International Journal of Applied Radiation and Isotopes, 1970, Vol. 21, pp. 183–191.

A Method for Simultaneous Electrolyte Investigations in Man Using ^{77}Br, ^{43}K and ^{24}Na

F. SKRABAL*, R. N. ARNOT, F. HELUS, H. I. GLASS and G. F. JOPLIN
Departments of Medicine, Medical Physics and M.R.C. Cyclotron Unit,
Hammersmith Hospital, London

(*Received* 31 *October* 1969)

The different gamma energies of ^{24}Na, ^{43}K and ^{77}Br allow analysis of mixtures of the three isotopes without any previous separation procedure, by gamma counting under three different conditions. A computer programme is used to perform the calculations.

^{77}Br and ^{43}K are cyclotron produced isotopes with half lives of 56 hr and 22·4 hr respectively. The principle gamma-ray emissions are at 240 keV and 520 keV for ^{77}Br and at 373 keV and 619 keV for ^{43}K. The radiation dose to the patient due to ^{77}Br is 0·3 mrad./μCi compared with 1·4 mrad./μCi for ^{82}Br; the dose due to ^{43}K is 0·6 mrad./μCi compared with 0·85 mrad./μCi for ^{42}K.

In vitro experiments show that mixtures of the three isotopes can be analysed with an error of less than 2 per cent.

The method is applied for simultaneous estimation of extracellular fluid volume, sodium space, exchangeable sodium and exchangeable potassium. The results are compared with a resin separation method and the findings in 10 subjects without electrolyte disorders are presented.

UNE MÉTHODE POUR DES RECHERCHES ELECTROLYTIQUES SIMULTANÉES DANS L'HOMME EMPLOYANT ^{77}Br, ^{43}K ET ^{24}Na

Les différentes énergies de ^{24}Na, ^{43}K et ^{77}Br permettent le dosage des mélanges des trois isotopessans aucun procédé de séparation préalable, en comptant les rayons gamma sous trois différentes conditions. Pour achever les calculs on employe un programme de calculateur.

Les isotopes ^{77}Br et ^{43}K sont produits dans le cyclotron et ont des demi-périodes, l'un de 56 hr et l'autre de 22,4 hr. Les principales émissions de rayons gamma sont à 240 KeV et 520 KeV pour le ^{77}Br et à 373 keV et 619 keV pour le ^{43}K. La dose de rayonnement au malade due au ^{77}Br est 0,3 mrad./μCi en comparaison avec 1,4 mrad./μCi pour le ^{82}Br; la dose due au ^{43}K est 0,6 mrad./μCi en comparaison avec 0,85 mrad./μCi pour le ^{42}K.

Des expériences *in vitro* montrent que l'on peut doser des mélanges des trois isotopes avec une erreur de moins de 2 pour cent.

La méthode s'applique à l'estimation simultanée du volume fluide extracellulaire, de l'espace de sodium, du sodium échangeable et du potassium échangeable. On compare les résultats à ceux d'une méthode de séparation à résine et on présente les résultats pour 10 sujets sans désordres électrolytiques.

МЕТОД ОДНОВРЕМЕННОГО ИССЛЕДОВАНИЯ ЭЛЕКТРОЛИТА В ЧЕЛОВЕКЕ ПРИ ПОМОЩИ ^{77}Br, ^{43}K И ^{24}Na

Гамма-излучения различных энергий от ^{24}Na, ^{43}K и ^{77}Br дают возможность анализировать смеси трех изотопов путем гамма-счета в трех различных условиях, без предварительной процедуры разделения. Вычисления производятся при помощи программы для вычислительной машины.

* Present address: Department of Medicine, Universitäts Klinik, Innsbruck, Austria.

^{77}Br и ^{43}K являются изотопами, полученными циклотроном; их сроки полураспада—56ч. и 22,4 ч. соответственно. Основные эмиссии гамма-лучей для ^{77}Br: 240 эв и 520 эв, а для ^{43}K: 373 эв и 619 эв. Доза облучения для пациента при ^{77}Br равна 0,3 мрад/μCi по сравнеиию с 1,4 мрад/μCi при ^{82}Br; доза при ^{43}K равна 0,6 мрад/μCi по сравнению с 0,85 мрад/μCi при ^{42}K.

