ciated with the ingested granules and apparently aid in bringing about their coalescence into masses which are stored by the cells. The changes found in the Golgi material never occur in cells which do not collect and store particulate matter.

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Excretion of Thiamin and its Degradation Products in Man.*

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The development of a simple procedure[1] to determine both thiamin and the pyrimidines in human urine permits the investigation of the possible relationship between the two.

Schultz, Atkins and Frey showed that the rate of glucose fermentation by a yeast is directly proportional to the concentration of thiamin present. In addition to thiamin, the pyrimidines give mol for mol stimulation effect on the rate of fermentation. Such pyrimidines are found normally in human urines. Since the pyrimidine nucleus constitutes an integral part of the thiamin molecule, it is of interest to determine the relationship between thiamin and urinary pyrimidine.

The total fermentation is a measure of thiamin and pyrimidine in the urine. The fermentation after oxidation of the free thiamin is a measure of the pyrimidines; the difference represents the free thiamin. This technic combines the gas method with the initial steps of the thiochrome procedure.

The urinary excretion of the thiamin and pyrimidine of a group of patients was studied under various conditions. Three patients were given a diet completely deficient in B_1 for 10 days. Two of these were normal and one had ileo-jejunitis. Fig. 1 and 2 and Table I illustrate that complete deprivation of dietary thiamin for a period of 10 days changed the thiamin-pyrimidine ratio from approximately 9:1 to 1:9. During this 10-day deprivation period,

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We are indebted to Dr. Charles Frey, of the Fleischman Laboratories, for his coöperation.

1 Schultz, A. S., Atkin, L., and Frey, C. N., *Science*, 1938, **88**, 547; *J. Biol. Chem.*, 1940, **136**, 713.

TABLE I.
Twenty-four-hour Excretion of Thiamin and Pyrimidine, During Administration of Low Thiamin Diet.
S.F. Male. Age 13. Diagnosis: Ileo-colitis.

March	Total fermentation (mol-equivalents)	Vitamin B_1 (m-equiv.)	Pyrimidines (m-equiv.)	% of fermentation due to free thiamin
3	640	282	358	44
4	172	109	63	63
5	750	487	263	65
6	644	322	322	50
7	286	28	258	10
8	270	38	232	14
9	184	0	184	0
10	402	54	348	18

the absolute amount of pyrimidine excreted remained at approximately the same level, while the free thiamin disappeared almost completely. It becomes apparent, then, that the determination of free thiamin in the urine is an index of the dietary intake immediately preceding the measurement, since the urinary excretion of thiamin decreases so rapidly on deprivation. Therefore, low values for free thiamin need not necessarily indicate a state of chronic insufficiency with respect to this vitamin since the same values are obtained with temporary, acute deprivation. On the other hand, the combined gas-thiochrome method can distinguish the low values of thiamin resulting from acute or normal deprivation. If the thiamin excretion is low in the presence of normal pyrimidine excretion, it is indicative of recent deprivation. However, if both the thiamin and pyrimidine are below normal, it can be interpreted as indicating a protracted insufficiency of B_1.

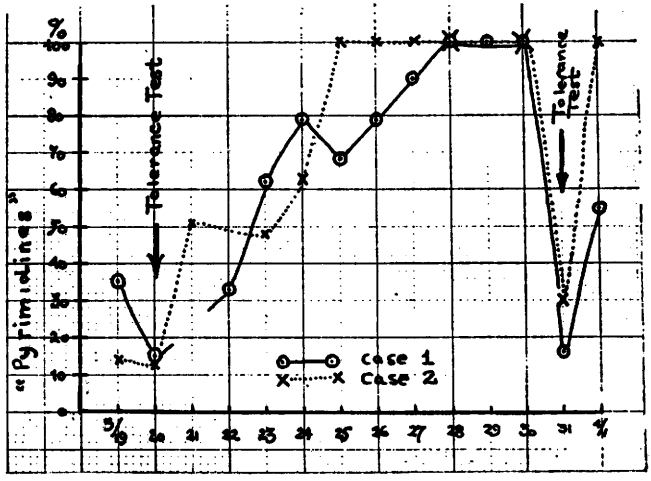

FIG. 1.

