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Water, Electrolyte and Nitrogen Content of Human Skin.

C. Wesley Eisele and Lillian Eichelberger.

From the Departments of Medicine and Biochemistry, The University of Chicago, Chicago, Ill.

This study on the distribution of water, nitrogen, and electrolytes in human skin (corium and epidermis) was made for the purpose of defining normal values which will serve as a basis of comparison for later investigations on abnormal skin. The report gives data on a group of patients from which skin was obtained during the course of surgery: fifteen specimens taken during radical mastectomies and three during leg amputations.

The electrolyte content of human skin has not been comprehensively studied in the past, and the limited data in the literature are unsatisfactory because the values are not expressed on a fat-free basis. The available analytical data on human skin are summarized in Table I.

Methods. Eighteen tissues were available for analysis: fifteen from the breast and three from the lower extremities. The tissues were removed immediately from an amputated part and placed in a glass-stoppered weighing bottle. The skins were taken as far from any pathological condition as possible. The preparation of the skin for analysis was as follows: Each skin was quickly placed on a tile and trimmed to remove any muscle and as much free fat as possible. It was wiped with gauze, cut into small strips approximately 0.5 x 2 mm and placed in a weighed glass-stoppered weighing bottle. After being weighed, the bottle was placed in a 100° oven and dried to constant weight.

The dried skin was then extracted for neutral fat[6] and the strips of skin were transferred quantitatively to a special apparatus[6-8] and pulverized. The smashed material was put through a No. 20 copper sieve after which it was transferred to an agate mortar and ground to a homogeneous mixture. This mixture was returned to a glass-stoppered weighing bottle and kept in a desiccator over sulfuric acid. Before each aliquot was taken from the bottle the mixture was stirred thoroughly with a stainless steel spatula.

The chemical methods used in the analyses were the same as those employed in our previous work.[9] The following determinations were made: water, chloride, sodium, potassium, calcium, magnesium, total nitrogen, and collagen nitrogen.

Results and Discussion. Values for Normal Skin. The analytical data of the skins from 18 patients are given in Table II, together with the mean values with standard deviations. Since skin is so complex in structure and since the samples of tissue analyzed comprised both the corium and epidermis layer, it was not surprising that the results were not as constant as have been found for other tissues. For example, the total water content on 15 of the 18 skins varied between 69.0 and 74.0%. It should be borne in mind that the skins were removed from different parts of the body that had been amputated. In our previous study on skins removed from the dog, the skins had been removed directly from the same location on the body, using a uniform technic in every animal. The difference in technic for the removal of the skins might account in part for the larger standard deviations for the sodium, chloride, and water in the group of human

1 Brown, H., *J. Biol. Chem.*, 1926, **68**, 729.

2 Nathan, E., and Stern, F., *Dermat. Z.*, 1928, **54**, 14.

3 Volk, R., and Fantl, P., *Dermatologica*, 1939, **79**, 91.

4 Lowry, O. H., Gilligan, D. R., and Katersky, E. M., *J. Biol. Chem.*, 1941, **139**, 795.

5 Cornbleet, T., Ingraham, R. C., and Schorr, H. C., *Arch. Dermat. and Syphilol.*, 1942, **46**, 833.

6 Eichelberger, L., and Bibler, W. G., *J. Biol. Chem.*, 1940, **132**, 645.

7 Graeser, J. B., Ginsberg, J. E., and Friedemann, T. E., *J. Biol. Chem.*, 1934, **104**, 149.

8 Eichelberger, L., *J. Biol. Chem.*, 1941, **138**, 583.

9 Eichelberger, L., Eisele, C. W., and Wetzler, D., *J. Biol. Chem.*, 1943, **151**, 177.

TABLE I.
Analytical Data in the Literature.
Values were calculated in units per 100 g of dry skin.

Investigator	Source of tissue	Cl mM	Na mM	K mM	Ca mM	Mg mM	H_2O g	Collagen g
Brown, 1926[1]	necropsy		15.6	6.1	1.15	1.23		
Nathan *et al.*, 1928[2]	15 patients			6.4	0.61		250	
Volk, 1939[3]	24 patients, biopsy	24.7*					275*	
Lowry *et al.*, 1941[4]	2 patients							79
Cornbleet *et al.*, 1942[5]	biopsy		15.2	6.3	1.07			

* Values expressed in terms of fat-free solids.

TABLE II.
Water, Electrolyte, and Nitrogen Content of Human Skin.
The values are expressed in units per kilo of fat-free skin.

