the type of connection which commonly links arterial and venous capillary networks; that the pulp space—not the venous sinus—is the primary physiological unit of the splenic vascular mechanism; and that contraction of the capsule and trabeculae may convert the structurally 'open' circulation of a relaxed or distended spleen into a functionally 'closed' circuit.

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Electrical Method for Studying Water Metabolism and Translocation in Body Segments.

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Although the electrical resistance of a mummified arm would, obviously, be very much greater than that of a fresh cadaver, no serious attempt has ever been made to measure the water content of a body segment in terms of its electrical resistance. One of the reasons for this would appear to have been the lack, until comparatively recently, of technics which would permit resistance measurements to be made. Using alternating current, it has now become possible to measure, with a fair degree of accuracy, not only the resistance of various parts of the arm-to-arm segment in man (the upper arm, the chest segment alone or the arm and chest segments together) but also changes in their dielectric properties.[1, 2, 3]

Hydration. In order to test out the possibility of measuring body water changes electrically, a liter of isotonic saline solution was injected intravenously into a normal individual weighing 50 kg who had been deprived of fluids for 3 hours previously and the electrical resistance of the arm-to-arm segment was measured before and 30 minutes after the injection. Resistance measurements were made by the immersion method at room temperature. The subject stood before a table 32 inches high and immersed the forearms in 9 liters of normal saline (11 cm deep) contained in a pair of arm baths supported on the table so that (1) the elbows rested on the arm-bath bottoms and (2) the upper arms were in a substantially

1 Horton, J. W., and Van Ravenswaay, A. C., *J. Frank. Inst.*, 1935, **220**, 557.
2 Barnett, A., and Bagno, S., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 543.
3 Barnett, A., *West. J. Surg.*, 1937, **45**, 380.

vertical position. Current was supplied to the arm baths at 11,160 cycles/second by the measuring instrument.[3] About 90% of the resistance measured by this method is due to the unimmersed segment.[4] Measurements over a control period of 2 hours were reproducible within ±2% and were made one minute after immersion.

The test subject excreted 150 cc of urine during the injection period (1 hour). Although the volume of retained saline (about 850 cc) was less than 2% of the total body weight (50 kg), a decrease of 10% in the measured resistance was observed. Confirming tests on a number of additional subjects yielded changes of the same order.

This surprisingly large decrease in body resistance demanded an explanation and the following working hypothesis was adopted. It is known that, when isotonic saline is injected intravenously, it does not distribute itself uniformly throughout the tissues but, after leaving the vascular system, accumulates in the extracellular or interstitial spaces.[5] Since these spaces are estimated to constitute only 20-30% of the total tissue volume,[5] a given volume of saline entering an extremity such as the arm, either fills in or increases the cross-section of the interstitial spaces by 3-5 times the amount that it would if it were also taken up intracellularly. The interstitial spaces in the arm lie in parallel relation to the muscle fibers. Current flowing along the arm splits up into parallel paths, part flowing along the inside of the muscle fibers and the rest along the interstitial spaces outside the latter. In the chest segment the current splits to flow in parallel paths through the chest muscles on the one hand and through the lung on the other. The reduction in resistance of the interstitial branches of these parallel circuits is the cause of the comparatively large resistance drop.

The distribution of extracellular isotonic saline following intravenous injection is variously reported in the literature. Skelton,[6] working with cats, found that none of the saline reached the muscles but was absorbed mainly by the skin. Hastings and Eichelberger,[7] on the contrary, working with dogs, traced considerable saline into the extracellular spaces of the muscles. The subject has been reviewed by Adolph.[8] From the electrical standpoint, whether the saline accumulates between the muscle fibers or in the subcutaneous

[4] Horton, J. W., Van Ravenswaay, A. C., Hertz, S., and Thorne, G., *Endocrin.*, 1936, **20**, 72.

[5] Peters, J. P., *Body Water*, C. C. Thomas, Baltimore, 1935.

[6] Skelton, H. P., PROC. SOC. EXP. BIOL. AND MED., 1925-6, **23**, 499.