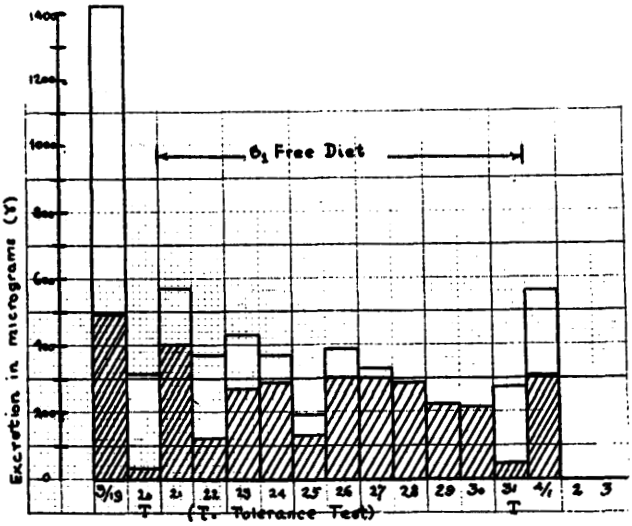

FIG. 2.

A further evidence in support of this concept is the result obtained with the 1 mg load test. By this test is meant the urinary response to the parenteral administration of 1 mg of thiamin hydrochloride, as previously reported.[2] This test was carried out before the experiment was started, and repeated after the 10-day deprivation period. It is highly significant that although the free thiamin was practically absent from the urine at the end of the 10-day period, the load test remained unchanged. This unchanged response to the 1 mg load test, (Fig. 2) indicates that the basic state of nutrition with respect to B_1 was unaltered by the temporary deprivation in

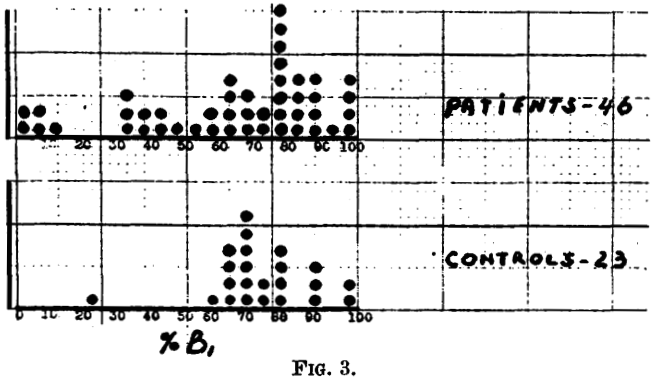

FIG. 3.

2 Pollack, H., Dolger, H., Ellenberg, M., and Cohen, S., PROC. SOC. EXP. BIOL. AND MED., 1940, **44**, 98.

a well-nourished individual. The laboratory data are supported clinically by the complete absence of any evidence of Vitamin B_1 deficiency either subjectively or objectively as measured by electrocardiogram, blood-sugar, cholesterol, total protein, hemoglobin, red blood cell count, blood pressure, pulse rate and weight.

Fig. 3 again demonstrates the importance of the pyrimidine concentration in relationship to the total thiamin excretion. When normal individuals are subjected to the 1 mg load test, over 60% of the yeast fermentation stimulating substance in the urine is free thiamin. Contrasting these results obtained from a group of unselected hospitalized patients, it is seen that 25% excrete more pyrimidine than thiamin. This indication that one-fourth of all patients admitted to the hospital showed atypical responses to the test is an independent correlation of a similar conclusion[3] arrived at by different means.

Table II shows the urinary excretion of pyrimidines following the daily parenteral administration of 100 mg of thiamin hydrochloride. It can be seen that the absolute amount of pyrimidine excreted is increased. This is evidence that urinary pyrimidine is derived from thiamin. Further, these data indicate that increasing the amount of thiamin administered increases its utilization, if the increased pyrimidine excretion in the urine is an index of actual utilization of thiamin. The administration of large doses of thiamin results in an absolute increase, but a relative decrease in the efficiency of utilization. Hence it might be suggested that frequent, divided dosage is the method of choice in administering this vitamin.

TABLE II.

Twenty-four-hour Excretion of Thiamin and Pyrimidine after Intravenous Administration of Vitamin B_1.

T. McN. Male. Age 35. Diagnosis: Avitaminosis B-Complex.

Date	Total fermentation (mol-equivalents)	Vitamin B_1 (m-equiv.)	Pyrimidines (m-equiv.)	% of fermentation due to free thiamin
9/27	87,500	83,000	4,500	95
28	24,400	20,100	4,300	82
29	73,100	63,600	9,500	87
30	112,000	69,000	43,000	62
10/3	82,500	67,600	14,900	82
4	106,000	90,000	16,000	85
7	9,390	2,490	6,900	27
8	9,550	3,150	6,400	33
17	312,000	288,000	24,000	92
18	145,500	116,500	29,000	80
19	19,300	2,300	17,000	12

This patient received 100 mg thiamin daily intravenously from 9/27 to 10/16. On 10/16 he was given 300 mg, 10/17 200 mg, 10/18 no thiamin administered.

3 Pollack, H., Ellenberg, M., and Dolger, H., *Arch. Int. Med.*, 1941, **67**, 793.