Эксперименты in vitro показывают, что смеси трех изотопов можно анализировать с погрешностью менее чем 2%.

Этот способ применяется для одновременной оценки объема жидкости, натриевого пространства, обменного натрия и обменного калия. Результаты сравниваются с результатами, полученными при методе разделения смолами; приводятся данные, полученные для 10-ти человек, не страдающих электролитическими расстройствами.

EIN VERFAHREN FÜR SIMULTANE ELEKTROLYTUNTERSUCHUNGEN IM MENSCHEN UNTER VERWENDUNG VON ^{77}Br, ^{43}K UND ^{24}Na

Da die Gammaenergien von ^{24}Na, ^{43}K und ^{77}Br verschieden sind, können Gemische der drei Isotopen ohne vorherige Trennungsverfahren analysiert werden, durch Gammazählung unter drei verschiedenen Verhältnissen. Für die Rechnungen wird ein Rechenautomatprogramm verwendet.

^{77}Br und ^{43}K sind in einem Zyklotron hergestellte Isotopen mit Halbwertzeiten von 56 hr bezw. 22,4 hr. Die hauptsächlichen Gammastrahlungen treten bei 240 keV und 520 keV für ^{77}Br und bei 373 keV und 619 keV für ^{43}K auf. Die Strahlungsdosis zum Patienten, die vom ^{77}Br herrührt, ist 0,3 mrad/μCi, verglichen mit 1,4 mrad./μCi für ^{82}Br; die Dosis von ^{43}K is 0,6 mrad./μCi, verglichen mit 0,85 mrad./μCi für ^{42}K.

In vitro-Experimente haben gezeigt, dass Gemische der drei Isotopen mit einem Fehler von unter 2 Prozent analysiert werden können.

Das Verfahren wird verwendet für die simultane Abschätzung des Flüssigkeitsvolumens ausserhalb der Zelle, des Natriumraums und des austauschbaren Natriums und austauschbaren Kaliums. Die Ergebnisse werden verglichen mit einem Kunstharztrennverfahren und der Befund in zehn Patienten ohne Elektrolytstörungen wird vorgelegt.

1. INTRODUCTION

THE SIMULTANEOUS measurement of exchangeable sodium, exchangeable potassium, extracellular fluid volume (ECFV) and total body water (TBW) not only gives information on the body stores, but also permits the calculation of distribution of electrolytes and water between the intra and extracellular compartments and of the intracellular concentration of sodium and potassium. ^{24}Na and ^{42}K have been the tracers most commonly used to estimate exchangeable Na and exchangeable K, while inulin,[1,2] $^{35}SO_4$[3,4] or ^{82}Br[5,6] have been used for estimation of ECFV, and deuterium oxide[7] and tritiated water[8,9] for measuring TBW. Bromide seems to be the most desirable[5,6,10] for ECFV measurement since both the fluid in connective tissue and transcellular water are measured, yet the ion penetrates the cells only to a small degree.

Hitherto, the disadvantages of using four isotopes simultaneously were impaired accuracy when compared with single isotope methods,[11] and the fact that only a restricted number of patients could be investigated owing to the lengthy analytical procedures involved.

Most workers[12,13] have separated ^{82}Br from ^{24}Na and ^{42}K by means of ion exchange resins and then assayed the mixture of ^{24}Na and ^{42}K by using a gamma counter for ^{24}Na and a G.M. tube to estimate ^{42}K. The introduction of ^{43}K[14] made it possible to assay all three isotopes in a gamma counter, but the resin separation of ^{82}Br from ^{24}Na and ^{43}K was still required.

The resin separation has several disadvantages. Apart from the time involved inaccuracies are introduced. Firstly, the passage of the sample through the resin may cause dilution of the sample and its tracers; this requires a correction to be made by measuring the stable element chemically before and after passing through the column. For example, the Na space requires the measurement of the stable Na concentration both on the counted sample as well as on untreated plasma. If undiluted plasma could be counted directly, the calculation of Na space would not involve any chemical estimation.

