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Water, Electrolytes and Epilepsy*

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> "A disturbance in water balance perhaps affecting the central nervous system more specifically appears to be closely identified with the aetiology of epilepsy."
>
> McQUARRIE, 1929

INTRODUCTION

The nature of epilepsy

The neurophysiological basis of an epileptic attack is the spontaneous repetitive discharge of a hyperexcitable aggregate of neurones (JACKSON 1890; AJMONE MARSAN 1961). Given the appropriate stimulus any human nervous system is capable of developing seizure activity and use is made of this phenomenon for therapeutic purposes in psychiatry (MEDUNA 1935, 1937). An epileptic seizure can be evoked in all vertebrates, but spontaneous attacks have only been observed in mammals (SERVÍT 1962). Spontaneous seizure susceptibility increases with increasing phylogenetic development of nervous systems and, therefore, reaches its highest incidence in man (SERVÍT 1962). The electroencephalographic correlate of seizures is the same spike and wave activity at all levels of the phylogenetic scale. Very different brain structures of different complexity are able to generate this typical electrical event in the same frequency range. This is true even in the frog paleopallium which has a very simple two-layer structure (SERVÍT 1966).

That the coordinated and complex activities of the majority of the human population are not continually interrupted by convulsions may be due to the development of mechanisms to prevent the occurrence of this property of nervous systems. It can be postulated that in human (and lower forms of) epilepsy these mechanisms are unstable and break down.

The biochemical basis of epilepsy

For some time human epilepsy has been classified into "idiopathic" and "focal" types. The "focal" irritant may be one of numerous vascular, atrophic, demyelinating

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or neoplastic neurological processes. However, this approach to the classification of epilepsy leaves unexplained the fact that many other patients who have similar or identical focal pathological lesions do *not* develop epilepsy. It seems more probable that the level of the convulsive threshold of the nervous system determines whether a patient develops epilepsy, either "idiopathic" or in response to a focal lesion. It is generally agreed that biochemical factors are *ultimately* responsible for alterations in convulsive threshold though this in no way undermines the importance of genetic, physical (brain damage), psychological and social factors in the precipitation of convulsions.

Probably many different biochemical factors can precipitate convulsions. Some of these are well known, for example, hypoglycaemia, hypocalcaemia, pyridoxine deficiency and phenylketonuria. However, with the growth of our understanding of the ionic basis of neuronal electrical activity (HODGKIN 1951, 1958, 1964) it may now reasonably be postulated that these biochemical factors (both known and unknown) ultimately produce their convulsive effects by their influence on the distribution of sodium and potassium across neuronal cell membranes. As it is the intracellular and extracellular concentrations of these two cations which determines the height of resting and action membrane potentials (and, therefore, susceptibility to spontaneous firing) this distribution may be looked upon as the *final common biochemical pathway* (to borrow a phrase from neurophysiology) in the generation of neuronal activity. The mechanisms by which hypoglycaemia and hypocalcaemia affect sodium-potassium distribution are already clearly understood in terms of energy requirements and membrane stability respectively (*e.g.* DAVSON 1964).

Water and electrolyte metabolism in epilepsy: review of previous literature

(a) Water. Although FRISCH AND WALTER (1922), KEITH *et al.* (1926) and HELMHOLZ (1927) were among the first to draw attention to a relationship between fit frequency and water intake, it is to MCQUARRIE (1929) and TEGLBJAERG (1936) that we owe the credit for first investigating and establishing under carefully controlled conditions, that fluid restriction (dehydration therapy) reduces fit frequency, and that hyperhydration leads to an exacerbation of epilepsy.

MCQUARRIE (1929) also concluded that the beneficial effects of ketogenic diets and inanition therapy, both of which were in vogue at the time, were due to the concurrent dehydration of the patient, a conclusion which CLEMMESON (1932) also reached with regard to inanition.

FAY (1929 and 1930) also studied the relationship between water intake and frequency of epileptic attacks, but his investigations were more orientated towards his hypothesis that the effects of excessive or restricted fluid intake were mediated through changes in intracranial pressure. His theory has been conclusively disproved by LENNOX AND COBB (1932), LENNOX AND MERRITT (1936) and TEGLBJAERG (1936), who were unable to substantiate his claim of elevated spinal fluid pressure in epileptic patients.

Following the initial observations of the effects of water ingestion, MCQUARRIE AND PEELER (1931) introduced the combined fluid loading and pitressin (antidiuretic) test as a diagnostic and investigative procedure in epilepsy. WACHTER (1939) obtained

convulsions in 9 out of 15 cases, and BLYTH (1943) precipitated seizures in 45 out of 49 epileptic patients by this method.

Prolonged and carefully-controlled observations of water balance in relation to seizure frequency have been carried out by TEGLBJAERG (1936), and by GREVILLE *et al.* (1940). TEGLBJAERG concluded that epileptic patients reacted just as quickly as did controls in their renal response to water ingestion or restriction, but that on a constant daily fluid (and salt) intake their daily weight and water excretion showed considerably greater variation than that shown by controls, though these variations were in no way specific, and showed no demonstrable relation to the seizures. GREVILLE *et al.* (1940) found that water retention sometimes, but not always, preceded seizures. At most, 10 out of 22 fits were preceded by a rise in weight. They concluded that water retention may be one of the factors which precipitate a seizure, or that unknown factors which determine the onset of a seizure may also influence water balance.

More recently, SCHNEIDER (1961) has studied urinary water and electrolyte excretion in children and adults suffering predominantly from petit mal (in order to exclude discrepancies which might arise from excessive disturbance in neuromuscular and autonomic function in convulsive seizures). He reported that exacerbations of petit mal were associated with reduction in urinary volume, and that electroclinical remission, whether spontaneous, drug-induced or hormone-induced, coincided generally with an increase in water excretion.

Finally, in relation to water balance it is appropriate to mention the well-known clinical exacerbation of epilepsy in relation to the menstrual cycle (GOWERS 1881). Although ALMQUIST (1955) concluded that menstrual events are unlikely to be a primary or dominant cause of attack rhythmicity, as a rhythmic fit pattern appears about as often in males as in females, and is also found in children, LAIDLAW (1956) appears to have re-established the existence of catamenial epilepsy in a further statistical study of the relationship between menstruation and epilepsy. ANSELL AND CLARKE (1956) attempted to investigate the role of water retention in relation to the menstrual aggravation of convulsions by measuring total body water by the antipyrine method in 7 epileptic patients, 3 of whom had catamenial convulsions. All their patients had total body water which fell within the wide normal range published for the method, and so they concluded that water retention was not directly responsible for the premenstrual and menstrual exacerbation of seizures. However in view of the few patients studied, the absence of controls and the omission of extracellular water measurements it is doubtful whether such a conclusion was justified.

In summary, there is abundant evidence, mostly accumulated between 1925 and 1945, linking epilepsy with water metabolism. The investigations of MCQUARRIE (1929) and TEGLBJAERG (1936) in particular, have established the ictogenic effect of excessive water ingestion, and the therapeutic value of dehydration. Evidence has also been quoted suggestive of spontaneous variations in water balance which, in some patients at least, are correlated with corresponding variations in fit frequency. In none of the studies referred to is there any evidence that the disturbances in water metabolism or the effects of altered fluid intake are related to any particular type of epilepsy.

(b) Sodium and potassium. Despite the early interest in water metabolism there has been surprisingly little investigation of sodium and potassium metabolism in *human* epileptics, and this possibly reflects the technical difficulties involved.

There is no evidence of a disturbance in serum electrolytes in epilepsy (McQUARRIE 1929; WADA *et al.* 1964).

In his study of urinary electrolyte and water excretion in petit mal epileptics, SCHNEIDER (1961) reported that fluctuations in the course of this type of epilepsy are associated with corresponding fluctuations in urinary sodium and water output. Electroclinical exacerbations were correlated with sodium and water retention. There was little change in potassium excretion in relation to the course of the epilepsy, but it was noted that calcium excretion tended to parallel that of sodium, high excretion rates occurring during periods of remission.

Two investigations of cerebrospinal fluid (CSF) electrolytes in epileptics and other neuropsychiatric disorders (EICHHORN 1954; SPINA-FRANC AND DEJORGE 1963) revealed normal values for sodium and potassium except in the immediate postictal period when significant elevations of CSF potassium were noted.

In a study of catamenial epilepsy ANSELL AND CLARKE (1956) measured total exchangeable sodium in 6 female epileptic patients by observing the decay curve following a single tracer dose of ^{22}Na. They concluded that there were no differences between the epileptics and controls or between the 3 patients with menstrual aggravation of fits and the other 3 epileptic patients.

Recently MEYER *et al.* (1966) reported changes in carotid arterial and jugular venous sodium and potassium concentrations during convulsive seizures. Their results indicated that during an attack there is a net uptake of sodium and loss of potassium by the brain, but there was no evidence of such changes *preceding* seizure activity.

Probably the most interesting studies in this field of electrolyte metabolism in epilepsy are those of TOWER (1960) who found that incubated slices of human epileptogenic cortex were unable to take up potassium and extrude excess sodium in the same way as control cortical samples. TOWER (1960 and 1965) has emphasised the difficulties in interpreting the significance of these findings which might be related to the *effects* of seizure activity as much as to its cause. Also our lack of understanding of the functioning and measurement of the various fluid spaces in brain tissue undermines attempts at interpretation (TOWER 1965; VAN HARREVELD 1966; DAVSON 1967). However, TOWER's findings for human epileptogenic cortex are supported by similar changes in ability to handle sodium and potassium in cortical slices from cats in which experimental epilepsy had been induced by megimide or methionine-sulfoximine, although not in experimental samples in which the epilepsy had been induced with thiosemicarbizone (TOWER 1960).