[7] Hastings, A. B., and Eichelberger, L., *J. Biol. Chem.*, 1937, **117**, 73.

[8] Adolph, E. F., *Physiol. Rev.*, 1933, **13**, 336.

tissues, the current path still remains a parallel one and the infiltrated saline shunts the intracellular branch of the circuit.

Since the cell walls in the arm are known to be dielectrics having capacitative properties, a change in arm resistance should modify the Q-factor which is the ratio between the reactances, due to these capacitances, and the resistance. Q-factor measurements were, therefore, made of a 10 cm length of the deep tissues of the right upper arm by the 4-electrode technic[1, 2, 3] before and after the injection of a liter of saline.

Results are given in Table I for 10 subjects on whom measurements of both resistance and Q-factor were made. Nine of these subjects were mental patients with negative physical findings.

The resistance changes vary from 9 to 17% with a mean of 11.4% and the Q-factors from 12 to 27%—mean 17.5%. Normal subject A.B. is remarkable for the large changes in the electrical values despite the retention of only 440 cc of saline. Subject C.P. was given an injection of 2 liters of saline over a period of 2 hours. 1250 cc were retained. The resistance change was 60 ohms and the Q-factor decreased 0.028 (27%). Subjects C.P. and M.B. were given injections of one liter of Ringer's solution instead of isotonic saline. No significant difference in the order of the electrical changes was observed.

Resistance measurements were made on 3 subjects 3½ hours and 24 hours after the end of the saline injection. The resistances after the 3½-hour interval were still decreased but had moved back towards the preinjection level roughly in proportion to the volume of urine excreted which took place at the rate of approximately 100 cc per hour. At the end of 24 hours, the resistances had returned to the preinjection levels.

Blood pressure measurements made before, after and during saline injections showed variations of the order of ±10 mm which may be considered as not significant.

Dehydration. As a test of the reversibility of resistance measurements, a female subject weighing 63 kg and normally excreting 1500-1700 cc of urine daily, was put on a restricted fluid intake of 500 cc daily and 50 cc of 50% glucose was given intravenously twice daily for 3 days. Her body resistance was 200 ohms at the beginning of the experiment. On the fourth day, there had been a total weight loss of 2 kg, the urine output had descended to 600 cc for the previous 24-hour period and the body resistance had risen 45 ohms, from 200 to 245 ohms.

Clinical Applications. (1) A female patient 16 years of age and

TABLE I.

Effect of Intravenous Injection of One Liter of Isotonic Salt Solution on the A.C. Resistance of the Arm-to-arm Segment and on the Q-factor of a 10 cm Arm Segment.

Subj.	Sex	Age	Wt in kg	Saline retained cc	Resistance in ohms by the immersion method			Q-factor of a 10 cm arm segment		
					Before injection	After injection	% difference	Before injection	After injection	% difference
L.G.	♀	15	40.2	900	275	245	10.9	.066	.058	12.1
M.W.	♀	27	46.9	960	235	205	12.8	.106	.077	27.4
J.M.	♀	23	44.0	700	306	275	10.1	.070	.058	17.2
M.B.	♀	25	53.6	975	315	282	10.5	.078	.064	17.9
R.N.	♀	32	63.4	800	210	182	13.3	.078	.068	12.8
C.D.	♀	19	64.1	750	225	200	11.1	.101	.089	11.9
A.B.	♀	26	43.6	440	345	314	9.0	.081	.063	22.2
C.P.	♀	43	50.7	850	290	262	9.6	.102	.080	21.6
I.D.	♂	21	64.9	900	221	200	9.5	.123	.102	17.1
L.B.	♂	20	50.9	800	234	194	17.1	.102	.087	14.7
							Mean 11.4%			Mean 17.5%

weighing 82 lb diagnosed as an hysteric had lost weight progressively as a result of prolonged vomiting. The vomiting episodes lasted for periods of several days during which time the patient regurgitated all food and liquid immediately after ingestion by inserting her fingers into her mouth to induce the vomiting reflex. The body resistance measured by the immersion method after 2 days of continual vomiting was the highest ever observed in a human subject—445 ohms. Suddenly the vomiting ceased and the patient ingested large quantities of food and liquid over a period of 48 hours. There was a gain in weight of 1½ kg. At this point the body resistance was found to be 405 ohms. An injection of one liter of isotonic saline was then given over a period of one hour intravenously. 745 cc were retained. The resistance fell from 405 to 334 ohms, a change of 71 ohms.