The same considerations apply to the Br space measurement if a cation exchange resin is used. Secondly, if an anion exchange resin is used and the resin containing the Br ions is counted, great care is required; the columns must be washed with a sufficient volume of water to remove all cations, and also the standard solutions must be prepared in the same way to avoid errors due to different counting geometries and sensitivities. Since it is small variations in the ratio of Na space to Br space that may be of particular interest,[15] it is undesirable to estimate these two quantities in different systems as described above.

The method described in this paper uses cyclotron produced ^{77}Br and ^{43}K together with ^{24}Na. The use of ^{77}Br instead of ^{82}Br makes it possible to estimate all these three isotopes simultaneously by direct gamma counting, thus enabling the calculation of the Na space, exchangeable Na, exchangeable K and extracellular fluid volume by counting of untreated plasma and urine samples. Tritium may be estimated on the same samples after decay of the other three isotopes. Gamma counting is performed on an automatic counter using three different energy bands, and a computer programme is used to perform the calculations of the equations, allowing for decay of the isotopes during the counting time. The method considerably decreases the time involved in sample preparation, and leads to improved accuracy and to a reduced radiation dose.

2. ISOTOPES

2.1 *Production of* ^{77}Br

^{77}Br is produced by the reaction ^{75}As (α, $2n$)^{77}Br. The target material As_2O_5, is bombarded with α-particles of approximately 28 MeV in the external beam of the Medical Research Council cyclotron. The yield of ^{77}Br at 20 μA beam current is about 3 mCi at the end of a 1 hr bombardment. After bombardment the target is left overnight to allow short-lived activities (e.g. ^{18}F and ^{78m}Br) to decay before beginning the chemical separation of the ^{77}Br.

The bombarded As_2O_5 is dissolved in hot water and the resulting solution is transferred to a distillation apparatus. Concentrated H_2SO_4 and $K_2Cr_2O_7$ are added, and on heating the radiobromine is distilled quantitatively, without the addition of carrier, into an ice-cooled water trap. The pH of this solution is then adjusted to 9 and a drop of $NH_2OH{\cdot}HCl$ solution is added to reduce the radiobromine to bromide before evaporating it to dryness and heating the residue to about 400°C to decompose possible pyrogenic contaminants. The residue is subsequently dissolved in water for injection and the resulting solution is filtered after re-adjusting the pH to 6–7. Full details of this procedure and of the methods used in checking the purity of the product are given elsewhere by one of us.[16]

2.2 *Production of* ^{43}K

^{43}K is produced by the ^{40}A(α, p)^{43}K reaction in the external beam of the Medical Research Council cyclotron. Details of the production are presented elsewhere.[14,17]

2.3 ^{24}Na

This was received in the form of NaCl in isotonic solution from the Radiochemical Centre, Amersham.

3. PHYSICAL CHARACTERISTICS AND RADIATION DOSAGE OF ^{77}Br

The principal emissions and physical constants of ^{77}Br are shown in Table 1. The constants of ^{82}Br are given for comparison. The whole body radiation doses from ^{77}Br and ^{82}Br have been calculated to be 0·3 and 1·4 mrad./μCi

TABLE 1. Physical properties of ^{77}Br

γ energy (MeV)	% disintegrations
0·24	30
0·30	6
0·52	24
0·58	7
0·75	2
0·82	3
1·00	1

Max. β energies: 0·34 MeV (^{82}Br: 0·44 MeV).

Specific γ ray constant: 2·2 r/mCi.hr at 1 cm (^{82}Br 14·6 r/mCi.hr at 1 cm).

Average β energy: 0·002 MeV/dis (^{82}Br: 0·150 MeV/dis).

