Muscle Biopsy Measurement of Body Water and Intracellular Electrolytes in Children

J. A. GRAHAM and W. G. SCOBIE

From the Department of Surgery, Western Infirmary, Glasgow, and Department of Paediatric Surgery, Oakbank Hospital, Glasgow

Graham, J. A., and Scobie, W. G. (1970). *Archives of Disease in Childhood*, 45, 473. **Muscle biopsy measurement of body water and intracellular electrolytes in children.** Body water and electrolytes have been measured in normal infants and children using a muscle biopsy technique. Extracellular water, sodium, and chloride contents per kilogram dry weight are high in infancy but fall to adult values by 18 months to 2 years. Intracellular water and potassium contents are initially high, but approximate to adult levels around 6 months of age. Large variations in water and electrolyte contents have been found in apparently normal children.

There is good correlation between extracellular water and sodium content, and between intracellular water and potassium content. Therefore intracellular electrolyte concentrations are similar for children of all ages.

This technique is presented as a useful method of obtaining information about fluid and electrolyte balance in children.

Body water content of infants and young children has been measured using indicator-dilution techniques (Friis-Hansen, 1957; Smull, 1958; Hanna, 1960; Cheek, 1961; Clapp, Butterfield, and O'Brien, 1962; Maclaurin, 1966). Electrolyte content has been measured using these techniques (Forbes, 1952; Cheek, 1954; Corsa *et al.*, 1956). Indicator-dilution studies have some limitations and are laborious to perform.

Measurement of body water and electrolyte contents by means of skeletal muscle biopsy is a well-recognized technique in adults (Bergström, 1962; Graham, Lamb, and Linton, 1967; Flear, Florence, and Williams, 1968). It is simple, quick, and easy, and gives results at least as accurate as indicator-dilution techniques. Nichols, Hazlewood, and Barnes (1968) have used percutaneous needle biopsy to study some aspects of skeletal muscle biochemistry in children. The following presentation gives the findings of muscle biopsy studies carried out on a series of normal children.

Subjects and Methods

Thirty-three normal children have been studied ranging in age from 2 weeks to 9 years. They were all

admitted to hospital for elective surgical procedures. None had clinical evidence of fluid and electrolyte imbalance or any disease process likely to cause this. The details of the procedure were explained to all the parents and their consent was freely given.

A small piece of skeletal muscle (100–150 mg.) was taken from a muscle exposed by the surgical incision (rectus abdominis or internal oblique in all cases). This biopsy was divided into three portions, after removing any excess blood and connective tissue. Analysis of the water and electrolyte contents and partition into extra- and intracellular phases was then carried out as previously described (Graham *et al.*, 1967).

Serum electrolytes were measured using standard laboratory techniques.

Results

Analysis of the results of the biopsy specimens into age-groups shows a large scatter of values in the first two years of life. The mean values for all patients over 2 years of age have an acceptable standard deviation, and Table I shows that they do not differ significantly from the mean values for normal adults found by Graham *et al.* (1967).

Individual results for all patients below 2 years of age are shown in Table II. Serum electrolytes are not shown, but were within normal limits except for

TABLE I

Comparison of Mean Muscle Water and Electrolytes for Subjects more than 2 years old, with mean values for Normal Adults (data from Graham et al., 1967)

Group	Value	Muscle Water (ml./kg. dry wt.)			Total Muscle Electrolytes (mEq/kg. dry wt.)			Intracellular Electrolytes (mEq/l.)		
		Total	Extracellular	Intracellular	Sodium	Potassium	Chloride	Sodium	Potassium	Chloride
Children aged 2-9 yr. (n=9)	Mean	3325	747	2579	154	424	88	20	165	4.3
	SD	336	128	320	19	36	11	7	11	0.2
Adults (n=40)	Mean	3179	710	2471	148	414	84	19	167	4.3
	SD	189	211	190	29	35	22	6	11	0.2

No difference is statistically significant.

TABLE II

Individual Muscle Water and Electrolytes for Subjects up to 2 Years of Age

Age (mth.)	Muscle Water (ml./kg. dry wt.)			Total Muscle Electrolytes (mEq/kg. dry wt.)			Intracellular Electrolytes (mEq/l.)		
	Total	Extracellular	Intracellular	Sodium	Potassium	Chloride	Sodium	Potassium	Chloride
0.5	5143	1769	3373	310	614	199	20	180	4.3
0.75	4119	1101	3017	233	494	129	26	162	4.4
1.25	3740	1040	2700	209	473	116	21	173	4.3
1.25	3695	1122	2573	226	466	130	27	179	4.4
1.75	3266	1077	2188	170	362	119	10	163	4.3
1.75	3732	1012	2720	205	468	128	22	170	4.3
3.0	3831	839	2992	155	490	100	13	162	4.3
5.0	3811	1182	2629	201	448	130	16	169	4.2
5.0	3689	727	2911	170	441	98	23	151	4.5
7.5	3314	789	2524	152	391	96	16	153	4.5
7.75	3219	666	2553	188	397	94	36	154	5.1
7.75	4482	956	3526	228	564	121	27	159	4.6
8.0	3319	1148	2171	218	407	126	24	187	4.3
8.5	3335	840	2495	186	416	96	27	166	4.3
10.0	3426	942	2483	148	411	112	8	164	4.5
10.0	3136	610	2536	134	447	79	19	167	4.6
12.0	3309	881	2428	176	412	105	23	168	4.5
15.0	3933	1185	2747	211	428	133	19	154	4.3
16.0	3369	862	2507	134	418	105	6	165	4.5
18.0	3265	927	2337	167	459	114	16	194	4.6
20.0	3505	1055	2449	205	391	122	26	159	4.4
21.0	3052	716	2336	156	451	86	25	191	4.4
24.0	3664	1004	2659	172	420	113	15	157	4.2
24.0	3402	944	2458	186	460	109	19	185	4.3

slight increase in the urea concentration in 7 subjects. There was no clinical evidence of abnormality in these patients and they have therefore been included as normal; possible causes for this will be discussed later. These biopsy specimen results are further analysed in Fig. 1 to 6.