(2) Resistance measurements were made in 2 cases of involutional melancholia (females) under treatment with testosterone propionate which is now widely used for menopausal disturbances.[9] 25 mg were given intramuscularly thrice weekly. Zuckerman and Bourne[10] have shown that, in primates, injections of testosterone propionate cause water retention. Recently Kenyon[11] and his coworkers have reported that this substance also produces water retention in man (normals). In both cases under treatment a progressive drop totaling about 10% in body resistance was observed in the course of a month. The absolute changes were 290 to 260 ohms and 285 to 251 ohms. Spontaneous resistance changes of this magnitude are not observed in conditions of this kind.

(3) Transverse resistance measurements were made on a female exhibiting a cyclic oedema of the ankles coincident with each menstrual period. The circumference at the ankle level increased by 4 cm during periods. Concentric electrodes[12, 13] were mounted on the leg by means of rubber bands at a level 3 inches above the ankle so that the current passed diametrically from the internal to the external lateral sides and the resistance of the deep tissues between electrodes was measured at, and 2 weeks after, a period. The measured resistance increased from 118 during oedematous infiltration to 212 ohms, when the oedema had been resorbed.

Remarks. It is important to note that both the resistance and Q-

9 Kurzrock, L., Birnberg, C. H., and Livingston, S., *Endocrin.*, 1939, **24**, 347.

10 Zuckerman, S., Palmer, A., and Bourne, G., *Nature*, 1939, **143**, 521.

11 Kenyon, A. T., Knowlton, K., Sandiford, I., Koch, F. C., and Latwin, G., *Endocrin.*, 1940, **26**, 26.

12 Barnett, A., *J. Physiol.*, 1938, **93**, 349.

13 Barnett, A., *West. J. Surg.*, 1937, **45**, 322.

factor decrease following infusion of isotonic saline. This is to be expected in a parallel type of circuit. In a circuit of the series type, a decrease in resistance would result in an increased Q. The studies here presented are of a preliminary nature and do not permit a judgment as to the contributory rôle of the various anatomical elements lying along the current path to the total result. A rough analysis of the probable relative effects of the extracellular and intracellular phases has been presented for the particular case where isotonic saline is injected intravenously. It is possible that vascular factors also intervene. Studies along these lines are now in progress.

I am indebted to A. N. Mayers for assistance during part of this investigation.

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Action and Toxicity of Vitamin B_6 Hydrochloride.

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In view of the increasing interest in vitamin B_6[1-4] as a nutritional accessory, the present investigation was undertaken in order to determine the degree of potency and limits of toxicity. All experiments were carried out with crystalline vitamin B_6 hydrochloride, m.p. 212°C (corrected) with effervescence.

General Properties. Vitamin $B_6 \cdot HCl$ is easily soluble in water. Its aqueous solutions are acid in reaction. A 1% solution has a pH of 2.44. *In vitro* a quantity of 4 mg caused hemolysis of sheep's washed erythrocytes, but if it was previously neutralized, no laking took place. Obviously the hemolytic effect was due to the acidity. When a 1% solution of $B_6 \cdot HCl$ in the amount of 0.5 cc was injected both subcutaneously and intramuscularly into 3 rabbits, practically no irritation occurred, but when 0.1 cc of the same

1 György, P., *Nature*, 1934, **133**, 498; *J. Am. Chem. Soc.*, 1938, **60**, 983.

2 Fouts, P. J., Helmer, O. M., and Lepkovsky, S., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 4; *Am. J. Med. Sc.*, 1940, **199**, 163.

3 Spies, T. C., Bean, W. B., and Ashe, W. F., *J. A. M. A.*, 1939, **112**, 2414.

4 Kark, R., Lozuer, E. L., and Meiklejohn, A. P., PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 97.