Half-life: 56 hr (^{82}Br: 35·4 hr).

respectively for a patient of 70 kg. The total whole body radiation dose due to our currently used 20 μCi of ^{24}Na, 50 μCi of ^{43}K and 30 μCi of ^{77}Br is 60 mrad. In comparison, the dose due to our former quantities of 20 μCi of ^{24}Na, 50 μCi of ^{42}K and 10 μCi of ^{82}Br is 78 mrad.

4. CLINICAL PROCEDURES

20 μCi of ^{24}Na and 50 μCi of ^{43}K were administered intravenously at 9 a.m. 30 μCi of ^{77}Br were given 12 hr later. Doses for injection were prepared in the same type of vial as was used for sample counting. After injection, the residue in the syringe was washed into the dose vial and made up to 10 ml for subsequent counting. Normal meals were permitted from 9 a.m. to 8 p.m., after which no fluids or food were permitted until 10 a.m. the next day. Urine was collected in polythene bottles as follows: 0–24 hr, 24–25 hr, 25–26 hr. Heparinised blood samples were taken at 24 hr and 25 hr.

5. RADIOACTIVE ASSAY AND CALCULATION OF RESULTS

A dose of each isotope, identical to that given to the patient, or of known ratio to it, was used to prepare three standard solutions by diluting each dose with distilled water up to 1 l. Duplicate 10 ml samples of each standard solution and 10 ml of each plasma and urine sample were transferred into counting vials. All vials, together with a background sample and with the two dose residues were counted twice on a two channel automatic gamma counter. The first time, the channels were arranged to accept energies between 320 keV and 447 keV (^{43}K), and between 1·2 MeV and 4·5 MeV (^{24}Na) respectively. The samples were counted again immediately (or up to 2 days later), using one channel arranged to accept energies between 190 keV and 275 keV (^{77}Br). Spectra of the three isotopes, showing the three gate widths used are given in Fig. 1. The counting efficiencies for the isotopes in each channel are also given.

The quantity of each isotope in the samples was calculated using a computer programme to solve the three relevant simultaneous equations. After correcting all samples for background, the mean net count rates of each standard in the three channels are corrected for decay to the midpoint of the counting period for every sample. Since the fraction of the dose contained

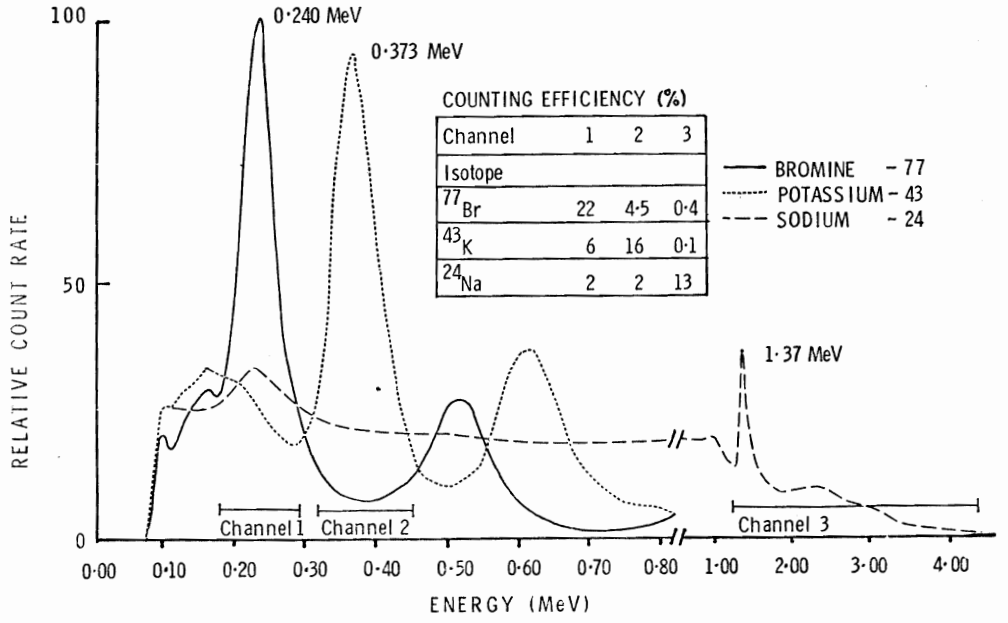

FIG. 1. Energy spectra of ^{77}Br, ^{43}K, ^{24}Na, showing the channels used and the counting efficiencies for each isotope.

