital with increasing muscular weakness and lethargy for four days. Seven months previously a diagnosis of tuberculous meningitis had been established which was being treated with streptomycin, isoniazid and sodium para-amino salicylic acid (3 g. four times daily in a mixture containing 5 minims of liquid extract of liquorice).

On admission blood urea was 17 mg./100 ml., serum potassium 1.7 mEq/l., serum bicarbonate 42 mEq/l., Ke 1,600 mEq. A urinary infection due to *Esch. coli* was present. Three days later, before any supplemental

potassium had been given, he developed status epilepticus, which was initially difficult to control. Potassium chloride (240 mEq the first day, then 80 mEq daily) and nitrofurantoin were given and he regained consciousness in four days. He then gradually recovered, though the blood urea rose to a maximum of 235 mg./100 ml. before it steadily fell to become normal after two months. Six weeks after admission Ke was 2,700 mEq, but by this time he had lost 12 kg. in body-weight during the prolonged illness, so it is probable that the true initial potassium deficiency was greater than the 1,100 mEq suggested by the changes in Ke.

Hypokalaemia is recognized as a complication of severe tuberculosis and PAS has frequently been implicated, particularly when liquorice had been used as a flavouring agent (Molhuysen, Gerbrandy, de Vries, de Jong, Lenstra, Turner and Borst, 1950; Strong, 1951). However, this is certainly not the only cause, for none of the four cases of hypokalaemia associated with tuberculosis described by Crofton, French and Sandler (1956) had received liquorice and only two had been given PAS. In this case the 24-hour urinary excretion of potassium was 26 mEq at a time when the serum potassium was only 1.7 mEq/l., which suggests that excessive renal potassium loss was the immediate explanation, but unfortunately the development of severe pyelonephritis precluded further study of the cause of the renal wastage.

Case 4. W.K., a female aged 47, was admitted to hospital with severe congestive cardiac failure, massive oedema and ascites. She was a known case of chronic rheumatic valvular disease with auricular fibrillation and tricuspid incompetence who had been treated for a long time with digoxin, mersalyl and oral diuretics of the benzodithiazine group.

On admission the serum potassium was 2.6 mEq/l., serum bicarbonate 34 mEq/l. and the Ke 1,100 mEq. Besides the routine treatment for cardiac failure she was given potassium chloride (89 mEq daily) for 12 days. There was some improvement in her general condition, but even in retrospect there had been no specific symptoms that could be ascribed to hypokalaemia. After treatment the serum potassium was 4.3 mEq/l. and Ke had risen to 2,070 mEq.

Case 5. H.F., a male aged 67, was admitted to hospital with symptoms due to chronic cor pulmonale and ischaemic heart disease, for which he had been given digoxin and oral diuretics for more than two years.

On admission he was given digoxin and bendrofluzide (20 mg. daily), but within a week he complained of abdominal pain and distension. The serum potassium was 2.7 mEq/l., serum bicarbonate 44 mEq/l. and the Ke 1,520 mEq. Potassium chloride (55 mEq daily) was given, with rapid improvement in the abdominal symptoms; three weeks later the serum potassium was 4.8 mEq/l., serum bicarbonate 29 mEq/l. and Ke had risen to 1,870 mEq.

Case 6. K.H., a female aged 67, was admitted to hospital with cardiac failure that had not responded to treatment with digoxin and oral diuretics.

On admission the serum potassium was 3.2 mEq/l., serum bicarbonate 30 mEq/l., blood urea 39 mg./100 ml. She was treated with chlorothiazide (1 g. daily) and enteric-coated potassium chloride (26 mEq daily) and she improved rapidly until three weeks later, when she became confused and restless; there was vomiting and incontinence of urine. Three days later the serum potassium was 2 mEq/l., serum bicarbonate 43 mEq/l., blood urea 40 mg./100 ml. Potassium chloride (405 mEq in two days) was given without im-

provement and at this time Ke was 1,800 mEq. 80 mEq of potassium had been excreted in the urine, indicating that the original Ke was about 1,525 mEq. Further potassium was given until the serum potassium rose to 6.8 mEq/l., but the confusional state persisted for a further week before recovery occurred, the blood urea rising to a maximum of 110 mg./100 ml. One week after complete recovery from the confusional state and cardiac failure the serum potassium was 3.5 mEq/l., serum bicarbonate 28 mEq/l., blood urea 28 mg./100 ml. and Ke 1,710 mEq.

