sick. The more effort we put into our work in teaching these visiting doctors—and, after all, we can only teach by example—the more we are likely to retain the respect of the leaders of the emergent nations of Africa and Asia.

We have achieved in this country, by a very substantial expenditure, a high standard of health and life expectancy. It costs less than 5% of our national income, or about £12 per head per annum. We must approach with sympathy and understanding the problems of the poorer countries in which the expenditure may hardly be as many shillings per head, and where obviously it will be many decades before they can apply our standards widely. We must be sympathetic to their efforts to adapt to the new knowledge. We must show them how to translate the results of research (which they themselves may not yet be able to pursue) into effective practical action. The sustained British tradition of shrewd and detailed bedside history-taking and clinical examination, backed by appropriately selected laboratory checks, is our greatest strength in transmitting "know-how," for we can frequently demonstrate that, by precise and accurate clinical observation, costly and extensive laboratory investigations may be merely confirmatory and often unnecessary for practical decisions. These working rules of bedside practice which we discern by careful study and research are available for the guidance of all. I believe that our standards of medical practice in this country stand at the highest ethical level in the world, and our ability to set an example of professional integrity combined with high scientific endeavour is a factor favouring British cultural leadership in medicine. William Harvey himself would have envied our opportunities to follow the example of the leadership of Padua in our own troubled century.

SENILE TYPE BODY-WATER CHANGES IN DEGENERATIVE DISEASES OF THE CENTRAL NERVOUS SYSTEM IN MIDDLE-AGED SUBJECTS*

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In an investigation of body-water distribution in aged normal subjects we showed that the lean body mass (L.B.M.) and the intracellular water (I.C.W.) diminished as age advanced, the ratio extracellular water to total body water remaining constant (Olbrich, Woodford-Williams, and Attwood, 1958). This finding was thought to be a true sign of ageing, as the proportion of extracellular water increased if somatic disease intervened. Certain degenerative diseases of the central nervous system (C.N.S.) occurring in middle age cause changes in the body characteristic of old age, such as presenile dementias (Huntington's chorea, Alzheimer's disease, and Pick's disease) and post-encephalitic Parkinsonism.

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Details of Findings in the Three Groups

