solutions is clear, with the figure for Ca notably smaller than the others.

In the second series, in which the salt solutions were followed by distilled water, the difference between the figures for water alone, and after the salt solutions is relatively little, except in the instances of Mg and Ca.

Since the same anion is present in both series, in each case of the individual salts, the bi-valent cations are apparently the chief factors of influence.

Where the same points are concerned, these results correspond in general to those of Haldi[4] and his associates in relation to swelling of brain tissue. They indicate an effect of Ca on brain tissue similar to that reported by Höber[5] on the plasma membrane and other parts of various cells, and to the findings of Langmuir and Blodgett[6] on the effect of salt solutions on mono-layers, and those of Herbst,[7] who observed that the individual cells of developing echinoderm eggs fall apart in Ca-free water, but are united again on the addition of Ca.

The findings have a bearing on the importance of these salts in maintaining normal water relations in the body tissues, notably in the brain.

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Vitamin C Nutrition in Artificial Fever.

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A number of studies have shown that Vitamin C requirement is increased in pneumonia, tuberculosis, and other diseases. It has been suggested that the decreased Vitamin C excretion in pneumonia may signify a greater requirement because of an increased metabolic rate.[1] Heise and Martin[2] have shown an increased rate of utiliza-

4 Haldi, J. A., and Rauth, J. W., *Am. J. Physiol.*, 1925-26, **75**, 294; *ibid.*, 1927, **80**, 631.

5 Höber, R., *loc. cit.*, p. 695.

6 Langmuir, I., and Blodgett, K. B., *Koll. Z.*, 1936, **73**, 257.

7 Herbst, C., in Höber, p. 695.

1 Bullowa, J. G. M., Rothstein, I. A., Ratish, H. D., and Harde, E., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 1.

2 Heise, F. H., and Martin, G. J., *Am. J. Dig. Dis. and Nutrit.*, 1937, **4**, 368.

tion or destruction of Vitamin C in tuberculosis. The assumption has been made that fever will increase Vitamin C requirement, but this has not been proved by direct experimental evidence. This paper is the report of an investigation of the effect of artificial fever on Vitamin C stores in guinea pigs and upon Vitamin C excretion in man.

Guinea Pigs: In order to study the rate of depletion of Vitamin C stores, all pigs were fed a scorbutic diet.[3] Twenty-three pigs were used as controls and 21 were given fever treatment. In a warm air chamber heated with light bulbs, temperatures were raised daily to 105°-106° for 2 to 6 hours. Temperatures were easily raised to 106° with a chamber temperature of 100°-102°. Groups of pigs were killed after 4, 7, 15 and 25 days and tissues analyzed by the method of Bessey and King.[4] Adrenals and kidneys of all animals and the brains of a few were analyzed. With the method used, reliable figures could not be obtained on liver extracts.

Results recorded in Table I show that Vitamin C stores are depleted faster in animals with fever than in their controls. However, when a state of scurvy is approached at 15 days, there is little difference between controls and fever treated animals. Since Vitamin C is stored in the adrenals, the rate of Vitamin C depletion in them should be more significant than great depletion in other tissues. When the results are analyzed with the method described by Dunn,[5] a highly significant difference is found between controls and fever treated pigs. There is approximately one chance in 4000 and one in 25,000,000 in the 4- and 7-day periods respectively that these results occur by pure chance.

TABLE I.
Effect of Fever on Vitamin C Stores of Adrenals and Kidneys.

	Fever treated pigs				Controls		
Days on diet	No. of pigs	Total hr of fever	Mg Vit. C per g tissue		No. of pigs	Mg Vit. C per g tissue	
			Adrenals	Kidneys		Adrenals	Kidneys
4	7	13	.17 ± .0126	.044 ± .007	7	.278 ± .041	.048 ± .017
7	7	15	.13 ± .0038	.020 ± .0003	7	.188 ± .016	.028 ± .002
15	4	30	.053	.018	4	.084	.021
25	3	45	.042	.017	5	.046	.018

Vitamin C concentrations found in the kidneys are less significant but interesting. After 4 days there is not a significant difference

[3] Eddy, Walter H., *Am. J. Publ. Health*, 1929, **19**, 1309.

[4] Bessey, Otto A., and King, C. G., *J. Biol. Chem.*, 1933, **103**, 687.