No alteration has been found in the sodium and potassium *content* of either human or experimental epileptogenic cortical samples (PAPPIUS AND ELLIOT 1954; TOWER 1960). But this does not exclude the possibility of abnormalities in sodium and potassium *distribution*. Such disturbance in distribution has in fact been reported in experimental samples by COLFER AND ESSEX (1947) (who employed a difficult microincineration technique) and by WOODBURY (1958). The potentially important aspect of WOODBURY's work in which convulsions were induced experimentally by

the withdrawal of anaesthetising doses of carbon dioxide was that the electrolyte changes could be detected *before* the onset of convulsions.

It has been shown that brain excitability in the rat varies inversely with the extracellular sodium concentration (SWINYARD 1949; DAVENPORT 1949; WOODBURY AND DAVENPORT 1949; WOODBURY *et al.* 1950; WOODBURY 1954; TIMIRAS *et al.* 1954). But it should be noted that in these experiments brain sodium (intracellular) was related to *plasma* sodium (extracellular) whereas, as will be discussed in more detail, it would be even more relevant to study intracellular and extracellular sodium concentrations *within the nervous system only*, and to relate these to brain excitability. A further interesting experiment was that of GLASER (1964) who induced seizure activity in cats by the intraventricular administration of hypertonic sodium chloride. However, the specificity of this effect is under investigation, as hypertonic potassium chloride produced similar activity.

The most important conclusion to be drawn from this survey of previous literature, especially the work of TOWER, is that sodium and potassium metabolism is central to our understanding of epilepsy, but that attempts to investigate it are considerably impeded by technical difficulties and by our lack of a thorough understanding of electrolyte metabolism in the normal brain, especially with regard to interrelationships between the various fluid compartments.

THE PRESENT INVESTIGATION

An indirect *in vivo* approach to the problem of water and electrolyte metabolism in human epilepsy is the study of the whole body distribution of water, sodium and potassium by radioactive isotope techniques. In this paper the results of such investigation in 42 epileptic patients from the National Hospital are presented.

The adoption of this "whole body" approach was stimulated by the observations already referred to of an aggravation of epilepsy by excessive water ingestion and the therapeutic value of dehydration therapy. Furthermore this technique has already been used with valuable results in the study of depression in which it is also believed there are disturbances in brain electrolyte distribution (COPPEN AND SHAW 1963; COPPEN *et al.* 1966; SHAW AND COPPEN 1966). Their findings will be discussed in some detail especially as they provide control material for the present investigation.

PATIENTS

Forty-two epileptic patients were studied. They were drawn from the epileptic population attending the Outpatient Department of the National Hospital.

The main clinical features of the cases are summarised in Tables 1 and 2.

Age and sex

There were 27 male patients whose ages ranged from 13–53 years (mean age 30.7 years). Fifteen female patients had an age range from 15–61 years (mean age 35.5). Mean age for all 42 patients: 32.4 years.

TABLE 1

SUMMARY OF MAIN CLINICAL FEATURES AND THERAPY OF 27 MALE EPILEPTIC PATIENTS

Patient	Age (years)	Epilepsy						Drugs and duration of treatment (years)				IMD score	Associated disorders
		classification	severity: idiopathic GM	idiopathic PM	focal	FH	age of onset (years)	duration (years)	phenobarb	phenytoin	primidone	others		
1 E.B.	30	focal TL (GM + M)			C		14	16					14	
2 T.B.	27	idiop. GM + PM	B	B		+	16	10	10	1	5		6	
3 W.B.	35	idiop. GM	B				9	26		19	6	sulthiame (0.5) folic acid (0.25)	16	
4 L.C.	23	idiop. GM	C			+	23	0.5					8	
5 J.D.	24	focal TL (GM + M)			A		14	10		10	5		9	migraine
6 H.D.	53	idiop. GM	B				23	30		2	9		7	writer's cramp
7 M.E.	41	focal TL (M)			B		4	37	30	23			0	
8 A.F.	18	idiop. GM + PM	B	B			9	9	9	4		sulthiame (2) folic acid (0.25)	5	
9 S.H.	45	focal GM			A		2	43	35	17			26	gastric ulcer
10 P.H.	13	idiop. GM	A				7	6	6	6		phenylethyl-acetylurea (6)		
11 J.H.	45	idiop. GM	A				15	30	30	20			36	subdural haematoma 10 years ago
12 E.K.	17	focal M			C	+	4	13					0	
13 R.L.	50	idiop. GM	A				15	35	25		9	chlordiazepoxide (3) dexamphetamine (6)	10	
14 F.M.	40	focal TL (M)			A		8	32	28	17	1	ethosuximide (3)	1	

15	D.N.	37	focal TL (M)			B		20	17	17	17	5		1	
16	B.N.	26	idiop. GM	C			+	13	13	13	11	8		11	
17	P.P.	23	focal TL (M)			A		7	16		14	14		0	
18	F.P.	51	focal TL (M)			C		20	31	31	12	2	folic acid (0.25)	3	
19	F.P.	26	idiop. GM + PM	C	C		+	10	16	16	10	1		14	
20	C.P.	31	idiop. GM	B				23	9	9	9	6	chlordiazepoxide (2)	4	progressive dementia 3 years
21	R.R.	17	focal TL (GM + M)			A		3	14	13	12			0	mental retardation
22	H.S.	31	focal TL (GM + M)			B		8	23		23	10	dexamphetamine (13)	0	
23	C.T.	21	idiop. GM	B				14	7	7	7			10	
24	D.T.	25	focal TL (GM + M)			A		18	7	6	6	3	amylobarbitone (2)	26	
25	P.W.	19	focal occip. (M)			B		2	17	13	9	5	chlordiazepoxide (1) ferrous gluconate (2)	7	
26	D.W.	21	idiop. GM	C				7	14	14	6			6	
27	G.W.	39	focal TL (M)			C		37	2					1	

In this and other tables the following abbreviations are used:
Idiop. = idiopathic
GM = grand mal
PM = petit mal
M = minor attacks
TL = temporal lobe
Occip. = occipital lobe

Severity:
A = severe
B = moderate
C = mild
FH = family history
IMD = inventory for measuring depression

TABLE 2

SUMMARY OF MAIN CLINICAL FEATURES AND THERAPY OF 15 FEMALE EPILEPTIC PATIENTS

Patient	Age (years)	Epilepsy: classification	Epilepsy: severity: idiopathic GM	Epilepsy: severity: idiopathic PM	Epilepsy: severity: focal	FH	age of onset (years)	duration (years)	Drugs and duration of treatment (years): phenobarb	phenytoin	primidone	others	IMD score	Associated disorders
28 L.A.	15	idiop. GM	C			+	13	2	2				6	
29 S.A.	17	idiop. GM	B			+	13	4	3	5	2		8	
30 P.B.	37	focal TL (GM)			B		10	27	27	20	12		4	
31 M.B.	45	focal TL (M)			B		26	19	12	12		trifluoperazine (1)	4	3 previous episodes of "schizophrenia-like psychoses"
32 F.D.	51	idiop. G.M.	A				10	41	30	15			13	
33 V.D.	21	idiop. G.M. + PM	A	A			9	12		10	2	chlordiazepoxide (1) trifluoperazine (1)	4	neuroticism
34 F.F.	27	focal TL (GM)			B	+	12	15	15	15		acetazolamide (5)	12	
35 M.G.	27	focal TL (M)			A		0.25	27		20	10	folic acid (0.5)	4	congenital left hemiparesis
36 M.G.	18	idiop. GM + PM	A	C			8	10	8	8		ethosuximide (8)	3	
37 D.G.	54	idiop. GM	B				14	39	39	22		sulthiame (0.25) dexamphetamine (6)	4	hysterectomy
38 D.H.	52	focal TL (M)			B		6	46	20		2		1	
39 M.H.	58	idiop. GM	B				7	51	22	22	4	prochlorperazine (0.5) folic acid (0.25)	10	series of attacks every 6 wks; last "bout" 1 wk ago
40 P.L.	18	idiop. GM	C			+	1	17					1	
41 E.M.	31	focal TL (M)			B		2	29	20	11	1	dexamphetamine (9) folic acid (0.25)	3	
42 M.W.	61	idiop. GM + PM	C	A			11	50			6	ethosuximide (4)	9	hysterectomy

Classification of epilepsy

The type and severity of the epilepsy was documented without any knowledge of the biochemical data.

(a) Type. Patients were classified as having either idiopathic or focal epilepsy on the basis of history, clinical examination and electroencephalographic (EEG) findings supported in many cases by carotid arteriography or air encephalography. Where there was a lack of correlation between the description of the attacks and the EEG then the clinical history was considered to provide the most reliable guide. In most cases of focal epilepsy the nature of the focus, which was temporal lobe in origin in all except 1 (an occipital focus in case 25), was not known with certainty but in no case was there a rapidly progressive lesion.

Amongst the male patients there were 13 with idiopathic and 14 with focal epilepsy. In 9 female patients the epilepsy was idiopathic and in 6 it was focal.

It was felt that any more elaborate classification would not be worthwhile as very many more patients would have to be studied in order to provide meaningful data, particularly as other variables, such as the severity of epilepsy, have also to be taken into consideration.

The presence of a positive family history of epilepsy is also recorded in Tables 1 and 2.

(b) Severity. This was graded on a 3 point scale, A—severe, B—moderate, C—mild. Patients with Grade A severity suffered from attacks either daily or on most days of the week. Those in Grade C experienced attacks less than once a month. The remainder were classified as Grade B. When patients had both grand mal and petit mal attacks the severity of each was recorded and in the analysis of the data when there was a difference in the comparative severities of the two types of attack, as in cases 36 and 42, the patient was graded according to the most frequent type of attack (*e.g.* cases 36 and 42 were both graded A). Amongst the group of patients with focal epilepsy there were many who experienced both minor (partial) attacks and major attacks (partial attacks becoming generalised). These patients are graded according to the most frequent type of attack.