TABLE 2. Results of *in vitro* experiments: Note: The expected result for each isotope in every sample was 0·5 per cent does per ml

Isotopes in mixture	^{24}Na		^{43}K				^{77}Br			
	% dose/ml	%error	% dose/ml	% error	% dose/ml*	% error	% dose/ml	% error	% dose/ml*	% error
^{24}Na	0.4978	−0·44	0·4885	−2·30	0.4832	−3·36	0·4975	−0·50	0·5074	1·48
	0·5015	0·30	0·4977	−0·46	0·4989	−0·22	0·4978	−0·44	0·4956	−0·88
^{43}K	0·5112	2·24	0·4882	−2·36	0·4910	−1·80	0·5051	1·02	0·4999	−0·02
	0·4877	−2·46	0·4901	−1·98	0·4897	−2·06	0·5012	0·24	0·5019	0·38
^{77}Br	0·5120	2·40	0·4846	−3·08	0·4872	−2·36	0·5126	2·52	0·5080	1·06
	0·5072	1·44	0·5031	0·62	0·5066	1·32	0·5112	2·24	0·5049	0·98
^{24}Na	0·5017	0·34					0·5025	0·50	0·5082	1·64
	0·5019	0·38					0·5044	0·88	0·5067	1·34
^{77}Br	0·5049	0·98					0·5092	1·84	0·5011	0·22
^{43}K			0·5139	2·78	0·5135	2·70	0·5035	0·70	0·5043	0·86
			0·5008	0·16	0·4985	−0·30	0·4996	−0·08	0·5039	0·78
^{77}Br			0·4961	−0·78	0·5023	0·46	0·5131	2·62	0·5018	0·36
^{24}Na	0·4982	−0·35	0·4997	0·05	0·4972	−0·55				
	0·5013	0·27	0·5062	1·25	0·5052	1·05				
^{43}K	0·5092	1·85	0·4986	−0·28	0·4974	−0·52				
	0·5076	1·52								
^{24}Na	0·5068	1·37								
	0·5052	1·05								
							0·5060	1·20	0·5035	0·70
^{77}Br							0·5015	0·30	0·5061	1·22
							0·4967	−0·65	0·5106	2·12
			0·5078	1·57	0·5053	1·07				
^{43}K			0·5108	2·17	0·5091	1·82				
			0·5028	0·57	0·5048	0·97				
Mean (%) and coefficient of variation	100·72 ± 1·42%		99·85 ± 1·73%		*99·88 ± 1·53%		100·82 ± 1·08%		*100·81 ± 0·74%	

* Results obtained by recounting the samples two days later under ^{77}Br conditions.

in each standard vial is known, the counting efficiency in each channel is calculated in counts/sec/per cent of dose. The results are expressed as the percentages of the three doses contained in each ml. of sample.

The expression used to calculate, for example, the total quantity of potassium in a sample is:

$$\%\text{K dose} = \frac{(B_3N_2 - B_2N_3)(B_2C_1 - B_1C_2) - (B_2N_1 - B_1N_2)(B_3C_2 - B_2C_3)}{(B_3N_2 - B_2N_3)(B_2K_1 - B_1K_2) - (B_2N_1 - B_1N_2)(B_3K_2 - B_2K_3)}$$

where K, N and B are the sensitivities in counts/sec/per cent of the ^{43}K, ^{24}Na and ^{77}Br doses respectively. The subscripts 1, 2 and 3 refer to the ^{43}K, ^{24}Na and ^{77}Br channels respectively. C_1, C_2 and C_3 are the count rates in counts/sec obtained from the sample in the ^{43}K, ^{24}Na and ^{77}Br channels respectively. Similar expressions are used for estimating sodium and bromine.