Comment

Cases 4, 5 and 6 were patients with chronic cardiac failure who developed hypokalaemia whilst taking oral diuretics of the benzothiadiazine group. The Ke measured before and after replacement therapy showed a variable degree of potassium deficiency which bore no relationship to the clinical picture. In Case 4 Ke rose by 960 mEq., indicating a severe deficiency, yet there were no special symptoms attributable to hypokalaemia. In Case 5 Ke rose by 350 mEq. and the symptoms were immediately relieved by potassium chloride but in Case 6 Ke rose by only 185 mEq. and the symptoms, which were not suggestive of potassium deficiency, did not improve when the hypokalaemia was corrected. However, in this patient the serum bicarbonate was very high and as the symptoms were characteristic of the classical syndrome of 'alkalosis' it is likely that the hypokalaemia was secondary to a metabolic alkalosis, rather than the reverse (see discussion). In Case 5, also, the serum bicarbonate was unusually high so it is possible that some of his improvement was due to chloride replacement as much as to the potassium.

Hypokalaemia following the administration of this group of drugs is usually attributed to excessive urinary excretion of potassium causing a potassium deficiency (*Lancet*, 1960) but hypochloraemic alkalosis may also complicate their use, though this is less often appreciated (Veygrat, 1960). No doubt a true potassium deficiency, which may be accompanied by an extracellular alkalosis, is the more common but an alkalosis due predominantly to chloride deficiency may not be so rare, as in Case 6 and possibly in Case 5, and this could explain why hypokalaemia may be so intractable in some of these cases (Slater and Nabarro, 1958).

Case 7. M.C., a female aged 26, was a typical case of acute intermittent porphyria in whom a severe relapse was precipitated by an injection of thiopentone given as an anaesthetic for a dilatation and curettage. Serial changes in the serum electrolytes and Ke were recorded from the third day, during the progression and ultimate partial recovery of a severe episode of polyneuritis. These changes and the treatment are shown in Fig. 1, the course of the polyneuritis being approxi-

FIG. 1.—Case 7. Serial changes in serum electrolytes and total exchangeable potassium in a patient with a severe episode of polyneuritis due to acute intermittent porphyria.

mately paralleled by the changes in body-weight therein depicted. Slight fever, tachycardia and mild hypertension were present during the first four weeks and the urine initially contained albumin, red blood cells and casts. Constipation and abdominal pain had been present for some weeks before the development of the paralysis, but there had been no vomiting.

Hyponatraemia, hypokalaemia and hypochloraemic alkalosis were present initially. The hyponatraemia and hypochloraemia responded to oral sodium chloride, but hypokalaemia and an elevated serum bicarbonate were present for the first two months, during which supplemental potassium was given mainly in enteric-coated tablets. The evidence indicates that these were ineffective, for the serum potassium had risen temporarily when a potassium citrate mixture was given for five days at the beginning and it became and remained normal when soluble potassium salts were finally given. The serum bicarbonate, on the other hand, remained elevated for a further two months after the correction of the hypokalaemia.

Corticotrophin gel was given early in the illness, but the dosage was gradually reduced, as it did not appear to alter its course. The change to soluble potassium salts was made at the nadir of the illness, which complicates the interpretation of the results, but there was no immediate improvement and it was considered to be a coincidence at the time.

There was a fall in the Ke of 165 mEq during the progression of the muscular paralysis and a subsequent slow gain of 320 mEq when recovery was well advanced. It should be noted that the Ke rose by only 75 mEq when 700 mEq of soluble potassium supplements were ultimately given, though the serum potassium had promptly reverted to normal, which suggests that the hypokalaemia was not due to potassium deficiency. In fact, the serial changes in Ke ran in parallel with the early muscle wasting and subsequent recovery, and they can be entirely explained by initial loss and later gain of muscle mass.

Comment

Abnormalities in the serum electrolytes may occur during an acute exacerbation of this condition and they have usually been attributed to excessive vomiting (Goldberg, 1959). Eales and Linder (1962) in a review of 80 cases in South Africa found hypokalaemia in 29% and they, too, attributed this together with hypochloraemic alkalosis to vomiting. However, hyponatraemia was just as common in their series and this they did not adequately explain. These workers also reported a high incidence of renal involvement, 8% having proteinuria and 69% an elevated blood urea.

It thus seems probable in the present patient, and possibly others in the literature, that the electrolyte abnormalities were part of a general metabolic disorder and that the hypokalaemia was secondary to a metabolic alkalosis especially as this persisted after correction of the hypokalaemia. The cause of the alkalosis has not been determined but it may, in part, have been of renal origin as there was evidence of such involvement in this case and renal tubular lesions have been described in acute intermittent porphyria. (Prunty, 1949). Alternatively there is such a profound metabolic disturbance in this condition that it could well be due to other unrecognized factors.