Case	Age	Height (cm.)	Weight (kg.)	E.C.W. (litres)	T.B.W. (litres)	E.C.W. T.B.W.	E.C.W. Body Weight (%)	T.B.W. Body Weight (%)	L.B.M.* (kg.)
Normal Subjects 40-59 Years									
32	49	166	68.2	11.6	44.5	0.26	17.0	65.2	62.0
33	49	160	49.1	11.2	36.0	0.31	22.8	73.3	50.0
33A	48	178	72.3	17.3	44.0	0.39	23.9	61.0	62.0
23	41	173	59.5	11.1	42.2	0.26	18.8	70.9	60.0
24	41	173	65.9	14.5	39.9	0.36	22.0	60.5	56.2
25	43	161	58.6	10.0	41.6	0.24	17.1	71.0	58.0
26	45	164	54.5	10.6	40.8	0.26	19.6	74.8	57.0
27	48	161	54.1	9.9	38.6	0.25	18.3	71.3	54.0
28	48	169	68.2	11.8	50.4	0.23	17.3	73.9	70.0
29	48	169	44.1	9.7	44.1	0.22	15.3	68.8	62.0
30	49	178	62.3	9.9	41.9	0.24	15.9	67.2	59.0
31	49	168	60.9	10.2	43.2	0.24	16.7	70.9	60.0
34	50	180	72.7	9.1	44.2	0.20	12.5	60.8	62.0
35	50	168	57.3	10.6	37.3	0.28	18.5	65.1	52.0
36	51	164	49.5	12.1	37.5	0.32	24.4	75.8	52.8
37	52	165	63.2	10.5	45.3	0.30	16.6	71.5	63.0
39	57	168	68.2	12.8	37.7	0.34	18.8	55.3	53.0
40	58	170	52.7	11.0	37.0	0.30	20.9	70.2	52.0
41	58	178	70.0	12.0	43.1	0.28	17.1	61.4	60.0
42	59	170	63.6	13.2	38.2	0.25	20.8	60.2	53.9
43	59	168	64.4	15.7	40.6	0.32	24.4	77.0	69.8
38A	54	152	58.2	13.0	41.3	0.32	22.3	70.9	58.0
Mean	50	168	60.7	11.7	41.7	0.28	19.0	68.0	58.4
Subjects with Degenerative Diseases of the C.N.S. (Pathological Group)—40-59 Years									
H	48	158	53.2	9.8	35.2	0.28	18.4	66.2	48.2
L	49	178	70.5	12.7	35.1	0.36	18.0	49.7	48.1
M	41	154	53.0	12.2	30.9	0.40	23.0	58.3	42.3
N	49	171	68.8	12.3	39.5	0.31	17.9	57.4	54.1
F	57	172	44.5	13.7	22.3	0.61	30.8	50.1	30.6
J	59	170	47.5	8.9	30.2	0.30	18.9	63.8	41.4
K	57	176	57.7	12.4	32.1	0.39	21.4	55.6	44.0
Mean	51	168	55.0	11.7	32.1	0.38	21.2	57.3	44.0
Normal Subjects—80-89 Years									
68	81	170	58.0	10.4	32.6	0.31	17.9	56.2	45.9
69	82	164	57.3	13.4	31.4	0.42	23.4	54.8	44.2
70	82	164	56.4	12.8	29.7	0.43	22.7	52.7	41.8
71	83	163	62.3	15.3	31.5	0.47	24.6	50.5	44.4
72	83	165	62.3	10.0	29.1	0.34	19.1	55.6	41.0
73	84	170	73.6	12.8	42.0	0.30	17.4	57.1	59.2
74	84	160	61.4	14.8	33.5	0.44	24.1	54.6	47.2
75	85	175	61.4	14.4	34.5	0.41	23.4	56.2	48.6
76	86	173	61.8	11.3	29.5	0.38	18.3	47.7	41.6
77	86	163	50.2	12.3	28.9	0.42	24.5	57.6	40.7
Mean	84	167	59.5	12.7	32.3	0.39	21.5	54.3	45.5

* Lean body mass = T.B.W. 0.73 kg.

Post-encephalitic Parkinsonism, for example, shows a posture imitating that seen in old age with head and neck craned forward, and a slight flexion of elbows, wrists, hips, and knees. To-day some neurologists (Stevenson, 1959) would agree with Gowers (1902) and classify these conditions as abiotrophies.

Histological changes also have been found in the brain in the above and other degenerative diseases of the C.N.S. which resemble closely those found in old age. There is, for instance, the accumulation of lipochrome in the cytoplasm of nuclear masses such as the inferior olives, thalamus, and dorsal ganglia (Altschul, 1938), and the deposition of lipofuscin very early in these diseases in the thalamus, a most constant finding in the aged. The presence of lipofuscin in the thalamus has been thought to account for the emotional lability of old age. Malfunction and atrophy of the internal secretory glands has also been attributed to similar changes in the nerve cells of the dorsal nucleus of the vagus in the medulla and of the hypothalamic nuclei (Wolf, 1959).

To determine whether these phenomena of premature ageing in subjects suffering from these degenerative diseases of the C.N.S. are also accompanied by characteristic changes in body water we have measured the distribution of total body water and extracellular water

in seven abnormal subjects between the ages of 41 and 59—four suffered from post-encephalitic Parkinsonism, one from progressive cerebellar atrophy, and two from presenile dementia. The techniques and methods employed were as described previously (Olbrich and Woodford-Williams, 1956; Olbrich *et al.*, 1958). Total body water was measured by estimation of the volume of distribution of urea, using 0.4 g. of urea per kg. body weight, and the extracellular water with sodium thiosulphate.