(c) Duration. The age of onset and duration of the epilepsy were also recorded.

Drugs

It is exceptionally difficult to study untreated epileptic patients as the majority have already been started on anticonvulsant therapy before they are referred to a Hospital Outpatient Department. There are, therefore, only 5 untreated patients in this series (cases 1, 4, 12, 27 and 40). As might be expected they are all mild (Grade C) epileptics. The study of a severe untreated epileptic patient is impossible as it is not justifiable to withdraw anticonvulsant therapy. In Tables 1 and 2 the drugs being taken by the patients at the time of the study are listed as well as the duration of therapy with each drug. The highest figure represents the total duration of drug treatment.

Main interest centres around the three major anticonvulsants, phenobarbitone (at least 30 mg b.d.), phenytoin (at least 100 mg b.d.) and primidone (at least 250 mg b.d.); but all other drug therapy, whether anticonvulsant or not, was also documented.

Depression

As whole-body disturbances in sodium, potassium and water distribution have been demonstrated by this multiple isotope technique in patients with depression (COPPEN AND SHAW 1963; SHAW AND COPPEN 1966), it was necessary to inquire whether any of the epileptic patients were also suffering from depression at the time of the investigation. This was assessed on a rating scale, the Inventory for Measuring Depression (IMD) (BECK *et al.* 1961; METCALFE AND GOLDMAN 1965), which was completed by the patient on the 1st day of the study. Nine of the 42 patients had scores indicative of depression, *i.e.* > 10, and their main clinical features are summarised in Table 3.

TABLE 3

CLINICAL SUMMARY OF FINDINGS IN 9 EPILEPTIC PATIENTS WITH DEPRESSION

Patient	*Sex*	*Age (years)*	*Epilepsy*		*Duration of therapy (years)*	*IMD score*
			type	*severity*		
1	M	30	focal	C	Nil	14
3	M	35	idiopathic	B	19	16
9	M	45	idiopathic	A	35	26
11	M	45	idiopathic	A	30	36
16	M	26	idiopathic	C	13	11
19	M	26	idiopathic	C	16	14
24	M	25	focal	A	6	26
32	F	51	idiopathic	A	30	13
34	F	27	focal	B	15	12

Associated disorders

The associated neurological, psychiatric or general medical disorders which were present or had occurred in the past in a few patients are recorded in Tables 1 and 2.

Intelligence and employment

Of the 42 patients, 38 were intellectually normal, 3 (cases 20, 22, 30) were borderline defective and 1 (case 21) was definitely defective (Wechsler Adult Intelligence Scale). Thirty patients were employed, 7 were housewives, 2 (cases 11 and 20) were unemployed, 2 lived sheltered existences in the care of relatives (cases 21 and 35) and 1 (case 10) was at school.

CONTROL PATIENTS

For ethical reasons it is not possible to provide *normal* controls for a study such as this employing the administration of three radioactive isotopes. However, two sources of control data are available.

(1) The techniques employed in this study were first used at this MRC Unit by COPPEN AND SHAW (1963) for the study of patients with depression. The data from

epileptic patients has, therefore, been compared with that obtained in patients who have *recovered* from depression and, where appropriate, with the data on depressed patients (COPPEN AND SHAW 1963; COPPEN *et al.* 1966; SHAW AND COPPEN 1966). The question of how normal may be the electrolyte distribution of patients who have recovered from depression is one to which no definite answer can be given at the present time. However, the similarity in the figures for mild (Grade C) epileptics (presumably the nearest to normal among the epileptic patients) and those for the patients who had recovered from depression does suggest that the latter patients are useful controls (Tables 8–14). The discrepancies that are present may be due to (*a*) the age difference between these two groups, (*b*) persistent constitutional disturbances in those patients who have recovered from depression (SHAW AND COPPEN 1966), or (*c*) slight deviations from normal in the mild epileptics. As there is a fall in ICW/ECW ratio with age (MOORE *et al.* 1963) allowance should be made for this when comparing the control data with that of the younger epileptic patients (see Discussion).

Because of the sex differences for most of the measurements in the epileptic patients all the control data have been separated and recalculated for males and females.

(2) Although there are no data available for normal control subjects in this country, MOORE *et al.* (1963) have published extensive data for normal American controls using techniques very similar to those employed in this study. As their findings have been used for comparative purposes in the studies of depression by COPPEN AND SHAW (1963), they have also, therefore, been utilised in this investigation (see ANALYSIS OF THE DATA, *F* values).

METHODS

The pattern of distribution of water, sodium, potassium and chloride was determined by an isotope dilution technique, using ^{24}Na, ^{82}Br and tritium, and whole-body counting to estimate the total body potassium. The details of this technique have been described by COPPEN AND SHAW (1963).

Timing of investigation

The patients were admitted for 3 days to the Clinical Investigation Ward of the Medical Research Council's Neuropsychiatric Research Unit at West Park Hospital, Epsom.

Day 1. On the morning of admission a full clinical history was taken and a neuropsychiatric examination was carried out. The Inventory for Measuring Depression (IMD) was completed by the patient. In the afternoon the total body potassium was estimated.

Day 2. At 9 a.m. a sample of venous blood was taken for haemoglobin and packed cell volume (PCV) estimation and the prepared solutions of ^{24}Na, ^{82}Br and tritium were administered. Urine collection was commenced.

Day 3. At 8 a.m. a 23-h collection of urine was completed. A further "spot" sample of urine was collected an hour later at 9 a.m. Also at 9 a.m. venous blood was taken for sodium, bromine and tritium counting and for chemical estimation of plasma electrolytes. Breakfast was not eaten until after the blood and urine samples had been collected.

During the period of admission the patients were kept up and about and activity such as walking in the hospital grounds was encouraged. A normal ward diet was taken. Any epileptic attacks were recorded, with particular reference to the type of attack and the time of day. The following values were measured or estimated:

SUMMARY OF ESTIMATED AND DERIVED VALUES

Estimated values	*Units*
Body weight (wt)	kg
Height (ht)	cm
24-h exchangeable sodium (Na_E)	mequiv

Distribution volume of bromine (DBr)		l
Total body water (TBW)		l
Total body potassium (K_T)		mequiv
Concentration of electrolytes in plasma ($(Na)_{out}$, $(K)_{out}$, $(Cl)_{out}$)		mequiv/l
Haematocrit (PCV)		%(v/v)
Haemoglobin (Hb)		g/100 ml
Derived values	*Derivation*	
Extracellular water (ECW)	DBr × 0.9	l
Intracellular water (ICW)	TBW − ECW	l
Sodium in extracellular space (Na_{ECW})	$(Na)_{out}$ × ECW	mequiv
Residual sodium (Na_R)	$Na_E - Na_{ECW}$	mequiv
Residual sodium concentration ($(Na)_{in}$)	$\frac{Na_R}{ICW}$	mequiv/l
Potassium in extracellular space (K_{ECW})	$(K)_{out}$ × ECW	mequiv
Intracellular potassium (K_R)	$K_T - K_{ECW}$	mequiv
Intracellular potassium concentration ($(K)_{in}$)	$\frac{K_R}{ICW}$	mequiv/l
Lean body mass (LBM)	$\frac{TBW}{0.732}$	kg
Body fat (BF)	Wt − LBM	kg
% Body fat (% BF)	$\frac{BF}{wt}$	%

ANALYSIS OF THE DATA

(a) Statistics

Conventional statistical procedures have been employed. Significance of differences between means was assessed by the *t* test. For assessment of the significance of differences for a variable which has been ranked on a 3-point scale, *e.g.* in relation to the severity of the epilepsy (Fig. 1) Kendall's τ method has been employed.

(b) F values

Among the variables that have been measured in this study, exchangeable sodium, residual sodium and extracellular water are highly correlated with total body water. MOORE *et al.* (1963) have derived regression equations from their normal data relating these three variables to total body water. These regression equations have been used to analyse this data by employing a procedure proposed by LINDEGAARD (1953) and utilised by COPPEN *et al.* (1966) who describe its application.

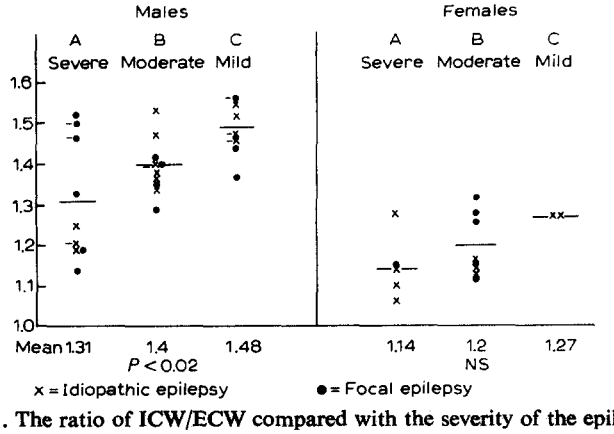

Fig. 1. The ratio of ICW/ECW compared with the severity of the epilepsy.

As ECW, Na_E and Na_R will vary among epileptic patients of *different body builds* it is necessary to standardise the data so as to be able to make meaningful comparisons between different groups of epileptics *i.e.* severe and mild, idiopathic and focal, etc. This is done by applying MOORE *et al.*'s (1963) regression equations to the epileptic data in order to find the *predicted* values of ECW, Na_E and Na_R for each patient. By subtracting the predicted value from the measured value we derive a figure which is known as the *F* value. Direct comparisons can then be made between the *F* values of each parameter, for the different groups of epileptic patients (see Tables 9–14).