The computer programme allows for volumes other than 10 mls to be used, and for variation of volumes between samples. More than one background sample may be used; this permits activity which may be left from a previous investigation to be taken into account, by counting plasma and urine samples taken prior to administration of the new dose. A correction may be applied for different chemical concentrations in active background samples and the new samples. The half-lives were taken to be 15·0 hr for ^{24}Na, 22·4 hr for ^{43}K and 56·0 hr for ^{77}Br.

Spaces and exchangeable electrolytes were obtained using standard calculations.[13] Plasma was used for the measurement of Na space, exchangeable Na and ECFV while urine was used to estimate exchangeable K. A factor of 0·9 was applied to correct the bromide space for serum water and Donnan equilibrium.

6. COMPARISON OF THE PROCEDURE WITH PREVIOUS METHOD

In studies on five patients, both the resin separation method and the new method were used simultaneously to confirm that there was no significant difference between the two methods.

7. *IN VITRO* EXPERIMENTS

Dilutions containing either all three isotopes, any combination of two of them, or each single isotope were prepared in concentrations that gave count rates similar to those obtained in an average urine or plasma sample. The three original solutions that were used to make the above dilutions were used as standards. Standards and triplicate "unknowns" were counted under the three conditions on the same day. The samples were recounted two days later under ^{77}Br conditions to investigate the effect of the differential decay of the three isotopes. The counting time was increased on the third day in order to obtain the same number of counts as on the first day. These data and the counts observed under ^{24}Na and ^{43}K conditions on the first day were used when recalculating the results.

TABLE 3. Results of comparison between resin method and triple isotope method in five patients

	Exchangeable Na (mEq)			Exchangeable K (mEq)			Extracellular fluid volume (l.)		
Patient	Resin	Triple	% Diff.	Resin	Triple	% Diff.	Resin	Triple	% Diff.
1	2791	2834	−1·5	2894	2781	−3·9	18·358	18·089	−1·5
2	3875	3760	−2·9	3655	3658	+0·1	24·224	23·487	−3·0
3	2902	2918	+0·5	2656	2804	+5·6	17·094	17·197	+0·6
4	2341	2369	+1·2	2043	2180	+6·7	14·688	15·188	+3·4
5	3026	3136	+3·6	2582	2684	+3·9	19·364	19·471	+0·6
Mean difference			0·18			2·48			0·02
Range			−2.9 to +3·6			−3·9 to +6·7			−3·0 to +3·4

TABLE 4. Results of clinical investigations

No.	Sex	Diagnosis	Age	Weight (kg)	Height (ft) (in.)	ECFV (ml/kg) at 12 and 13 hr	ECFV (ml/kg) Mean	ECFV (ml/kg) % Diff.	Na space (ml/kg) at 24 and 25 hr	Na space (ml/kg) Mean	Na space (ml/kg) % Diff.	Na space/ ECFV	Exchangeable Na (mEq/kg) at 24 and 25 hr	Exchangeable Na (mEq/kg) Mean	Exchangeable Na (mEq/kg) % Diff.	Exchangeable K (mEq/kg) at 24 and 25 hr	Exchangeable K (mEq/kg) Mean	Exchangeable K (mEq/kg) % Diff.
1	M	Normal	22	63·7	5 10	269·3 270·5	269·9	0·4	327·5 322·1	324·8	−1·6	1·20	46·2 45·4	45·8	−1·7	45·3 42·7	44·0	−5·7
2	F	Normal	25	55·5	5 6	268·3 278·9	273·6	3·8	302·5 307·3	304·9	1·6	1·11	42·3 43·0	42·7	1·7	39·2 39·2	39·2	0·0
3	F	Normal	30	76·4	5 11	239·2 242·2	240·7	1·2	285·4 280·4	282·9	−1·8	1·18	39·3 38·7	39·0	−1·5	30·8 30·7	30·8	−0·3
4	M	Normal	46	68·1	5 4	219·1 221·1	220·1	0·9	258·5 256·7	257·6	−0·7	1·17	36·7 36·4	36·6	−0·8	37·5 38·0	37·8	1·3
5	F	Simple obesity	24	120·0	5 7	164·3 160·1	162·2	−2·6	184·0 184·0	184·0	0·0	1·13	26·1 25·9	26·0	−0·8	22·3 24·2	23·3	8·5
6	F	Simple obesity	32	105·1	5 1	171·8 172·3	172·1	0·3	187·5 195·9	191·7	4·5	1·11	26·0 27·0	26·5	3·8	28·0 26·9	27·5	−3·9
7	F	Simple obesity	33	91·9	5 3	174·5 172·3	173·4	−1·3	200·5 202·0	201·3	0·7	1·16	27·6 27·8	27·7	0·7	29·3 28·8	29·1	−1·7
8	F	Simple obesity	68	87·6	5 6	190·2 190·2	190·2	0·0	221·6 216·6	219·1	−2·3	1·15	30·4 29·6	30·0	−2·6	20·4 21·0	20·7	2·9
9	F	Osteoporosis	49	61·5	5 3	231·4 222·4	226·9	−3·9	267·0 254·2	260·6	−4·8	1·15	37·9 36·1	37·0	−4·7	31·1 31·9	31·5	2·6
10	F	Osteoporosis	57	52·9	5 4	288·3 290·1	289·2	0·6	348·1 347·8	348·0	−0·1	1·20	49·7 49·7	49·7	0·0	26·7 26·9	26·8	0·7
		Mean difference (%)						−0·06			−0·45				−0·59			+0·44
		Standard deviation						±2·1			±2·5				±2·4			±3·9