Results

The results in respect of serum potassium and the corresponding Ke , $Ke/(kg. \text{ body-weight})$ and the increase in Ke after treatment with potassium supplements are summarized in Table 1. The absolute increase in Ke ranged from 185 to 1,100 mEq. The patients varied greatly in weight and general body habitus and a better indication of the significance of the changes is obtained if the initial values, when hypokalaemia was present, are expressed as a percentage of the values after treatment, which is here assumed to be the 'optimum' for their body-constitution at that time. With these criteria the initial Ke ranged from 53 to 89% of the 'optimum'.

$Ke/(kg. \text{ body-weight})$ when the patients were hypokalaemic, ranged from 18.5 to 28 mEq/kg. In the six patients without oedema; after treatment the range was from 30 to 42 mEq/kg.

Discussion

There is considerable difficulty in the interpretation of single estimations of Ke , particularly in patients with chronic illnesses. Even in healthy subjects there is a wide variation when Ke is related to body-weight but a better correlation is found by reference to the lean body mass (Muldowney, Crooks and Bluhm, 1957). Unfortunately, though, this parameter is not valid

TABLE I
CHANGES IN SERUM POTASSIUM AND TOTAL EXCHANGEABLE POTASSIUM BEFORE AND AFTER THE ADMINISTRATION OF
POTASSIUM SUPPLEMENTS

Case	Sex	Age	Diagnosis	Date	Weight (kg.)	Serum K (mEq/l.)	Ke (mEq)	Ke/kg. (mEq)	Percentage of Optimum Ke*	Treatment and Comments
1 M.H.	F	55	Chronic purgation. Inadequate diet	15. 5.59	30	2.0	780	26	54	Before K supplements
				8. 6.59	35	5.5	1,405	42	100	After " " "
				21. 7.59	35	5.4	1,445	41	99	No further K supplements
				19. 1.60	38	2.5	1,180	31	72	" " " "
				3. 2.60	39	6.5	1,630	42	100	After K supplements "
2 E.P.	F	62	Anorexia nervosa. Frequent rectal washouts	3.10.62	36	2.1	650	18	53	Before K supplements
				17.10.62	37	4.1	825	22	67	" " " "
				24.10.62	38	5.1	1,215	32	98	After " " "
				31.10.62	38	4.4	1,240	33	100	" " " "
3 W.W.	M	35	Treated military tuberculosis	19. 5.60	76	1.7	1,600	21	59	Before K supplements
				29. 6.60	64	4.5	2,700	42	100	After " " "
4 W.K.	F	47	Heart failure. Oral diuretics	12.10.61	78	2.6	1,110	—†	54	Before " " "
				26.10.61	78	4.3	2,070	—	100	After " " "
5 H.F.	M	67	Heart failure. Oral diuretics	22. 2.61	60	2.7	1,520	25	81	Before " " "
				15. 1.61	60	4.8	1,870	31	100	After " " "
6 K.H.	F	67	Heart failure. Oral diuretics	10.11.59	55	2.0	1,525‡	28	89	Before " " "
				24.11.59	50	3.5	1,710	34	100	After " " "
7 M.C.	F	26	Acute porphyria polyneuritis	3. 2.60	43	2.7	1,215	28	—§	Before " " "
				16. 2.60	39	3.0	1,095	28	—	After enteric-coated K
				16. 3.60	33	2.8	1,050	32	—	" " " "
				6. 4.60	35	3.8	1,060	30	—	After soluble K supplements
				26. 4.60	37	4.3	1,125	30	—	" " " "
				14. 6.60	44	4.4	1,370	31	—	" " " "

Notes: * The optimum Ke is the value after administration of potassium supplements and correction of true potassium deficiency.
† Not valid because of gross oedema.
‡ Initial calculation determined after chemical balance following potassium supplements for 48 hours.
§ Not valid because of muscle wasting due to polyneuritis.

in chronic illness, particularly if there has been much loss of muscle bulk (Staffurth, 1962). Numerous other parameters have been assessed in healthy subjects but none has proved to be of value in illness and probably because of this, reference to body-weight has been most used in studies on patients.

