CXLVII. INORGANIC CONSTITUENTS OF CEREBROSPINAL FLUID.

IV. THE POTASSIUM IN SERUM, SERUM-ULTRAFILTRATE AND CEREBROSPINAL FLUID.

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A number of investigators have examined the cerebrospinal fluid for potassium and reported that it contains 25–50 % less than the serum. The averaged serum values of the different observers vary very much, and, although their averaged cerebrospinal fluid values are more consistent, the range of scatter of the individual cases differs considerably from one observer to another. Thus in serum Parhon and Werner [1932] found relatively little scatter (16·4–18·9 mg. per 100 cc.), but figures ranging from 15 to 27 mg. have been given by others. The lowest and most constant values (13·7–14·0 mg. per 100 cc.) have been reported by Dulière [1931], who separated the plasma from oxalated blood as rapidly as possible after removal from the body.

In the C.S.F. Dulière again found relatively constant potassium values, which averaged 11·17 mg. per 100 cc. Others, however, while agreeing on this average have found much wider variations, for example 10–18 mg. [Ballif and Gherscovici, 1932].

The literature on this subject has been reviewed by Nourse, Smith and Hartman [1925] and more recently by Lierle and Sage [1932] and need not be further discussed.

It is generally agreed that the whole of the potassium of serum is diffusible [*e.g.* Rona *et al.* 1924; Massaut, 1931, 1, 2], but Greene and Power [1931], who used *in vivo* dialysis in dogs, found 24 % non-diffusible.

If the whole of the potassium is in fact diffusible one would expect to find that any body fluid formed from the serum by simple physical means would contain about as much potassium as the serum. Thus, whatever may be true of the cerebrospinal fluid, this relationship might be expected in pleural effusions, hydroceles and ascitic fluids. Here again an investigation of the literature showed widely differing results. Loeb *et al.* [1922] obtained an average of 9·77 mg. K per 100 cc. in a series of fluids, mostly ascitic, whereas the corresponding serum value was 16·03 mg. per 100 cc. Three examples of potassium in oedema fluid given by Salvesen and Linder [1923] were 70–80 % of the serum values. The individual figures varied greatly and are higher than those given by Loeb *et al.* Greene *et al.* [1931], in experimental oedema in dogs, found that the potassium content of the fluid was the same as that of the serum. On the other hand ascitic fluid from human subjects had an average of 13 mg. K per 100 cc. compared with 17 mg. in their sera. Contrary to these findings are those of Dumitresco-Mante and Petrovano [1931] who found the potassium of centrifuged pleural fluid to be equal to, or (more generally) somewhat higher than, that of the corresponding serum.

Comparison has also been made between serum and ocular fluids, with equally divergent results. Tron [1926] using ox and horse, and Lebermann [1925] using rabbit, found only some 70 % of the serum-K in the vitreous and aqueous humours. Duke-Elder [1927], however, who has brought forward very complete evidence that the ocular fluids are true ultrafiltrates, obtained a close approximation between the serum- and aqueous-potassium. Stary and Winternitz [1932] also found close agreement between the potassium of the ventricle fluid of the eye and that of the serum-ultrafiltrate, both being somewhat higher than the serum value. Cohen *et al.* [1928] compared vitreous with cerebrospinal fluids and found average values of 24·9 mg. per 100 cc. for the former and 19·5 mg. for the latter. Both these figures are high and no serum values are given; nevertheless the ratio of the two suggests that they are not both formed from the serum in the same way.

In considering the reason for serum values being higher than those of the C.S.F. or other body fluids, one must remember the possibility that the higher serum values may be due to the potassium in the corpuscles leaking into the serum during the formation of the clot, since the lowest figures for serum potassium have been obtained on rapidly separated plasma [Dulière, 1931]. There is also the fact that some 24 % of the serum-potassium has been held by one group of workers to be non-diffusible [Greene and Power, 1931].

The present investigation has been prompted by these uncertainties and by the importance of the result in assessing how far the C.S.F. can be regarded as a serum-ultrafiltrate.

Methods.