The following three regression equations derived from MOORE *et al.*'s data have been employed (see COPPEN *et al.* 1966).

	95% Confidence limits	*Correlation coefficient*
1. $Na_E = 68.10\ (TBW) + 253$	$\pm$ 376 mequiv	0.94
2. $Na_R = 12.83\ (TBW) - 76$	$\pm$ 160 mequiv	0.68
3. $ECW = 00.38\ (TBW) + 3.58$	$\pm$ 2.03 l	0.90

It must be emphasised, as was done by COPPEN *et al.* (1966), that this procedure is not being employed to compare the epileptic patients directly with the normal Americans, but merely as a way of standardising the data for body size so that meaningful comparisons can be made between patients of different body sizes, and also so that the present findings could be compared with the control data of COPPEN AND SHAW (1963), COPPEN *et al.* (1966) and SHAW (1966), who used this statistical method.

For analysis of the TBW results I have similarly employed the procedure adopted by COPPEN *et al.* (1966) for the control data, which is based on the use of Leanness Index (NICHOLSON AND ZILVA 1964).

(c) Body potassium and obesity

A correction factor for per cent body fat (see DRENICK *et al.* 1966) has been applied to K_T according to the equation:

$$K_0 = \frac{K_T(0.404x + 84.1)}{84.1}$$

where K_0 = total body potassium corrected to 0% body fat, K_T = estimated total body potassium and x = body fat as a percentage of body weight.

This factor has been derived from studies of total body potassium, exchangeable potassium and obesity in schizophrenic patients using the same whole body counter as in the present investigation (COPPEN AND SHAW 1964).

RESULTS

Details of all the results are set out in Tables 4 and 5.

Patient 14 did not have a total body potassium estimation because of a technical fault with the body counter and patient 21 did not have his exchangeable sodium measured because of a failure of supply of ^{24}Na.

Table 6 summarizes the number of epileptic patients and their mean ages in the various groups, when broken down according to sex, severity or type of epilepsy, presence or absence of depression. This table, which has been compiled to correspond with the presentation of the data on the main parameters in Tables 9–14 also includes information about numbers and mean ages of patients in the control data of COPPEN AND SHAW (1963) for depression and recovered depression.

Table 7 shows the number of epileptic patients in each group, when sex, type and severity of epilepsy are considered together.

The data obtained for individual parameters in the various groups of epileptic and control patients are set out in Tables 8–15 (means and standard errors).

The fact that the data on most of the biochemical variables have to be considered

TABLE

BODY COMPOSITION, WATER, SODIUM, POTASSIUM AND

Case	Wt. (kg)	Ht. (cm)	Body build				Water						Sodium			
			lean body mass (kg)	leanness index	body fat (kg)	% body fat	TBW (l)	F TBW	ICW (l)	ECW (l)	F ECW	ICW: ECW ratio	Na_E (mequiv)	F Na_E	Na_{ECW} (mequiv)	Na_R (mequiv)
1	76.8	169.5	61.9	0.0634	14.9	19.4	45.3	+ 74	27.7	17.6	−3.2	1.57	3553	+215	2436	1117
2	74.0	179	69.1	0.0775	4.9	6.6	50.6	+ 89	29.0	21.6	−1.2	1.34	3423	−276	3021	402
3	54.3	171.7	55.9	0.0932	—	—	40.9	+ 73	23.9	17.0	−2.1	1.40	2707	−331	2308	399
4	74.0	182	67.3	0.0959	6.7	9.1	49.3	+ 49	29.7	19.6	−2.7	1.52	3123	−487	2878	245
5	61.5	164.5	62.0	0.0724	—	—	45.4	+176	27.4	18.0	−2.8	1.52	3009	−335	2641	368
6	75.2	166	56.3	0.0505	18.9	25.1	41.2	+ 46	25.0	16.2	−3.0	1.54	2808	−250	2273	535
7	81.0	171	62.8	0.0617	18.2	22.4	46.0	−100	26.8	19.2	−1.9	1.40	2994	−392	2670	324
8	60.2	173.5	53.0	0.0867	7.2	12.0	38.8	− 16	22.4	16.4	−1.9	1.37	2746	−149	2411	335
9	79.2	175	64.1	0.0677	15.1	19.1	46.9	+ 69	27.9	19.0	−2.4	1.47	3984	+537	2671	1313
10	39.5	150	33.2	0.0854	6.3	15.9	24.3	−139	13.2	11.1	−1.7	1.19	1856	− 51	1564	292
11	87.3	177.5	59.0	0.0640	28.3	32.4	43.2	+111	23.6	19.6	−0.4	1.20	3481	+286	2848	633
12	60.2	170	57.2	0.0819	3.0	5.0	41.9	+ 78	24.3	17.6	−1.9	1.38	2630	−476	2526	104
13	77.9	164	58.1	0.0566	19.8	25.4	42.5	+ 68	23.6	18.9	−0.8	1.25	2937	−210	2560	377
14	65.7	171.5	55.0	0.0762	10.7	16.3	40.3	+ 22	21.5	18.8	−0.1	1.14	2796	−201	2581	215
15	82.7	175.8	68.2	0.0653	14.5	17.6	49.9	+110	28.1	21.8	−0.7	1.29	3550	−101	3027	523
16	59.3	177.5	55.5	0.0972	3.8	6.4	40.6	− 50	24.1	16.5	−2.5	1.46	2785	−233	2276	509
17	68.9	176.5	64.6	0.0797	4.3	6.2	47.3	+197	27.0	20.3	−1.2	1.33	3338	−136	2956	382
18	63.5	173.8	55.0	0.0882	8.5	13.4	40.3	+110	23.8	16.5	−2.4	1.44	2824	−173	2280	544
19	102.9	184	83.7	0.0605	19.2	18.7	61.3	+112	36.5	24.8	−2.1	1.47	3893	−534	3438	455
20	91.7	172	62.8	0.0555	28.9	31.6	46.0	+ 80	27.4	18.6	−2.5	1.47	3274	−111	2716	558
21	60.1	164	46.7	0.0733	13.4	22.3	34.2	+ 22	18.6	15.6	−1.0	1.19				
22	58.0	174.5	56.0	0.0959	2.0	3.4	41.0	+ 31	23.1	17.4	−1.7	1.36	2810	−235	2172	638
23	67.9	175.8	59.6	0.0988	8.3	12.2	43.6	+ 32	25.3	18.3	−1.8	1.38	2982	−240	2649	333
24	80.5	171	63.2	0.0621	17.2	21.4	46.3	+ 84	27.8	18.5	−2.7	1.50	3037	−369	2675	362
25	56.0	159	48.8	0.0733	7.2	12.9	35.7	+ 75	20.9	14.8	−2.4	1.41	2336	−348	2044	292
26	71.7	172	65.8	0.0710	5.9	8.3	48.2	+ 13	29.2	19.0	−2.8	1.54	2994	−541	2638	356
27	59.0	164.4	52.9	0.0750	6.1	10.3	38.7	+ 13	23.0	15.7	−2.6	1.46	2626	−262	2162	464

TABLE

BODY COMPOSITION, WATER, SODIUM, POTASSIUM AND

Case	Wt. (kg)	Ht. (cm)	Body build				Water						Sodium			
			lean body mass (kg)	leanness index	body fat (kg)	% body fat	TBW (l)	F TBW	ICW (l)	ECW (l)	F ECW	ICW: ECW ratio	Na_E (mequiv)	F Na_E	Na_{ECW} (mequiv)	Na_R (mequiv)
28	57.3	162	44.1	0.0741	13.2	23.0	32.3	− 44	18.1	14.2	−1.6	1.27	2279	−174	2017	262
29	60.2	161.5	46.2	0.0713	14.0	23.2	33.8	− 18	18.2	15.6	−0.8	1.17	2628	+ 73	2167	461
30	68.9	167	50.4	0.0691	18.5	26.9	36.9	− 43	19.5	17.4	−0.2	1.12	2975	+209	2402	573
31	58.4	167	45.2	0.0809	13.2	22.6	33.1	− 35	17.8	15.3	−0.8	1.16	2365	−142	2093	272
32	51.4	149.5	32.2	0.0652	19.2	37.4	23.6	− 33	12.1	11.5	−1.0	1.05	1831	− 29	1637	194
33	59.0	158	44.3	0.0669	14.7	24.9	32.4	+ 14	17.3	15.1	−0.8	1.14	2433	− 26	2085	348
34	71.4	168.1	52.9	0.0664	18.5	26.0	38.7	− 11	21.6	17.1	−1.2	1.26	3238	+350	2420	818
35	39.2	151.4	28.8	0.0884	10.4	26.6	21.1	− 56	11.3	9.8	−1.8	1.15	1713	+ 23	1395	318
36	41.1	155.8	33.7	0.0922	7.4	18.0	24.7	− 90	13.9	10.8	−2.2	1.28	1991	+ 56	1504	487
37	64.3	155.4	42.7	0.0597	21.6	33.6	31.3	+ 94	16.7	14.6	−0.8	1.14	2493	+109	2094	399
38	65.5	163.5	40.8	0.0667	24.7	37.7	29.9	− 70	16.8	13.1	−1.8	1.28	2269	− 20	1800	469
39	46.7	160	36.9	0.0877	9.8	21.1	27.0	− 72	14.3	12.7	−1.1	1.13	2149	+ 57	1796	353
40	59.2	169	47.1	0.0815	12.1	20.4	34.5	− 35	19.3	15.2	−1.5	1.27	2380	−222	2064	316
41	55.3	160.5	43.7	0.0749	11.6	21.0	32.0	− 90	18.2	13.8	−1.9	1.32	2260	−172	1876	384
42	70.5	158.8	46.6	0.0581	23.9	33.9	34.1	+ 9	17.9	16.2	−0.3	1.10	2818	+243	2347	472