8. RESULTS

The results of the *in vitro* experiments shown in Table 2 indicate that the error in the simultaneous measurement for ^{24}Na, ^{43}K and ^{77}Br is 1·42, 1·73 and 1·08 per cent respectively. Using the differential decay in addition the errors were 1·5 per cent for ^{43}K and 0·74 per cent for ^{77}Br. The results for ^{24}Na were unchanged. The computer calculated estimates for the isotopes that were not present in the mixture are not given in Table 2; they were all close to zero, with a mean of 0·0013 per cent of dose and a range from −0·004 to +0·006.

Table 3 shows the results of the comparison between the formerly used resin method and the current non resin method in five clinical studies. The average difference for the estimation of exchangeable Na is 0·54 per cent (range −2·9 to +3·6 per cent); the corresponding values for exchangeable K were +2·0 per cent (range −3·9 to +6·7 per cent), and for the Br space were −0·3 per cent (range −3·0 to +3·4 per cent).

The results in 10 subjects without electrolyte disorders are given in Table 4. The mean per cent differences between results at the paired sampling times were less than 0·6 per cent. The standard deviations of the differences were as follows: Br space 2·1 per cent, Na space 2·5 per cent, exchangeable Na 2·4 per cent, and exchangeable K 3·9 per cent.

9. DISCUSSION

The results of the *in vitro* experiments indicate that the method is accurate to within 2 per cent for analysis of a mixture of the three isotopes, any two or any one of them. No significant improvement is obtained by allowing the ^{43}K and ^{24}Na to decay for two days before counting under ^{77}Br conditions. Full results could therefore be obtained a few hours after collections are completed.

Table 3 shows that no significant difference exists between the established resin method and the present method.

The results for the four normals given in Table 4 agree well with the values of other workers.[18–20] An equilibration period of 24 hr for Na and of 12 hr for Br was chosen, since it has been shown that equilibration is virtually complete at this time.[21,22] Exchangeable K was estimated at 24 hr and a second sample at 25 hr; the similarity of these values indicates that at 24 hr the slowly mixing phase of equilibration had been reached.[18] Furthermore, it has been shown[23] that only a small increase of exchangeable K occurs between 24 and 40 hr if patients are kept on a K free diet. These two facts led us to adopt the 24–hr equilibration period.

The mean value of the Na/Br space ratio in normals was found to be 1·16 with a range from 1·11 to 1·20. This compares well with the values obtained by other workers.[15,21] As the method permits the estimation of the Na space and Br space in the same counting vial in the presence of radioactive K, errors due to the different handling of the samples are avoided. With this improved accuracy it may be possible to study some outstanding clinical problems in detail such as an investigation of intracellular Na gains and bone Na exchangeability.