Blood was collected chiefly from in- and out-patients of King's College Hospital; some specimens were obtained from the National Hospital, Queen Square. The general technique has been described previously [McCance and Watchorn, 1931]. When for special purposes (see Table III) it was desired to separate the serum from the corpuscles as quickly as possible, the following procedure was adopted. A S.I.M.A. serum needle (Down Bros.) with rubber tubing attached was inserted into the vein. The patient was then bled with light constriction direct into a large paraffin-coated tube which was immediately centrifuged at high speed for 4–5 minutes. The supernatant fluid was pipetted off rapidly into another smaller centrifuge-tube and allowed to clot. This white clot was later broken up and clear serum obtained by centrifuging. The C.S.F. was withdrawn 15 minutes after the blood.

For the majority of the analyses Kramer and Tisdall's [1921] method was used. Determinations were made in duplicate at least, frequently in triplicate or quadruplicate. Some idea of the accuracy of the method may be obtained from the following figures obtained on the same large sample of mixed sera. Each ultrafiltrate figure represents a separate filtration.

Serum (mg. per 100 cc.)	Ultrafiltrate (mg. per 100 cc.)
26·40	29·04
27·09	27·59
26·40	27·22
26·08	29·74
26·71	27·59
—	29·24

A few of the later determinations (including all those in Table IV) were made by Jacobs and Hoffman's [1931] colorimetric modification of Kramer and Tisdall's method. This enables the precipitate of potassium cobaltinitrite to be

washed with alcohol, in which it is completely insoluble. This excludes also the possibility of high serum results being due to the oxidation of organic matter, *e.g.* protein debris, by the permanganate in the titration method. The colorimetric method gave closer agreement between duplicates than did the titrimetric and was of particular advantage in dealing with body fluids other than serum and C.S.F. in which a great deal of organic matter is sometimes precipitated. In these cases the coloured solutions were lightly centrifuged before matching in the colorimeter.

The method of ultrafiltration used was the same as that previously described [McCance and Watchorn, 1931].

Results.

Table I shows the amount of potassium found in a series of sera, their corresponding ultrafiltrates and cerebrospinal fluids. The whole of the serum-potassium appears to be diffusible. The percentage shown in the ultrafiltrates

Table I. *Potassium in serum, serum-ultrafiltrate, and C.S.F.*

Diagnosis	Serum per 100 cc.	Ultra-filtrate	C.S.F.
Cerebral tumour	18·15	20·76	13·06
Taboparesis	17·63	19·06	12·93
Parenchymatous nephritis	20·24	21·55	11·23
Diabetes	18·54	20·24	—
Disseminated sclerosis	21·03	23·64	12·80
,,	19·98	21·81	13·71
,,	23·90	25·07	12·93
Neuro-syphilis	20·37	20·37	12·41
Cerebral tumour	23·05	24·14	10·82
Tabes	21·81	22·72	10·82
Amyotrophic lateral sclerosis	17·15	18·56	15·00
Cirrhosis of liver	18·56	18·69	—
? Syphilis	17·02	17·15	12·67
Cerebral tumour	17·66	19·58	10·75
Epilepsy	22·53	23·68	—
Meningo-vascular syphilis	17·56	19·27	12·67
Average	19·70	21·20	12·45

Table II. *Additional C.S.F.-potassium values.*

Diagnosis	C.S.F. (mg. per 100 cc.)
T.B. meningitis	13·19
,,	11·49
,,	13·45
,,	14·07
,,	11·62
,,	12·95
Meningococcal meningitis	12·22
,,	8·16
Chronic nephritis	9·79
Trauma with neurological signs	11·78
Spinal tumour	11·01
Tumour of cauda equina	11·44
Meningeal haemorrhage	7·96
Cerebral arterio-sclerosis	12·69
Cerebral cyst and tumour	11·87
Average	11·58

is actually higher than that in the serum because no correction has been made for the space occupied by the serum-proteins. Cerebrospinal fluid taken from the same patients at the same time invariably contained less potassium than the

serum. A further series of cerebrospinal fluids (Table II) also failed to give values approaching those usual for serum. All the sera in Table I had been left in contact with the corpuscular clot for some 6 to 18 hours before separation. A further series of comparisons therefore was undertaken in which the effect on the serum-K of leaving the serum in contact with the corpuscles was studied. From Table III it appears that there is no appreciable diffusion of potassium