4

CHLORIDE DISTRIBUTION IN 27 MALE EPILEPTIC PATIENTS

			Potassium						Blood		
F Na_R	$(Na)_{in}$ (mequiv/l)	$(Na)_{out}$ (mequiv/l)	K_T (mequiv)	K_T %BF (mequiv)	K_{ECW} (mequiv)	K_R (mequiv)	$(K)_{in}$ (mequiv/l)	$(K)_{out}$ (mequiv/l)	$(Cl)_{out}$ (mequiv/l)	Hb (g/100 ml)	PCV (%)
+612	40.3	138	3785	4138	81	4057	146	4.6	—	14.4	47
−171	13.9	140	4169	4301	99	4202	145	4.6	109	14.8	46
− 50	16.6	136	3864	3864	70	3794	159	4.1	111	12.3	40
−311	8.2	147	4194	4385	94	4291	144	4.8	113	14.2	45
−138	13.4	146	3760	3760	97	3663	134	5.4	—	15.6	48
+ 82	21.4	140	2916	3267	81	3186	127	5.0	108	14.8	47
−190	12.1	139	3529	3909	90	3819	143	4.7	109	16.2	52
− 86	15.0	147	3836	4057	83	3974	177	5.1	105	15.4	51
+787	47.1	141	3376	3686	97	3589	129	5.1	105	15.0	45
+ 56	22.1	141	2251	2423	52	2371	180	4.7	114	13.7	44
+155	26.8	145	2762	3192	86	3106	132	4.8	109	14.4	46
−357	4.3	144	3478	3561	90	3471	143	5.1	110	15.9	49
− 92	16.0	136	3760	4219	83	4136	175	4.4	108	13.3	44
−226	10.1	137			83			4.4	—	14.2	44
− 41	18.6	139	3555	3857	96	3761	134	4.4	104	14.4	49
+ 65	21.1	138	3683	3796	82	3714	154	5.0	105	17.4	55
−149	14.1	145	3939	4057	90	3967	147	4.4	110	16.0	46
+103	22.9	138	3325	3539	66	3473	146	4.0	109	14.9	50
−255	12.5	138	4859	5296	124	5172	142	5.0	107	15.4	45
+ 44	20.4	147	2376	2737	82	2655	97	4.5	107	16.4	51
		138	2788	3086	68	3018	162	4.4	110	14.8	44
+188	27.0	144	3325	3379	74	3305	143	4.9	—	16.4	47
−150	13.2	144	3708	3925	86	3839	152	4.7	119	14.4	—
−156	13.0	145	3581	3949	100	3849	138	5.4	112	15.2	51
− 90	14.0	138	3427	3639	68	3571	171	4.6	—	15.5	53
−186	12.2	139	4015	4175	105	4070	139	5.5	105	15.1	44
+ 44	20.2	138	2967	3125	61	3064	133	3.9	109	13.0	42

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CHLORIDE DISTRIBUTION IN 15 FEMALE EPILEPTIC PATIENTS

			Potassium						Blood		
F Na_R	$(Na)_{in}$ (mequiv/l)	$(Na)_{out}$ (mequiv/l)	K_T (mequiv)	K_T %BF (mequiv)	K_{ECW} (mequiv)	K_R (mequiv)	$(K)_{in}$ (mequiv/l)	$(K)_{out}$ (mequiv/l)	$(Cl)_{out}$ (mequiv/l)	Hb (g/100 ml)	PCV (%)
− 76	14.5	142	2711	3011	59	2952	163	4.2	113	13.7	40
+103	25.3	139	2660	2957	76	2881	158	4.9	109	14.3	44
+176	29.4	138	2558	2888	87	2801	144	4.7	105	14.6	47
− 77	15.3	137	2532	2806	72	2734	154	4.7	106	12.7	40
− 32	16.0	142	1995	2354	59	2295	190	5.1	109	12.4	42
+ 8	20.1	138	2404	2691	68	2623	152	4.5	109	13.4	42
+398	37.9	142	2916	3280	82	3198	148	4.8	113	14.6	43
+123	28.1	142	1765	1991	44	1947	172	4.5		12.4	40
+246	35.0	139	2583	2807	48	2759	198	4.4	106	14.6	44
+ 74	23.9	143	2276	2643	62	2581	155	4.2	111	14.1	45
+162	27.9	137	2046	2416	60	2356	140	4.6	105	13.1	43
+ 83	24.7	141	2353	2592	64	2528	177	5.0	110	14.5	44
− 51	16.4	135	3274	3595	81	3514	182	5.3	111	14.0	42
+ 50	21.1	136	2890	3182	59	3123	172	4.3	110	13.1	42
+111	26.4	145	1969	2290	79	2211	124	4.9	112	14.0	45

TABLE 6

NUMBER AND MEAN AGE OF GROUPS OF EPILEPTIC AND DEPRESSED PATIENTS ACCORDING TO SEX AND TYPE OR SEVERITY OF EPILEPSY (SEE TABLES 9–14)

		Epilepsy	*Epilepsy and depression*		*Epilepsy (severity)*			*Epilepsy (type)*		*Controls*	
			depressed epileptics	*non-depressed epileptics*	*group A*	*group B*	*group C*	*idiopathic group*	*focal group*	*depression*	*recovered depression*
										(sodium and water study)[a]	
Total	No.	42	9	33	14	18	10	22	20	23	23
	mean age (years)	32.4	34.4	31.8	32.8	35.2	26.6	31.9	32.9	55.6	55.6
Male	No.	27	7	20	9	10	8	13	14	10	10
	mean age (years)	30.7	33.1	29.9	31.3	31.3	29.1	29.9	31.4	52.6	52.6
Female	No.	15	2	13	5	8	2	9	6	13	13
	mean age (years)	35.5	39.0	35.0	35.6	40.1	16.5	34.7	36.5	57.8	57.8
					(Excluding 9 with depression)					*(potassium study)*[b]	
	Total		No.		10	16	7	17	16	16	14
			mean age (years)		29.4	35.8	26.3	30.5	33.2	57.3	55.5
	Male		No.		6	9	5	9	11	8	8
			mean age (years)		27.8	30.9	30.2	28.6	30.8	53.0	53.4
	Female		No.		4	7	2	8	5	8	6
			mean age (years)		31.8	42.0	16.5	32.8	38.4	56.4	58.3

[a] From COPPEN AND SHAW 1963.
[b] From SHAW AND COPPEN 1966.

TABLE 7

NUMBER OF PATIENTS IN GROUPS RELATED TO SEX, TYPE AND SEVERITY OF EPILEPSY

Sex	*Severity*						*Total*
	A		*B*		*C*		
	idiopathic	*focal*	*idiopathic*	*focal*	*idiopathic*	*focal*	
Male	3	6	6	4	4	4	27
Female	4	1	3	5	2	–	15

separately for both sexes, only emerged as a result of this study. In spite of this unforeseen reduction in the number of patients in the various groups (*i.e.* because of the sex factor), much significant information has been obtained. It will be noted that although significant levels are often not reached in the analysis of the data for females (because of the lack of numbers), in nearly all the results the trends are similar to the findings in the male patients.

Sex differences in electrolyte distribution

It can be seen in Tables 9–14 that there are highly significant differences between the two sexes for ICW/ECW ratios, F ECW, F Na_E, F Na_R, $(Na)_{in}$, and $(K)_{in}$ values. This applies also to the control data of COPPEN AND SHAW (1963). The levels of significance vary between $P < 0.05$ and $P < 0.001$.

Body water

F TBW/kg (Table 8). There are no significant differences in leanness index or F TBW/kg values between epileptic patients and controls. In particular there are no significant differences between the various subgroups of epilepsy, nor between these values and zero. This suggests that TBW is not raised in epilepsy and does not alter in relation to the severity, type of epilepsy or presence of depression.

ICW/ECW ratio (Table 9). The ICW/ECW ratio for all the epileptic patients (mean 1.32) is almost identical to that for control patients (depressed or recovered from depression, mean 1.31).

There are no significant differences between epileptic patients with depression and those without depression, nor between idiopathic and focal epileptics.

There are significant differences between patients with different severities of epilepsy (Fig. 1). For all epileptic patients: A (mean 1.25) *vs.* B (mean 1.31) *vs.* C (mean 1.44), $P < 0.02$. For male epileptics: A (mean 1.31) *vs.* B (mean 1.40) *vs.* C (mean 1.48), $P < 0.02$. There are not enough female epileptic patients to draw any significant conclusion but the trend is the same: A (mean 1.14), B (mean 1.20), C (mean 1.27).

Extracellular water, F ECW (Table 10). There are no significant differences between F ECW values for epileptic patients and controls, between depressed and non-depressed epileptics, or between idiopathic and focal epileptics.

There are significant differences between the F ECW values for the three grades of severity of epilepsy (see Fig. 2). For all epileptics: A (mean -1.37) *vs.* B (mean -1.54) *vs.* C (mean -2.33), $P < 0.01$. For the male patients A (mean -1.46) *vs.* B

TABLE 8

LEANNESS INDEX AND *F* TBW/kg

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity)*			*Epilepsy (type)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
No.[a]	42	9	33	14	18	10	22	20	10	9
Leanness index	0.0746 ±0.00196	0.0711 ±0.0046	0.0760 ±0.0022	0.0720 ±0.0030	0.0732 ±0.0033	0.0789 ±0.0039	0.0750 ±0.0033	0.0741 ±0.0021	0.0691 ±0.0051	0.0708 ±0.0042
F TBW/kg [(ml/kg)]	22.5 ± 11.6	47.6 ± 20.2	15.7 ± 13.7	32.4 ± 25.2	10.2 ±16.1	32.0 ± 19.2	13.1 ± 14.4	32.8 ± 18.5	23.1 ± 14.1	61.4 ± 26.8

There are no significant differences between values for leanness index or *F* TBW/kg between any of the groups.
[a] Sexes combined (see NICHOLSON AND ZILVA 1964).