In the present cases the initial Ke in relation to body weight ranged from 18.5 to 28 mEq/kg. and if cases 6 and 7 in whom the hypokalaemia is not considered to be due primarily to potassium deficiency, are excluded the range was from 18.5 to 25 mEq/kg. body-weight, values which are well below the normal range for either sex. These results are similar to other cases of hypokalaemia in the literature but there are numerous instances where Ke/kg. has been of this order in chronically ill patients without hypokalaemia or other evidence of potassium deficiency, particularly in patients with cardiac failure, cirrhosis of the liver and steatorrhoea (Moore, Edelman, Olney, James, Brooks and Wilson 1954; Flear, Cawley, Quinton and Cooke, 1958; Birkenfeld, Leibman, O'Meara and Edelman, 1958; Nagent de Deuxchaisnes, Collet, Busset and Mach, 1961).

A low value for Ke in relation to body-weight may be found if there is a disproportionate loss of muscle bulk, in true potassium deficiency and in many chronic diseases where a reduced intra-

cellular potassium concentration is an obligatory part of the general metabolic disorder. Birkenfeld and others (1958) called this last group 'potassium depletion' in contrast to a true potassium deficiency which alone could be corrected by the administration of potassium supplements.

Although Ke measures only about 80% of the total body potassium it probably represents most that is readily available (Burrows, Ashley and Sisson, 1952) for the remainder, which is about equally divided between bone and cell mitochondria, is more firmly bound and is only slowly exchangeable (Fourman, 1957). In presenting the results in the present cases it has been assumed that the administration of potassium supplements will have corrected any potassium deficiency and therefore that Ke is the 'optimum' that could be expected for the body status then pertaining, both as regards total muscle bulk and any coexistent general illness. The increase in Ke gives an approximate indication of the magnitude of the original potassium deficiency. Because of the very different body habitus of patients, for instance Case 1 was a small woman and Case 3 a large man, a better indication of the significance of the changes is obtained if the initial values are expressed as a percentage of those found after repletion, namely the 'optimum'. This method has been applied also to the few instances in the

literature where similar measurements have been reported.

Chobanian, Burrows and Hollander (1961) investigated 11 patients with primary hyperaldosteronism, all of whom had a low serum potassium, in seven of whom it was less than 3.0 mEq/l. The initial Ke in these patients ranged from 19.6 to 30.5 mEq/(kg. body-weight). In two cases Ke was measured a second time before operation after the administration of potassium supplements. The increases amounted to 430 mEq. in each instance and if the second value is considered as the 'optimum', the original values were 76.5 and 84% respectively. In nine of the whole group Ke was determined after successful operation, usually several months later. By this time the increases in Ke were much larger ranging from 200 to 1,382 mEq, the mean being 720 mEq. However, they had probably increased their muscle mass and intracellular potassium concentration following operation so it is not justifiable to assume that the last values were the preoperative 'optimum'.

Blainey, Cooke, Quinton and Scott (1954) determined Ke in five cases of steatorrhœa before and after potassium supplements and found increases between 386 and 1,744 mEq. If the last values from their data are considered as the 'optimum' the initial values were between 58 and 76% in four cases. The fifth patient had severe muscle paralysis on admission, with serum potassium only 1.8 mEq/l., and the Ke was only 500 mEq. After potassium supplements for 40 days Ke was 1,048 mEq., which would indicate that the initial value was 48% of the 'optimum'. A later value of Ke was 2,352 mEq., a further gain of 1,304 mEq., but this was at least four months from the first reading by which time it seems probable that there had been a considerable improvement in general health and probably therefore in muscle mass.

Schwartz and Relman (1953) reported two cases of hypokalaemia due to chronic purgation. In one Ke rose from 1,120 to 1,659 mEq. after treatment, a gain of 539 mEq. In this instance the initial value was 67.5% of the final or 'optimum'. The absolute values of Ke are not given in the second case but Ke/(kg. body-weight) rose from 27.0 to 39.4 mEq. so that if the body-weight remained constant the original value was 68.5% of the 'optimum'.

In the present series Cases 1, 2 and 3 can be considered together for they all had severe symptoms typical of the clinical syndrome of hypokalaemia. The initial Ke was between 53 and 59% of the 'optimum' and these values can be compared with the most severe case of Blainey and others (1954), who had marked muscular

weakness and profound hypokalaemia, where the initial Ke was only 48% of the 'optimum'. Thus it would appear that in severe cases of hypokalaemia, accompanied by paralysis or severe weakness, the potassium deficiency is about half the available body potassium. In less severe instances of potassium deficiency: Cases 1 on second admission, 5 and 6 in the present series and in most of the other cases already quoted from the literature, the deficiency amounts to about one third.