Table III. *Potassium content of serum in contact with clot and of C.S.F.*

Serum (mg. per 100 cc.)	Time in contact with clot	Serum (mg. per 100 cc.)	Time in contact with clot	Increase (mg. per 100 cc.)	C.S.F. (mg. per 100 cc.)
18·31	0 hours	23·05	18 hours	4·74	10·82
17·66	0 ,,	20·22	18 ,,	2·56	—
15·78	0 ,,	17·09	10 ,,	1·31	11·44
18·23	0 ,,	21·08	18 ,,	2·85	13·37
17·87	0 ,,	18·27	20 ,,	0·40	15·15
18·27	0 ,,	21·15	19 ,,	2·88	13·26
15·39	0 ,,	17·58	18 ,,	2·19	12·69
17·15	0 ,,	17·15	5 ,,	Nil	—
18·51	0 ,,	18·82	7 ,,	0·26	—
17·02	0 ,,	17·28	7 ,,	0·26	—
19·70	0 ,,	19·91	7 ,,	0·21	11·97

out of the corpuscles for the first 7 hours after taking blood, but that later the serum-K slowly increases. These results therefore show that the potassium in the C.S.F. is generally much below that in the serum and that although potassium does tend to leak from the corpuscles after about 7 hours this does not account for the serum/C.S.F. relationship.

Table IV. *Potassium in various fluids.*

	Potassium		Protein	
	Serum (mg. per 100 cc.)	Fluid	Serum %	Fluid %
Hydrocele fluid	16·43	16·57	—	—
,,	14·33	15·26	—	—
,,	16·57	15·10	—	—
,,	—	18·27	—	—
,,	16·95	18·04	—	—
,,	14·91	17·18	—	—
Pleural fluid	16·56	14·06	—	—
,,	18·69	18·74	—	—
,,	18·02	19·91	7·2	5·1
Ascitic fluid	19·30	17·96	—	—
,,	17·44	16·08	2·7	0·18
,,	13·32	16·28	—	—
Average	16·59	16·87		

Table IV shows that the amount of potassium in effusions was found to be approximately equal to the amount in the corresponding sera. This is the relationship characteristic of the ultrafiltrates and is in agreement with the findings of Dumitresco-Mante and Petrovano [1931].

Discussion.

The average C.S.F.-potassium was 12·05 mg. per 100 cc., which is slightly higher than the figure usually given. Most of the values are close to this average, but the range of variation seems to be greater than in the case of calcium and

magnesium [McCance and Watchorn, 1931; 1932; Watchorn and McCance, 1932]. No constant variation of the cerebrospinal fluid-potassium in any one direction in any specific disease has been observed. The fall in magnesium in the C.S.F. in cases of meningitis is not accompanied by a fall in potassium. Further, Tables I and III show that no constant relationship has been found between the serum and the corresponding C.S.F.-potassium; high serum values were frequently accompanied by low C.S.F. values and *vice versa*. The average value for serum separated as rapidly as possible without the use of anticoagulant was 17·6 mg. per 100 cc., and the average for the corresponding cerebrospinal fluids was 12·7 mg. per 100 cc. In no case did we succeed in obtaining a serum value as low as that of the corresponding cerebrospinal fluid, nor such low values as Dulière [1931] reported. Even Dulière's sera figures were, however, higher than those of his cerebrospinal fluids.

Whatever may be true of sodium [see Dailey, 1931] it appears that, whereas the whole of the potassium of serum is ultrafiltrable (and the amount found in effusions can be thus explained), the level found in the C.S.F. represents at most 65–70 % of that found in the serum. Massaut [1931, 1, 2] and Kral *et al.* [1929], discussing similar results, consider that they are not in keeping with the view that cerebrospinal fluid represents an ultrafiltrate of the blood-plasma. With this opinion we are in complete accord and suggest that the C.S.F. should be compared with the intestinal secretions [Gilman and Cowgill, 1933] which are isotonic with blood but contain very different ionic concentrations.

Conclusions.

1. The whole of the potassium of serum was found to be ultrafiltrable and the level of potassium found in hydrocele, pleural and ascitic fluids may be explained in this way.

2. The potassium in the cerebrospinal fluid was always found to be lower than that in the serum, and consequently lower than that found in serum-ultrafiltrates or effusions. So far as potassium is concerned, therefore, the C.S.F. does not represent a serum-ultrafiltrate.

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