TABLE 9

ICW/ECW RATIOS

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity)*			*Epilepsy (type)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
Total	1.32 ± 0.02	1.38 ± 0.06	1.30 ± 0.02	1.25 ± 0.04	1.31 ± 0.03	1.44 ± 0.03	1.30 ± 0.03	1.34 ± 0.03	1.31 ± 0.04	1.31 ± 0.04
Male	1.39 ± 0.02		1.38 ± 0.03	1.31 ± 0.05	1.40 ± 0.02	1.48 ± 0.02	1.39 ± 0.02	1.39 ± 0.03	1.4 ± 0.04	1.35 ± 0.05
Female	1.19 ± 0.03		1.19 ± 0.02	1.14 ± 0.04	1.20 ± 0.03	1.27 ± 0.00	1.17 ± 0.09	1.22 ± 0.03	1.24 ± 0.06	1.27 ± 0.07

Depressed *vs* non-depressed epileptics: N.S.; A *vs.* B *vs.* C: Total $P < 0.01$, Male $P < 0.02$; I. *vs.* F: N.S.; Depression *vs.* recovered depression: N.S. (SHAW AND COPPEN 1966).

TABLE 10

EXTRACELLULAR WATER (F ECW ON TBW)

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity)*			*Epilepsy (type)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
Total	-1.69 ± 0.15	-1.96 ± 0.24	-1.60 ± 0.18	-1.37 ± 0.24	-1.54 ± 0.17	-2.33 ± 0.17	-1.62 ± 0.17	-1.73 ± 0.19	-1.74 ± 0.23	-1.35 ± 0.33
Male	-2.03 ± 0.18		-1.85 ± 0.18	-1.46 ± 0.34	-1.92 ± 0.21	-2.53 ± 0.14	-1.96 ± 0.22	-1.92 ± 0.24	-1.99 ± 0.36	-1.77 ± 0.28
Female	-1.07 ± 0.16		-1.20 ± 0.18	-1.22 ± 0.34	-1.08 ± 0.20	-1.55 ± 0.28	-1.12 ± 0.29	-1.28 ± 0.28	-1.55 ± 0.29	-1.02 ± 0.55

Depressed *vs.* non-depressed epileptics: N.S.; A *vs.* B *vs.* C: Total $P < 0.02$. Male $P < 0.02$; I. *vs.* F. N.S.; Depression *vs.* recovered depression: N.S. (SHAW AND COPPEN 1966).

TABLE 11

EXCHANGEABLE SODIUM (F Na_E ON TBW)

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity) (Excluding 9 patients with depression)*			*Epilepsy (type) (Excluding 9 patients with depression)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
Total	-124 ± 38	-12 ± 125	-155 ± 34	-71 ± 57	-124 ± 43	-334 ± 61	-129 ± 54	-184 ± 39	$+51 \pm 75$	-133 ± 61
Male	-208 ± 48		-262 ± 32	-187 ± 47	-234 ± 33	-388 ± 72	-257 ± 67	-266 ± 15	-60 ± 111	-155 ± 48
Female	$+22 \pm 42$		$+1 \pm 41$	$+74 \pm 59$	$+16 \pm 52$	-198 ± 24	$+15 \pm 54$	-20 ± 68	$+137 \pm 98$	-115 ± 104

Depressed *vs.* non-depressed epileptics: N.S. (but similar trend to controls). Depressed epileptics *vs.* male non-depressed epileptics: $P < 0.02$; A *vs.* B *vs.* C: Total $P < 0.02$, A + B *vs.* C: Total $P < 0.01$. Male $P < 0.01$; I. *vs.* F. N.S.; Depression *vs.* recovered depression: N.S. (COPPEN AND SHAW 1963).

(mean −1.92) *vs.* C (mean −2.53), $P < 0.02$. The females do not show the same trend: A (mean −1.22), B (mean −1.08), and C (mean −1.55). However, as has already been emphasised the numbers in this sex group are small.

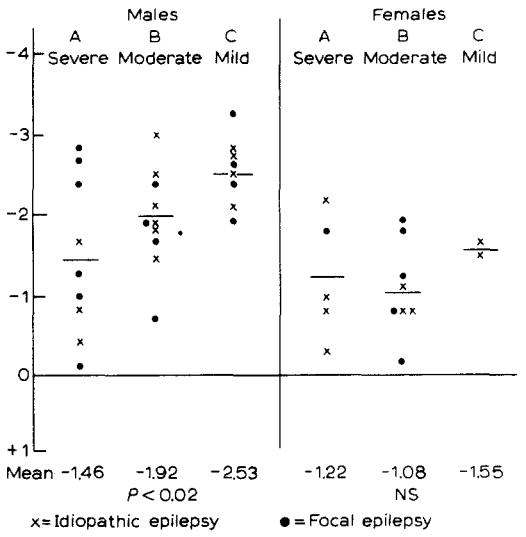

Fig. 2. *F* ECW compared with the severity of the epilepsy.

Body sodium

Exchangeable sodium F Na_E. *(Table 11).* There are no significant differences in *F* Na_E values between epileptic patients and controls (recovered depressed) or between idiopathic and focal epileptics.

In both the epileptic patients and the control patients there are trends towards more positive values (*i.e.* higher exchangeable sodium) in association with depression. This does not reach significant proportions in the controls, but for the epileptics, $P < 0.02$ (see also Table 17).

Because of significant differences in *F* Na_E among the depressed epileptics these 9 patients have been excluded in the analysis of results in relation to the severity of epilepsy. For the remaining 32 patients there are significant differences between the three grades: A (mean −79) *vs.* B (mean −124) *vs.* C (mean −334), $P < 0.02$. (If the 9 depressed patients are *included* these values change to A (mean −16), B (mean −110) and C (mean −289) and the significance increases to $P < 0.01$). The figures for the two sexes considered separately show a trend towards increasingly positive values (*i.e.* increasing exchangeable sodium) with increasing severity. When the severer (A and B) grades are combined and compared with the C grade for all patients and for male patients, significantly higher values are found in the severer patients ($P < 0.01$); the same trend is seen in the females but there are only 2 female patients in grade C.

Residual sodium F Na_R *(Table 12).* There are no significant differences in *F* Na_R values between epileptic patients and controls (recovered from depression) or between idiopathic and focal epileptics.

TABLE 12

RESIDUAL SODIUM ($F\,Na_R$ ON TBW)

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity) (excluding 9 patients with depression)*			*Epilepsy (type) (excluding 9 patients with depression)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
Total	+19 ± 35	+169 ± 119	−23 ± 26	− 7 ± 49	+10 ± 31	−118 ± 66	−19 ± 34	−28 ± 43	+179 ± 37	−17 ± 44
Male	−20 ± 51		−88 ± 34	−110 ± 47	−46 ± 42	−141 ± 93	−90 ± 44	−86 ± 52	+169 ± 48	−68 ± 75
Female	+87 ± 34		+72 ± 28	+122 ± 49	+82 ± 31	− 64 ± 11	+62 ± 36	+87 ± 46	+187 ± 62	+23 ± 52

Depressed *vs.* non-depressed epileptics: $P < 0.02$; Depressed epileptics *vs.* male non-depressed epileptics: $P < 0.01$; A + B *vs.* C: Total $P < 0.05$; I. v. F. N.S.; Depression *vs.* recovered depression: Total $P < 0.001$. Males $P < 0.01$. Females $P < 0.01$ (COPPEN AND SHAW 1963).

TABLE 13

RESIDUAL SODIUM CONCENTRATIONS, $(Na)_{IN}$ (mequiv/l)

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity) (excluding 9 patients with depression)*			*Epilepsy (type) (excluding 9 patients with depression)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
Total	20.5 ± 1.4	25.7 ± 4.3	19.0 ± 1.2	20.6 ± 2.7	20.2 ± 1.4	14.1 ± 2.3	19.3 ± 2.0	18.6 ± 1.9	28.3 ± 2.4	18.3 ± 2.4
Male	18.3 ± 1.8		15.7 ± 1.9	15.1 ± 2.0	17.3 ± 1.8	13.6 ± 3.6	15.8 ± 1.6	15.7 ± 2.1	26.3 ± 3.4	15.5 ± 2.6
Female	24.1 ± 1.8		23.7 ± 1.1	27.4 ± 3.1	23.9 ± 1.8	15.4 ± 1.1	23.3 ± 2.3	24.4 ± 2.7	29.9 ± 3.1	20.5 ± 3.6

Depressed *vs.* non-depressed epileptics: $P < 0.05$; Depressed epileptics *vs.* male non-depressed epileptics: $P < 0.001$; A + B *vs.* C: Total $P < 0.02$. Male $P < 0.05$; I. *vs.* F: N.S.; Depression *vs.* recovered depression: Total $P < 0.001$. Male $P < 0.01$. Female $P < 0.001$ (COPPEN AND SHAW 1963).