This simple procedure for simultaneous electrolyte studies in man makes the isotopes ^{77}Br and ^{43}K particularly suitable for large scale investigations. Their half lives (56 and 22 hr) make it practicable to consider their use in locations remote from a cyclotron. The lower radiation dosage is another advantage of these isotopes.

Acknowledgements—We wish to thank Dr. R. Haslam and her staff for performing the chemical estimations, and Mr. A. Richards for the radiation dosimetry calculation. The ^{24}Na and expendables were purchased with a grant to G. F. J. from the Ernest and Minnie Dawson Cancer Trust. F. S. gratefully acknowledges an Austrian Government Fellowship. We are also pleased to acknowledge critical comments on the manuscript from Professor Russell Fraser.

REFERENCES

1. Gaudino M. *Proc. Soc. exp. Biol.* **68,** 507 (1948).
2. Schwartz I. L., Schachter D. and Freinkel N. *J. clin. Invest.* **28,** 1117 (1949).
3. Cardozo R. H. and Edelman I. S. *J. clin. Invest.* **31,** 280 (1952).
4. Murphy B. *Can. J. Biochem.* **41,** 497 (1963).
5. Berson S. A. and Yalow R. S. *Science* **121,** 34 (1955).

6. Bradley J. E. S., Davidsson D., MacIntyre I. and Rapaport A. *Biochem. J.* **62,** 33p (1956).
7. Schloerb P. R., Friis-Hansen B. J., Edelman I. S., Solomon A. K. and Moore F. D. *J. clin. Invest.* **29,** 1296 (1950).
8. Prentice T. C., Siri W., Berlin N. I., Hyde G. M., Parsons R. J., Joiner E. E. and Lawrence J. H. *J. clin. Invest.* **31,** 412 (1952).
9. Edelman I. S., Haley H. B., Schloerb P. R., Sheldon D. B., Friis-Hansen B. J., Stoll G. and Moore F. D. *Surgery Gynec. Obstet.* **95,** 1 (1952).
10. Gamble J. L., Robinson J. S., Hannigan C. A., Foster C. G. and Farr L. E. *J. clin. Invest.* **32,** 483 (1953).
11. James A. H., Brooks L., Edelman I. S., Olney J. M. and Moore F. D. *Metabolism* **3,** 313 (1954).
12. Robinson C. V., Arons W. L. and Solomon A. K. *J. clin. Invest.* **34,** 134 (1955).
13. Veall N. and Vetter H. *Radioisotope Techniques in Clinical Research and Diagnosis*, p. 209. Butterworth, London (1958).
14. Skrabal F., Glass H. I., Clark J. C., Jeyasingh K. and Joplin G. F. *Int. J. appl. Radiat.* **20,** 677 (1969).
15. Crooks J., Bluhm M. M. and Muldowney F. P. *Clin. Sci.* **18,** 175 (1959).
16. Helus F. *Radiochem. Radioanalyt. Lett.* (in press 1970).
17. Clark J. C. and Silvester D. *Radiochem. Radioanalyt. Lett.* (submitted 1970).
18. Corsa J., Jr., Olney J. M., Jr., Steenburg R. W., Ball M. R. and Moore F. D. *J. clin. Invest.* **29,** 1280 (1950).
19. Forbes G. B. and Perley A. *J. clin. Invest.* **30,** 558 (1951).
20. McMurray J. D., Boling E. A., Davis J. M., Parker H. V., Magnus I. C., Ball R. and Moore F. D. *Metabolism* **7,** 651 (1958).
21. Forbes G. B., and Perley A. M. *J. Lab. clin. Med.* **34,** 1599 (1949).
22. Davies R. H., Kornberg H. L. and Wilson G. M. *Biochim. biophys. Acta* **9,** 703 (1952).
23. *Compartments, Pools and Spaces in Medical Physiology*, p. 42. U.S. Atomic Energy Commission (1967).