Fig. 1 and 2 show, respectively, the total and extracellular water content of muscle. There is a tendency for both to decrease with age.

Fig. 3 and 4 show the total sodium and chloride content of muscle. The values are initially high but tend to fall into the adult range around 18 months to 2 years.

Fig. 5 shows the muscle intracellular water content and Fig. 6 the total potassium content. Again there is an increase in both in the youngest children, but after about 6 months both approximate closely to the normal adult range.

A highly significant correlation exists between the extracellular water and total sodium content of muscle, throughout the entire age range studied (Fig. 7). A similar correlation is found between intracellular water and total potassium content (Fig. 8). These correlations have been shown for normal adults (Graham *et al.*, 1967), and therefore appear to hold good at all ages. Because of these

FIG. 1.—Total muscle water content of children up to 2 years of age (shown against ± 1 SD normal adult mean).

FIG. 2. Extracellular muscle water content of children up to 2 years of age (shown against ± 1 SD normal adult mean).

FIG. 3.—Total muscle sodium content of children up to 2 years of age (shown against ± 1 SD normal adult mean).

FIG. 4.—Total muscle chloride content of children up to 2 years of age (shown against ± 1 SD normal adult mean).

FIG. 5.—Intracellular muscle water content of children up to 2 years of age (shown against ± 1 SD normal adult mean).

FIG. 6.—Total muscle potassium content of children up to 2 years of age (shown against ± 1 SD normal adult mean).

FIG. 7.—Correlation between sodium content and extracellular water in muscle.

close relationships, the intracellular electrolyte concentrations lie within relatively narrow limits at all ages, and the mean values for this whole series are close to that of normal adults, being: potassium 167 ± 13 mEq/litre cell water ($\pm$ one SD); sodium 20 ± 7 mEq/litre; and chloride 4.4 ± 0.2 mEq/litre.

Discussion

Previously reported work on body water and electrolyte content in young children has utilized tracer-dilution methods which have distinct limitations. Incomplete equilibration or entry into compartments other than those under study, and loss of tracer from the body, can introduce error, especially under pathological conditions. Furthermore, there may be a possible radiation hazard in the administration of radioisotopes to children.

The advantage of muscle biopsy studies is that no tracer substances are given, only endogenous water and electrolytes being measured. The method is quick and simple, and the results obtained correlate well with measurements of total body content both in adults (Muldowney and Williams, 1963) and children (Nichols *et al.*, 1969).

We have only taken specimens from children having surgical procedures, using muscles exposed by the surgical incision. This, however, raises some problems. It is difficult to find very young children who are having surgery and in whom it seems fairly certain that the body water and electrolyte contents have not been altered. Furthermore, these children may have had normal eating and drinking habits upset by admission to hospital. The high blood urea values in some of our cases were probably due to a degree of dehydration; McCance and Widdowson (1947) have shown that the blood urea rises very quickly in dehydrated

FIG. 8.—Correlation between potassium content and intracellular water in muscle.

normal infants. Part of the variability of the results for water and electrolyte content in this and other series (e.g. Friis-Hansen, 1957; Hanna, 1960) may be likewise due to alterations in intake.

Our results, expressed per unit of body weight, show a similar trend to those of previous investigators. Extracellular water and the extracellular ions, sodium and chloride, are high in the newborn and then fall slowly to reach adult values around 2 years of age. Friis-Hansen (1957) and Corsa *et al.* (1956) believe that there is a further slow fall in extracellular water and chloride content after this age, and that adult values are not reached till adolescence, but this is not obvious in our series.

On the other hand, high intracellular water and potassium contents in the newborn fall quickly to adult levels by about 6 months. Clapp *et al.* (1962) have shown a similar fall in intracellular water; Friis-Hansen (1957) believes, however, that cell water remains relatively constant throughout growth and Corsa *et al.* (1956) and Forbes (1952) found that the potassium content remained steady with growth. These investigators express their results per wet weight of tissue, which tends to mask minor changes in water and electrolyte content, and may explain this discrepancy.

The most interesting findings of this series are the excellent correlations between extracellular water and sodium content, and between intracellular water and potassium content. This has the effect of maintaining the intracellular electrolyte concentrations within narrow limits at all ages, the values in growing children being similar to adults. The mean intracellular potassium concentration in this series is similar to that of Corsa *et al.* (1956) who

calculated a value of 165 mEq/litre cell water. Despite changes in water and electrolyte content during growth, the cellular concentrations of electrolytes remain steady; this appears vital for the maintenance of normal electrical activity and therefore of function in the cell. This result directly contradicts the finding of Nichols *et al.* (1969) that the cell potassium concentration was low at birth and increased with age.

We find, in company with other investigators, that because of the large variation in water and electrolyte content in the tissues of children of the same age, it is impossible to evaluate 'normality' at any age. However, muscle biopsies are easy to take and to analyse, either at open operation or by percutaneous needle biopsy, and the results obtained will help to provide a more accurate picture of the fluid and electrolyte status of individual children.

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Correspondence to Dr. J. A. Graham, Department of Surgery, Western Infirmary, Glasgow W.1.