Comparison has been made with our previous findings in "normal" individuals of the same age and with "normal" subjects aged 80–89 years. The findings have been tabulated in three groups (see Table) represented as follows: group 1—normals aged 40–59; group 2—pathological aged 40–59; group 3—normals aged 80–89.

The "t" test has been applied to differences between the means of the total body water, lean body mass, and the ratio extracellular water to total body water in the following pairs: normal and pathological young (groups 1 and 2); normal young and normal aged (groups 1 and 3); and pathological young and normal aged (groups 2 and 3).

Results

Total Body Water.—The mean total body water in the young normals of 40–59 years, pathological young of the same age range, and aged normals of 80–89 years was 41.7, 32.1, and 32.3 litres respectively. Comparing the total body water of the young normals and pathological young normals revealed a highly significant difference between the two— $t=5.14$ at 1% level. There was also a significant difference in the total body water between the normal young and normal aged— $t=7.05$ at 1% level—but no significant difference was found between the pathological young and normal aged— $t=0.445$.

Lean Body Mass.—Here the findings were similar: a significant difference was found between normal young and pathological young— $t=6$. There was also a significant difference between the lean body mass of young normals and old normals— $t=6.5$ —but again no significant difference was found between the pathological young and normal old— $t=0.23$.

Ratio of Extracellular Water to Total Body Water.—Comparing the young normals with the pathological young, and the normal young and normal aged, again showed significant differences— $t=3.1$ and 5.75 respectively. No difference was found between the pathological young and normal aged— $t=0.31$.

Extracellular Water.—The differences here were not significant in any of the groups. The values for t were 0.012, 1.37, and 1.2 between groups 1 and 2, 1 and 3, and 2 and 3 respectively.

Discussion

The theory that ageing is associated with a change in the direction of greater inertia or stability of something in or around the cell has been held for some time. Child (1915) suggested that changes in the chemical constitution of the cellular substratum during differentiation might result in the accumulation of structural substances which might lower the cell's metabolic activity. Heilbrunn (1943) likewise concluded that senescence is fundamentally due to protoplasmic changes. Bechhold (1912) showed that the cells of the human body, which are colloidal masses, lose their affinity for water progressively with age and become less elastic—the water content of the foetus being 94%, as compared with 70% at birth

and 58% in adult life. As we have shown, this dehydration continues to progress in old age. According to Marinesco (1904), dehydration of the colloids in the cells is an inherent progressive change in evolution leading to senescence and death.

It would seem, therefore, that cells of any complex organism depend for their duration of life not so much on an inborn store of vitality as on metabolic changes in the colloids, which in their turn may be modified by extrinsic factors of various kinds. Růžicka (1924) investigated the progressive condensation of colloids—a phenomenon called "hysteresis." He attributed the diminished water-binding capacity of aged cells to the same process.

Our findings give quantitative expression to these opinions and show that the process of colloid condensation may occur before old age in degenerations of the C.N.S. This evidence offers some confirmation of the view expressed by Groen (1958) that senescence is primarily due to exhaustion of the diencephalon, which becomes the weakest chain in the feed-back mechanism regulating food intake, metabolism, and endocrine activity.

Summary

In an investigation of body water distribution in normal young, normal aged, and young subjects suffering from degenerative diseases of the central nervous system significant differences were found between the normal and pathological groups, and between the normal and old age-groups in total body water, in lean body mass, and in the ratio of extracellular water to total body water; but there were no significant differences between the pathological young and the normal old age-groups. In the case of extracellular water, however, there were no significant differences between any of the groups. These findings are discussed in relation to the colloid theory of ageing.

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A doctor's bill to George Washington for £27 8s. 9d. fetched £430 at a New York sale on the first president's birthday anniversary. The bill, bought by a dealer, itemized visits between 1786 and 1788 and showed that the doctor was paid partly in barrels of fish. (*Daily Telegraph*, February 24.)