Patient unit No.	Source of skin	H_2O g	Cl mM	Na mM	K mM	Ca mM	Mg mM	Total N, g	Collagen N, g
x	Breast	725.5	73.5	88.2	15.41			44.3	35.4
155220	Thigh	740.5	76.1	96.2	18.60	3.75	2.06	40.65	29.35
281123	Breast	725.0	79.8	95.0	10.17	2.77	1.58	44.37	
78716	"	725.0	78.8	93.6	13.28	2.84	2.02	42.0	28.7
141323	"	695.5	74.6	85.8	10.58	2.43	2.50	49.3	41.9
285023	"	677.0	84.8	93.1	14.88	1.62	2.39	52.3	
290098	"	695.2	83.3	83.8	19.07	3.52	1.94	47.56	
206536	Leg	713.6	72.9	89.2	16.88				
y	Breast	708.1	84.2	93.7	23.46	3.04	2.66	45.2	31.1
238104	"	691.5	81.8	85.9	16.2	2.98	3.45	52.1	40.7
23792	"	741.9	82.8	102.8	16.8	2.72	1.79	42.1	28.7
326543	"	704.8	74.3	81.7	14.64	2.09	2.12	49.7	38.6
323121	Leg	728.9	90.1	108.9	20.80	3.24	2.25	44.9	30.0
45193	Breast	731.5	85.5	95.4	19.6	2.40	2.10	44.2	33.0
330802	"	706.0	76.6	88.6	17.6	2.50	1.82	48.2	38.8
244188	"	715.0	78.8	94.1	15.8	2.48	1.88	46.0	35.0
280907	"	756.0	84.2	112.0	16.6	2.23	1.91	38.6	28.3
335101	"	738.8	76.0	85.4	16.08	2.33	1.66	41.4	32.6
No. of determinations		18	18	18	18	16	16	17	14
Mean		717.7	79.9	93.0	16.47	2.68	2.13	45.5	33.7
σ		20.1	4.8	8.0	3.36	0.52	0.30	3.8	4.5
			Dog Skin.[9]						
Mean		708.3	86.7	96.5	22.46	3.01	3.03	46.8	33.1
σ		20.1	2.5	4.2	2.7	0.52	0.37	3.7	3.0

σ = Standard deviation.

skins than in the dog skins.

It will be noted, however, that a number of similarities of analytical results did occur between human and dog skin, the most pronounced exception being potassium (Table II and IV). If the results are expressed in units per 100 g of fat-free skin solids (Table III), the similarities are more apparent, with the lower potassium values in human skin still prevailing. The total nitrogen content (45.5 g per kilo, ±3.8 g) and the collagen nitrogen content (33.7 g per kilo, ±4.5 g) of the human skin were the same within experimental limits of error, as that found in dog. The 33.7 g of collagen nitrogen represents 188 g (5.58 × 33.7) of collagen per kilo of fat-free skin and since the total solid matter of human skin was 282 g per kilo, the remaining 94 g must be allocated to the other proteins found in skin. Thus collagen represents two-thirds of the solid matter of skin.

From the collagen nitrogen content the connective tissue nitrogen and therefrom the connective tissue weight were calculated by the method that Manery *et al.*[10] used for muscle; that is, by assuming that the connective tissue of skin corresponds to tendon and that the

[10] Manery, J. F., Danielson, I. S., and Hastings, A. B., *J. Biol. Chem.*, 1938, **124**, 359.

TABLE III.
Skin Analyses of Human and Dog Skin.
Values are expressed in units per 100 g of fat-free solid.

	H_2O g	Cl mM	Na mM	K mM	Ca mM	Mg mM	Total N. g	Collagen N, g
Human skin (18 subjects)	254	28.3	32.9	5.83	0.95	0.75	16.1	11.9
σ	23	2.6	4.5	1.27	0.22	0.12	0.2	1.1
Dog skin[9] (10 subjects)	243	29.7	33.1	7.71	1.03	1.04	16.0	11.3
σ	24	2.3	3.2	1.14	0.20	0.08	0.3	0.8

σ = Standard deviation.

TABLE IV.
Estimated Weight of Connective Tissue in Human Skin with Calculated Concentrations of Water, Chloride, Sodium, and Potassium in This Tissue.
The values are expressed in units per kilo of fat-free skin.

Exper. No.	Collagen N g	Connective tissue N g	Connective tissue weight, g	Connective tissue H_2O g	H_2O* g	Connective tissue Cl mM	Cl* Mm	Connective tissue Na mM	Na* mM	Connective tissue K mM	K* mM
x	35.4	38.5	572	347	378	44.7	28.8	53.4	34.8	3.41	11.92
155220	29.4	32.0	476	289	452	37.2	38.9	44.5	51.7	2.90	15.70
78716	28.7	31.3	455	276	449	36.4	42.4	43.4	50.2	2.78	10.50
141323	41.9	45.6	677	411	285	52.9	21.7	63.2	22.6	4.13	6.45
y	31.1	33.9	504	306	402	39.4	44.8	47.1	46.6	3.07	20.39
238104	40.7	44.3	658	399	292	51.5	30.3	61.5	24.4	4.01	12.19
23792	28.7	31.3	465	282	460	36.4	46.4	43.4	59.4	2.84	13.96
326543	38.6	42.0	624	378	326	48.8	25.5	58.2	23.5	3.81	10.83
323121	30.0	32.7	486	295	434	37.8	52.3	45.4	63.5	2.96	17.84
45193	33.0	35.9	533	323	408	41.7	43.8	49.7	45.7	3.25	16.35
330802	38.8	42.3	628	381	325	49.1	27.5	58.6	30.0	3.83	13.77
244188	35.0	38.1	566	343	372	44.3	34.5	52.8	41.3	3.45	12.35
280907	28.3	30.8	458	278	478	35.8	48.4	42.9	69.1	2.79	13.81
335101	32.6	35.5	528	320	419	41.3	34.7	49.3	36.1	3.22	12.86
Mean	33.7	36.7	546	330	391	42.7	37.1	51.0	42.8	3.32	13.50
σ	4.5	4.9	73	45	61	5.7	9.1	6.8	14.5	0.45	3.29
					Dog Skin.[9]						
Mean	33.1	34.7	540	328	381	42.5	44.4	48.9	46.5	3.29	19.14
σ	3.0	3.1	46	28	36	3.6	4.5	4.5	7.4	0.89	2.78