[5] Dunn, Halbert L., *Physiol. Rev.*, 1929, **9**, 275.

between the 2 groups. After 7 days there is a difference which is as significant as values found in the adrenals for the corresponding period. Seven days, with 15 hours of fever, lowered the concentration to .02 mg per g of tissue which corresponds to 15 days for the controls. This is apparently the scorbutic level because only slightly lower values were obtained in pigs with severe scurvy.

A few analyses were made on the brains which indicated only slight loss of Vitamin C. One animal which had .07 mg per g of tissue in the adrenals still had .12 mg per g of tissue in the brain compared with a normal value of .14 to .16 mg per g.

Scurvy appeared in two fever treated pigs 5 days before any symptoms were visible in controls.

Human Studies: In patients receiving artificial fever, studies were made on Vitamin C excretion in urine and on its concentration in the blood. Urinary Vitamin C excretion was determined the day before fever treatment, the day of treatment and the day following treatment. Blood Vitamin C was determined before treatment and immediately after treatment. A modification of Bessey and King's[4] method was used to determine Vitamin C in urine; and the method of Pijoan and Klemperer[6] was used to determine it in blood plasma.

Because of difficulty in collection of complete 24-hour samples of urine from patients studied, reliable results were obtained on only 4. Two of these had previous fever treatment, and each excreted 17 mg of Vitamin C the day before treatment. Each of the others excreted 23 mg. The day including the fever treatment, none excreted more than 10 mg. Following fever, the first 2 excreted 8.0 and 15.0 mg, the last 2 each excreted 16 mg. Since Vitamin C is excreted in sweat[7, 8] no significance can be attached to the low values obtained during fever. In all cases, however, excretion was lower following fever than before.

Since excretion did not return immediately to pre-treatment level and those individuals who had previous treatments were excreting very little Vitamin C (normal excretion in 24 hours is 25 mg or more[9]), lowering of Vitamin C stores is indicated. Whether fever increases the physiological need for Vitamin C or induces an excessive loss in sweat cannot be determined by this type of experi-

6 Pijoan, M., and Klemperer, F., *J. Clin. Invest.*, 1937, **16**, 443.

7 Cornbleet, Theodore, Klein, R. I., and Pace, E. R., *Arch. Dermatol., Syphilol.*, 1936, **34**, 253

8 Lilienfeld, A., Wright, I. S., and MacLenathen, E., PROC. SOC. EXP. BIOL. AND MED., 1936, **35**, 184.

9 Youmans, John B., Corlette, M. B., Akeroyd, J. H., and Frank, H., *Am. J. Med. Sciences*, 1936, **191**, 319.

ment. However, when the results with guinea pigs are considered, an increased physiological need for Vitamin C during fever is indicated.

Studies on blood were interesting but did not aid in judging Vitamin C utilization. It seemed that the blood Vitamin C concentration should be reduced during fever if an excessive amount was lost in sweat, or tissues required more than normal. However, a decrease was not observed in any of 6 patients studied. In all of them, values after treatment were equal to or greater than the values before treatment which indicates that Vitamin C, like blood chlorides and blood sugar,[10] concentrates with the concentration of blood during fever.

Summary. Studies of Vitamin C excretion before and after periods of artificial fever show that fever increases the Vitamin C requirement of man. Studies of Vitamin C stores in adrenals and kidneys of guinea pigs show that artificial fever increases the requirement or accelerates the destruction of Vitamin C. Since guinea pigs cannot lose Vitamin C in sweat, an increase in the physiological need for Vitamin C during fever is indicated.

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Localization of the Neural Inductor and Tail Mesoderm in a Frog Egg (*Hyla regilla*)*

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The Neural Inductor. In the urodeles the dorsal and lateral blastoporal lips of the early gastrula induce a secondary neural plate when implanted under presumptive epidermis.[1, 2] Although in *both* urodeles and anurans the anlagen of chorda and somites occupy the dorsal and lateral lips,[3] it has been reported that in anurans the neural plate inductor is limited to the dorsal lip.[4] Is this a general characteristic which distinguishes the anuran from

10 Krusen, Frank H., *Am. J. Med. Sciences,* 1937, **193**, 470.

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1 Bautzmann, H., *Arch. f. Entw.-mech.,* 1926, **108**, 283.

2 Schechtman, A. M., *Univ. Calif. Publ. Zool.,* 1934, **39**, 277.

3 Vogt, W., *Arch. f. Entw.-mech.,* 1929, **120**, 384.

4 Schmidt, G. A., *Zool. Anzeiger,* 1936, **116**, 323.