Cases 6 and 7 seem to be different from the remainder for in the light of the serial changes in Ke and the clinical picture it seems improbable that the hypokalaemia was due to true potassium deficiency. In Case 7 the lowest value of Ke was 77% of the highest, but, as explained in the Case protocol, at the time of the last measurement there had been a considerable increase in muscle power and gain in weight due to concomitant recovery from the polyneuritis. It is unfortunate that added potassium was initially given in enteric-coated form as it was probably not absorbed but in the first three weeks on soluble potassium supplements the Ke rose by only 75 mEq., though the serum potassium had promptly become normal, which suggests that there was no potassium deficiency. Consequently it is considered that the hypokalaemia was part of the general metabolic disorder which had caused a metabolic alkalosis and this is supported by the fact that the serum bicarbonate remained elevated for a further two months after the hypokalaemia had been corrected. In Case 6 the clinical picture was that of 'alkalosis' and potassium supplements, which had caused a rapid elevation of the serum potassium, had no effect clinically. In this instance the initial Ke was 89% of the 'optimum', a difference which is barely significant, so it seems probable that here, too, the hypokalaemia was due to a metabolic alkalosis rather than being its cause.

There is no doubt that clinical and experimental potassium deficiency, severe enough to cause hypokalaemia, may be accompanied by an extracellular alkalosis and as a result there has been a tendency to assume that this association is always due to potassium deficiency. However, electrolyte abnormalities are seldom simple and the role of other factors, particularly chloride depletion, has been neglected. Moore, Bollig, Dittmore, Sicular, Teterick, Ellison, Hoyer and Ball (1955) showed that loss of chloride, particularly when combined with a high sodium intake or after stress, may lead to an alkalosis and hypokalaemia without any significant potassium deficiency, and recently Aber, Simpson, Whitehead and Brooke (1962) have stressed the necessity of chloride in the treatment of hypokalaemic alkalosis. It has also been shown that the serum

potassium level falls as arterial pH rises and that this is independent of the total body potassium (Burnell, Villamil, Uyeno and Scribner, 1956; Leibman and Edelman, 1959).

The paucity of similar studies in the literature is surprising but is no doubt due to the innumerable difficulties that exist in the application and interpretation of this method in the study of patients with hypokalaemia, for these are usually acute situations that require immediate treatment. The half-life of ^{42}K (12.5 hours) is so short that even with regular deliveries the isotope may not be available; moreover, because of the short half-life the radioactive measurements cannot be checked a few days later if unexpected results emerge, a practical point which may be of great disadvantage. In order to reduce technical errors to a minimum repeat determinations should be made under standard conditions, preferably by starting the investigation early one morning and collecting the spot urine samples 24 hours later (Staffurth, 1961). During this period added potassium should not be given, partly because Ke will change during the equilibrium period if potassium deficiency exists and also because its administration may affect the specific activity in the urine (Corsa and others, 1950). In practice this means that there is usually a delay of at least 48 hours from the time of the discovery of hypokalaemia before added potassium can be given. In severe cases such a delay is not justified and it may have been a factor in the severe complications that occurred in Case 3.

In spite of these practical difficulties it is apparent that much useful information can be derived from repeat determinations of Ke before and after potassium supplements. This method gives some indication of the magnitude of any true potassium deficiency and if applied to more patients with hypokalaemic alkalosis it should help

in elucidating the relative importance of potassium deficiency and other factors, particularly chloride deficiency, in the cause of this syndrome.

Summary

1. The total exchangeable potassium (Ke) has been determined in patients with hypokalaemia from a variety of causes and the initial values have been compared with one or more subsequent determinations after the administration of potassium supplements.

2. The initial values have been expressed as a percentage of those found after treatment, at which time Ke was considered to be 'optimum' for the state of health then pertaining. It is apparent that in severe hypokalaemia with paralysis there is a deficiency of nearly half of the body potassium. In less severe instances there is a deficiency of about one-third.

3. In two cases serial changes in Ke did not demonstrate a significant change in Ke and it is considered that the hypokalaemia may have been secondary to a metabolic alkalosis.

4. Isolated values of Ke are difficult to interpret because of the absence of a valid parameter with which to compare them. Ke per unit body-weight is the most convenient and the most frequently used in the literature but it is not a satisfactory index for the diagnosis of potassium deficiency.

5. Some of the difficulties in the application of the method to the study of acute clinical conditions are discussed and the limitations of the method has been stressed in these situations.

I am grateful to Dr. E. N. Allott for his encouragement and for help with the presentation and I thank Mr. John Whale for technical assistance. This work was done during the tenure of a part-time personal grant from the Clinical Research Board of the Medical Research Council, to whom I am very grateful.

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