TABLE 14

INTRACELLULAR POTASSIUM CONCENTRATIONS, $(K)_{IN}$ (CORRECTED TO 0% BODY FAT) (mequiv/l)

	Epilepsy	*Epilepsy and depression*		*Epilepsy (severity)*			*Epilepsy (type)*		*Controls*	
		depressed epileptics	*non-depressed epileptics*	*A*	*B*	*C*	*idiopathic*	*focal*	*depression*	*recovered depression*
Total	152 ± 3	149 ± 6	153 ± 4	156 ± 7	150 ± 5	149 ± 5	156 ± 5	147 ± 5	151 ± 5	143 ± 9
Male	146 ± 4		147 ± 5	150 ± 7	145 ± 7	143 ± 2	148 ± 6	144 ± 3	146 ± 6	140 ± 7
Female	162 ± 5		161 ± 5	167 ± 13	156 ± 5	173 ± 10	167 ± 8	155 ± 6	157 ± 8	147 ± 19

Depressed *vs.* non-depressed epileptics: N.S.; A *vs.* B *vs.* C: N.S.; A + B *vs.* C: N.S.; I. *vs.* F.: N.S.; Depression *vs.* recovered depression: N.S. (SHAW AND COPPEN 1966).

Control patients with depression (mean 179) have a significantly higher residual sodium than those who have recovered from depression (mean −17), $P<0.001$ (COPPEN AND SHAW 1963). In the present study comparable differences are seen between depressed epileptics (mean 169) and non-depressed epileptics (mean −23), $P<0.02$. As 7 of the 9 depressed epileptics are male it is appropriate to compare them with the *male* non-depressed epileptics (mean −88), $P<0.01$ (Table 17).

The 9 epileptic patients with depression have again been excluded in the analysis of $F\,Na_R$ in relation to the severity of epilepsy. A Kendall's τ test on the remaining patients does not reveal significant differences between the three grades of severity, though there is a trend towards increasing residual sodium with increasing severity in the females (A mean 122; B mean 82; C mean −64). The combined (A and B) groups have significantly higher values than the C group for the two sexes considered together ($P<0.05$). There is a similar trend for the two sexes considered separately.

Residual sodium concentration $(Na)_{in}$ (Table 13). There are no significant differences in residual sodium concentration values between epileptic patients and controls (recovered from depression) or between idiopathic and focal epileptics.

Control patients with depression have very significantly higher intracellular sodium concentrations than those who have recovered from depression ($P<0.001$) (COPPEN AND SHAW 1963). In the present study comparable differences are seen between depressed epileptics (mean 25.7) and non-depressed epileptics (mean 19.0), $P<0.05$. As 7 of the 9 depressed epileptics are male it is again appropriate to compare them with the male non-depressed epileptics (mean 15.7) and the difference is even more significant ($P<0.001$).

The 9 epileptic patients with depression have again been excluded in the analysis in relation to the severity of epilepsy. A Kendall's τ test on the remaining 32 patients does not reveal significant differences between the three grades of severity, though there is a definite trend in the female patients (A mean 27.4; B mean 23.9; C mean 15.4), which does not reach significance because of lack of numbers in this group. When the severe (A and B) groups are combined and compared with the C group, significantly higher values are found in the severe group, for male patients ($P<0.05$), and for both sexes together ($P<0.02$).

Body potassium

Intracellular potassium concentration $(K)_{in}$ (Table 14). There are no significant

TABLE 15

PLASMA ELECTROLYTES
(mequiv/l)

	$(Na)_{out}$	$(K)_{out}$	$(Cl)_{out}$
Epilepsy	140.6 ± 0.5	4.71 ± 0.6	109.2 ± 0.5
Recovered depression[a]	141	4.8	105
Depression[a]	141	4.8	105

[a] Controls (COPPEN AND SHAW 1963; SHAW AND COPPEN 1966).

differences in intracellular potassium concentration between epileptic patients and controls. Nor are there any differences within the various subgroups of epilepsy, in relation to severity, type or presence or absence of depression.

Serum electrolytes (Table 15)

Serum sodium, potassium and chloride concentrations are normal in epileptic and control patients, and in all subgroups of epilepsy.

Haemoglobin and PCV

There was no evidence of anaemia except in patient 3 whose haemoglobin was 12.3 g as a result of drug-induced folate deficiency.

DISCUSSION

Body water

The most interesting finding in relation to body water distribution is the significant decrease of the ICW/ECW ratio with the increasing severity of epilepsy (Table 9, Fig. 1). This phenomenon is demonstrable whether the sexes are considered together or separately.

How abnormal are these ratios in the epileptic patients? When comparing the results with the control data of COPPEN AND SHAW (1963) it must be remembered that their patients were older than the epileptics (Table 6) and that changes in body water occur with ageing. It is likely therefore that the mean values of the ICW/ECW ratio for male controls (1.35 in those who had recovered from depression and 1.4 in the depressed, Table 9) are higher when corrected to the age of the younger epileptics and are probably similar to the mean value for the mild (C) grade of epileptics (*i.e.* 1.48). Similarly the control mean values for female patients (1.27 and 1.24) are probably a little higher than the mild (C) female epileptics (mean 1.27). It might reasonably be predicted that the C grades of epileptic patients approximate closest to normality and to the extent that COPPEN AND SHAW's (1963) patients are "normal" this appears to be true. With the increasing severity of epilepsy the ICW/ECW ratio changes significantly and deviates further from the control ratio in both sexes.

To what extent are the changes in ICW/ECW ratio due to alterations in ECW or ICW? That the changes are at least partly due to ECW is suggested by the findings

TABLE 16

COMPARISON OF DATA FOR IDIOPATHIC AND FOCAL GROUPS OF MALE PATIENTS

	No. of patients	*ICW/ECW ratio*	*F ECW*	*F Na_E*	*F Na_R*	*$(Na)_{in}$ (mequiv/l)*	*$(K)_{in}$ (mequiv/l)*
Idiopathic	13	1.39 ± 0.03	-1.96 ± 0.22	-257 ± 67	-90 ± 44	15.8 ± 1.6	148 ± 6
Focal	14	1.39 ± 0.03	-1.92 ± 0.24	-266 ± 15	-86 ± 52	15.7 ± 2.1	144 ± 3

The findings are very similar for idiopathic and focal groups of epileptic patients.

TABLE 17

COMPARISON OF DATA FOR MALE DEPRESSED AND NON-DEPRESSED EPILEPTICS AND NON-EPILEPTICS

		No. of patients	*ICW/ECW ratio*	*F ECW*	*F Na_E*	*F Na_R*	*$(Na)_{in}$ (mequiv/l)*	*$(K)_{in}$ (mequiv/l)*
Epileptics	Depressed	9[a]	1.38 ± 0.06	−1.96 ± 0.24	− 12 ± 125	+169 ± 119	25.7 ± 4.3	149 ± 6
	Non-depressed	20	1.38 ± 0.03	−1.85 ± 0.18	−262 ± 32	− 88 ± 34	15.7 ± 1.9	147 ± 5
Non-epileptics (controls)[b]	Depressed	10[c] 8[d]	1.4 ± 0.04	−1.99 ± 0.36	− 60 ± 111	+169 ± 48	26.3 ± 3.4	146 ± 6
	Recovered from depression	10[c] 8[d]	1.35 ± 0.05	−1.77 ± 0.28	−155 ± 48	− 68 ± 75	15.5 ± 2.6	140 ± 7
Epileptics	Depressed *vs.* non-depressed		N.S.	N.S.	$P < 0.02$	$P < 0.01$	$P < 0.001$	N.S.
Non-epileptics	Depressed *vs.* non-depressed		N.S.	N.S.	trend but N.S.	$P < 0.01$	$P < 0.001$	N.S.

The changes in depression are very similar in epileptic and non-epileptic (control) patients.

[a] Includes 2 females

[b] From COPPEN AND SHAW 1963; COPPEN *et al.* 1966; SHAW AND COPPEN 1966 (Data recalculated for males and females separately).

[c] Number for sodium and water study.

[d] Number for potassium study.

for *F* ECW (Table 10, Fig. 2) which indicate a significant rise in ECW with increasing severity of epilepsy both in the male patients and in the combined sexes, though not in the smaller number of females when considered separately. However as there is no evidence of any change or abnormality in TBW in relation to the severity of the epilepsy (Table 8) this implies that there must be a corresponding fall in ICW in relation to the rising ECW and that the changing ICW/ECW ratio is the result of an altered distribution of body water.

There is no evidence of differences in body water distribution between idiopathic and focal epileptics (Table 16) or between depressed and non-depressed epileptics (Table 17).

Body sodium and potassium

Sodium. In this study, significant increases in exchangeable sodium have been found in patients with increasingly severe epilepsy. As extracellular (serum) concentrations of sodium are normal despite the increases in extracellular water with increasing severity of the epilepsy, it may be concluded that there is extracellular sodium retention in association with the water changes and that this at least contributes to the rise in exchangeable sodium. The corresponding rise in residual sodium and residual sodium concentrations in relation to severity were not so clear-cut, but when the two severe grades (A and B) were combined, a significant increase in the severe patients was noted. However, an even more significant finding was the considerable elevation of residual sodium and residual concentration in the 9 depressed epileptics. This is in close agreement with the data of COPPEN AND SHAW (1963) for patients with depression (see Table 17) and seems to reflect a more striking change in intracellular sodium than is found in the severe epileptics. No abnormalities were noted in serum sodium values, and there were no differences in any of the sodium variables between idiopathic and focal epileptics (Table 16).

Potassium. No differences in intracellular or extracellular (serum) potassium concentrations were apparent in any of the subgroups of epilepsy considered, or between epileptics and depressed patients or those who had recovered from depression.