*Total skin concentrations minus connective tissue concentration.
σ = Standard deviation.

ratio of collagen nitrogen to total nitrogen is the same in all connective tissue as it is in tendon. Employing the assumption that the ratio of collagen nitrogen to total nitrogen in the tendons of man is the same as that found in the tendons of dog, the data from dog tendons were used to calculate the weight of the connective tissue in the human skin: average total nitrogen content, 67.3 g; collagen nitrogen, 61.8 g; total water 606.2 g and chloride 78.2 mM per kilo of fat-free tendon.[11]

From the data in Table II the weight of the connective tissue of skin was estimated; and the amounts of water, chloride, sodium, and potassium identified with this connective tissue were calculated using the above tendon data along with the sodium and potassium data given by Muntwyler *et al.*[12] The results of these calculations are presented in Table IV. The water, chloride, sodium, and potassium in excess of that accounted for by the connective tissue should represent the amounts associated with the remaining part of the corium and the entire epidermis, since no

[11] Eichelberger, L., and Brown, J. D., *Proc. Am. Soc. Biol. Chem.*, 1944, **3**, 56.

[12] Muntwyler, E., Mellors, R. C., Mautz, F. R., and Mangun, G. H., *J. Biol. Chem.*, 1940, **134**, 389.

collagen is found in the epidermis. In a kilo of skin, therefore, 546 g may be allocated to the connective tissue and 454 g to the cells of the skin and their surrounding ultrafiltrate. The numerical amount of water, chloride, and sodium that can be assigned to the ultrafiltrate volume cannot be satisfactorily estimated on the basis of what we know now; nevertheless, the low concentration of potassium (13.5 mM) suggests that the amount of the intracellular phase of the skin is small; and if magnesium is ascribed to the intracellular fluids of a tissue, the low concentration found in the skin (2.13 mM) should further corroborate this small intracellular phase.

Although the total water of the extracellular phase cannot be calculated at this time, the calculated 330 g of water identified with the 546 g of connective tissue per kilo of fat-free skin demonstrates that the volume of available water is considerably larger in the skin than any other tissue of the body. This finding corresponds to the results obtained by Flemister[13] for his work on mice.

Summary. Total water, nitrogen, collagen nitrogen, and electrolyte concentrations were determined in human skin which was removed at once from amputated parts during the course of surgery. The total skin (corium plus epidermis) gave the mean average results which are expressed as units per kilo of fat-free skin: total water, 717.7 ± 20.1 g; chloride, 79.9 ± 4.8 mM; sodium, 93.0 ± 8.0 mM; potassium, 16.47 ± 3.36 mM; calcium, 2.68 ± 0.52 mM; magnesium, 2.13 ± 0.30 mM; total nitrogen, 45.5 ± 3.8 g; and collagen nitrogen, 33.7 ± 4.5 g.

By applying methods now accepted as valid for calculating the weight of connective tissue in a tissue, the weight of connective tissue in human skin was estimated to be 546 ± 73 g per kilo of fat-free skin. The calculated 330 ± 45 g of water identified with this amount of connective tissue demonstrates that the volume of available water is considerably larger in skin than in any other tissue of the body. The skin may be regarded as one of the most important water-storage organs of the body.

We wish to express our appreciation to various members of the Department of Surgery for making the tissues used in this study available to us.

[13] Flemister, L. J., *Am. J. Physiol.*, 1942, **135**, 430.

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Effect of Penicillin on Experimental Staphylococcus Osteomyelitis in Rats.*

J. EMERSON KEMPF AND J. ARTHUR HERRICK. (Introduced by Malcolm H. Soule.)

From the Hygienic Laboratory, University of Michigan, Ann Arbor.

Experimental staphylococcal infections in animals which simulate natural occurring infections in man are difficult to produce. In order to evaluate the recently introduced chemotherapeutic agents it would be desirable to have access to readily reproduceable *in vivo* procedures. The purpose of this study was to develop methods for the production of chronic staphylococcal infections in mice and determine the value of penicillin in the treatment of such infections.

With economy of penicillin in mind, several animals were considered, and on investigation the rat was found to be suitable for the purpose. The production of osteomyelitis in this animal did, however, present a major problem which was quite distinct from that of treatment. Because of the nature of the problem

* The penicillin was provided by the Office of Scientific Research and Development from supplies assigned by the Committee on Medical Research for experimental investigations recommended by the Committee on Chemotherapeutic and Other Agents of the National Research Council.