Idiopathic and focal epilepsy

The results of this study provide some support for the concept of an essential unity between idiopathic and focal epilepsy. The 27 male patients studied provide comparable groups of idiopathic and focal epileptics, especially as the three grades of severity are fairly evenly distributed between the two groups (Table 7). Table 16 demonstrates the striking similarity between the two groups for all the biochemical variables considered. One reservation must be that if all the changes reported in this paper are the *result* of epilepsy or its treatment then possibly one might not expect to find differences between these two groups. However, as is later discussed this is unlikely to be the principal explanation for the findings, although a contributory role for the effects of seizures and drugs cannot be excluded.

Epilepsy and depression

The pattern of distribution of water and electrolytes found in the depressed epileptic

patients is very similar to that reported in non-epileptic depressed patients (COPPEN AND SHAW 1963; COPPEN *et al.* 1966; SHAW AND COPPEN 1966). Table 17 relates the findings in the 7 male and 2 female depressed epileptics to the male non-depressed epileptics and the corresponding male patients of COPPEN AND SHAW (1963). In both groups of patients there was a rise in exchangeable sodium (which was only significant in the epileptics) and a highly significant and comparable rise in residual sodium and residual sodium concentration in the *depressed* state. There were no differences in body water and potassium distribution between depressed and non-depressed in either epileptic or control patients.

The main differences in water and electrolyte distribution between severe epileptic patients and patients suffering from depression are that the elevation in residual sodium concentration is more marked and more significant in depression than in epilepsy and that there are disturbances in body water distribution in epilepsy in proportion to the frequency of attacks. COPPEN (1965) and SHAW (1966) have not yet been able to come to any definite conclusion about the mechanism of production and the significance of the change in residual sodium concentration in depression. They do suggest, however, that it is part of a more complex biochemical process involving amine and hormone metabolism and that it is aetiologically related to depression, particularly as lithium, which has marked effects on sodium metabolism and electrolyte distribution (COPPEN *et al.* 1965), has very encouraging therapeutic effects in manic-depressive and depressive illnesses (BAASTRUP AND SCHOU 1967).

The relationship of the biochemical changes in epilepsy to those in depression is of more than theoretical interest in view of our ignorance of the mode of action of electroconvulsive therapy in depression and in other psychiatric illnesses. It may be significant that there are differences in water and electrolyte distribution in these two disorders and it is possible that future research into the homeostatic mechanisms which determine these different fluid and electrolyte patterns may ultimately provide some insight into this intriguing problem.

CONCLUSIONS

The main findings in this study have been summarised in Table 18. What is the significance of the redistribution of body water in relation to the severity of epilepsy and the rise of residual sodium concentration in the more severe epileptics? It is not possible at the present time to draw any definite conclusions, and one can only discuss what seem to be possible explanations. The main reason for this necessary caution is our incomplete knowledge of water and electrolyte metabolism in the normal brain and its relationship to extracerebral water and electrolyte metabolism. Our present knowledge in these fields has been summarised and reviewed by DAVSON (1964 and 1967), DAVSON AND BRADBURY (1965) and VAN HARREVELD (1966). One point is worth stressing. The nervous system seems to have elaborated processes (as yet ill-understood) to provide a more rigidly-controlled and stable extracellular environment for neurones than is present in other cellular tissues. Thus brain extracellular fluid has a different ionic composition from body extracellular fluid. For example its potassium concentration in man (which is believed to be the same as

TABLE 18

SUMMARY OF FINDINGS

	Parameter	Direction of change	Significance	
			all patients	*male patients*
Severity of epilepsy	ICW/ECW ratio	fall	$P < 0.01$[a]	$P < 0.02$[a]
	F_{ECW}	rise	$P < 0.02$[a]	$P < 0.02$[a]
	F_{Na_E}	rise	$P < 0.02$[a]	$P < 0.01$[b]
	Na_R	rise	$P < 0.05$[b]	N.S.
	$(Na)_{in}$	rise	$P < 0.02$[b]	$P < 0.05$[b]
			Epileptics	*Controls* (COPPEN AND SHAW 1963)
Depression (Table 17)	F Na_E	rise	$P < 0.02$	N.S.
	Na_R	rise	$P < 0.01$	$P < 0.01$
	$(Na)_{in}$	rise	$P < 0.001$	$P < 0.001$
Focal *vs.* idiopathic epilepsy			no significant differences (Table 16).	

[a] Grades A *vs.* B *vs.* C.
[b] Grades A + B *vs.* C.

the cerebrospinal fluid potassium concentration—BRADBURY AND DAVSON 1965) shows little variation from a mean of 2.9 mequiv/l despite normal fluctuations in serum potassium between 3.4 and 5.8 mequiv/l (BRADBURY *et al.* 1963). The advantages of this specialised "milieu interior within a milieu interior" in terms of membrane stability and the consistent and efficient functioning of the ion-mediated electrical processes in neurones are readily apparent.

Bearing these points in mind it is possible to consider three interpretations of the present findings.

(1) Are the changes in the body the same as those occurring in the brain?

Until such time as the relationship between cerebral and whole body water and electrolyte distribution has been clarified it is dangerous to assume that changes in the concentrations of sodium and potassium across body cell membranes reflect similar changes in the brain. It may be noted, however, that if the rise in residual sodium concentration in severe epileptic patients is also occurring in neurones, then the resulting fall in membrane potential would render them less stable and enable them to generate seizure activity more easily. However, this interpretation would leave unexplained why depressed patients, who have even higher residual sodium concentrations, are not suffering from severe epilepsy.

(2) Are the changes in the body different from those occurring in the brain but nevertheless reflecting a breakdown in homeostatic control mechanisms resulting in an unknown cerebral water and electrolyte pattern which underlies seizure activity?

In addition to the fact that the nervous system has its own specialised mechanisms for providing and maintaining a *different* and more stable extracellular environment

than that in the rest of the body, there is evidence that at least some homeostatic controlling influences have different effects on nervous tissues than on other tissues. An example is WOODBURY AND DAVENPORT's (1949) experimental finding that desoxycorticosterone markedly *reduced* brain intracellular sodium concentrations in the intact rat whereas it *increased* intracellular sodium concentrations in other tissues (*e.g.* muscle, liver, skin, heart). These authors also found that this reduction in brain intracellular sodium concentration was associated with an increase in electroshock *threshold* (*i.e.* a decrease in brain excitability). WOODBURY (1958) has since reviewed the relationship of adrenal function to cerebral excitability and has concluded from his own and other experimental work that steroids which predominantly affect electrolyte metabolism *decrease* excitability whereas steroids which predominantly affect carbohydrate metabolism *increase* brain excitability. This conclusion appears to be supported by clinical experience for whereas convulsions are a well-recognised complication of Cushing's syndrome (SPILLANE 1951; STARR 1952) and glucocorticoid therapy (LOWELL *et al.* 1951; WAYNE 1954), I have been unable to trace a single report of epilepsy complicating aldosteronism.

(3) Are the changes in the body the result of epilepsy or its drug treatment?

There are three possible mechanisms by which the occurrence of convulsions or its drug treatment may have contributed to these findings. *(a)* Frequent fits may increase adrenocorticotrophin output (WOODBURY 1958), and in some patients it is also likely that the psychological and social stresses which so often accompany epilepsy may contribute to adrenal cortical stimulation. *(b)* On the other hand chronic phenytoin administration has been shown to depress adrenocortical function both experimentally (WOODBURY 1958) and in man (COSTA *et al.* 1955). *(c)* As a result of his studies of the effect of phenytoin on the distribution of electrolytes and on radiosodium movement between plasma and brain in rats WOODBURY (1955) has suggested that this drug stimulates the active extrusion of sodium from brain and other cells.

It has not been possible to assess definitely whether anticonvulsant drug therapy has influenced the pattern of water and electrolyte distribution found in this study. For reasons already discussed there were only 5 untreated patients and 1 of these was depressed. There was, however, no difference in water and electrolyte distribution between the remaining 4 *untreated* and 5 other mild (Grade C) *treated* epileptics.

Although one cannot exclude the possibility that these factors have contributed to the body water and sodium changes, the extent of these alterations in distribution seems too large to be wholly explicable on this basis, apart from which factors *a* and *b*, for example, might be predicted to have *opposing* effects on electrolyte distribution and would possibly therefore reduce each other's contribution to the findings.

Finally it is worth emphasising that the therapeutic effects of dehydration or diuretic therapy in epileptic patients suggest that the present findings are not the result of convulsions but are linked in a way, as yet obscure, to the aetiology of epilepsy.

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SUMMARY

Body water, sodium and potassium distribution have been studied in 27 male and 15 female epileptic patients. Nine (7 male, 2 female) of the epileptic patients also suffered from depression.

Total body potassium was measured by whole-body counting of natural ^{40}K. Exchangeable sodium, bromine space (for extracellular water) and total body water (TBW) were estimated with ^{24}Na, ^{82}Br and tritium respectively.

The data have been analysed for various subgroups of epilepsy, according to type, severity and the presence or absence of depression. The results have also been compared with previously published findings obtained with the same technique in patients who have recovered from depression or (where appropriate) were suffering from depression.

With increasing severity of epilepsy the TBW remains unaltered but there is a significant fall in ICW/ECW ratio which is due partly to a rise in extracellular water (ECW) and partly to a corresponding fall in intracellular water (ICW). There is a significant rise in exchangeable sodium in severe epileptics and also in epileptic patients with depression.

There is an elevation of residual sodium and residual sodium concentration in severe epileptics but the increase is not as great as that which occurs in epileptic patients with depression or in control patients with depression.

No disturbances were found in the body distribution of potassium in epilepsy.

There are no differences in body water, sodium or potassium distribution between idiopathic and focal epileptic patients.

The possible interpretations of these results are discussed and it is concluded that the changes in body water and sodium are linked, in a way as yet obscure, to the aetiology of epilepsy.

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