VITAMINS B_1 AND C IN EFFORT SYNDROME.

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" EFFORT syndrome " is a comprehensive term applied conveniently to a group of conditions not apparently due to organic disease, characterized primarily by effort intolerance and manifesting breathlessness, palpitation, left chest pain and a subjective feeling of fatigue on even mild exertion. Vegetative lability on emotional excitement, e.g. palpitation, sweating, giddiness, etc., are described by the patient and may be objectively observed. We have found the simplest and most convenient classification of E.S. patients to be into (*a*) primarily constitutional, and (*b*) primarily neurotic groups. In the former (Group 1) the patient has had a poor physical endowment since earliest recollection, to which he has responded in a neurotic manner. In this sense there is a psychological aetiology, but the constitutional factor is the basic one. In the primarily neurotic group (Group 2) there is a definite psychopathology and the usual factors determining a neurosis apply: constitutional physical inferiority, if present, colours the whole picture, but is of only secondary importance. The whole problem has been studied in some detail in the E.S. Unit at this hospital, where more than 2,000 cases have been treated since the end of 1939 (Guttmann and Jones, 1940; Wood, 1941; Lewis, 1941; Jones and Lewis, 1941; Jones and Scarisbrick, 1941, 1942 and 1943).

In considering the factors that may give rise to effort intolerance the question arose whether certain types of effort syndrome might be attributable to malnutrition. Fatigue is prominent among the symptoms of dietary deficiency, and it has been associated in particular with deficiencies of vitamins B_1 and C. Point was given to this suggestion by the studies of Jolliffe, Goodhart, Gennis and Cline (1939), who observed the effects of mild vitamin B_1 deprivation on normal volunteers, and found " the symptoms observed were fatigue and lassitude, anorexia, precordial pain, burning of the feet, dyspnoea on exertion, muscle cramps and palpitation." The picture has much in common with that observed in effort syndrome, and emphasizes the unspecific character of this condition. Apart from a deficiency in the diet, a deficiency due to failure in absorption had also to be considered.

In the present investigation a series of patients in the Effort Syndrome Unit at the Mill Hill Emergency Hospital were examined by means of vitamin excretion and saturation tests with regard to their vitamin B_1 and C nutrition.

METHODS.

Vitamin B_1.—Vitamin B_1 estimations in urine were done by the improved thiochrome method of Harris and Wang (1941), using an Osira ultraviolet lamp and Chance glass filter. The vitamin B_1 saturation test was similar to that described by McAlpine and Hills (1941), and consisted in measuring the vitamin B_1 excreted in the period of $4\frac{1}{2}$ hours immediately following the oral ingestion of 1 mgrm. vitamin B_1.

Vitamin C.—The resting level of vitamin C excretion was estimated on 3-hour samples by the " true ascorbic acid " method of Richter and Croft (1943). The saturation tests were done by the method of Harris (1942), which consists in estimating the daily excretion of vitamin C in a 3-hour sample after the oral ingestion

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of 700 mgm./70 kgm. ascorbic acid. The blood vitamin C estimates were done by the lead precipitation method of Richter and Croft (1944).

Results.

Vitamin B_1.—Of a series of 21 effort syndrome patients who were selected for investigation, 11 were chosen as typical of the " constitutional type " and 10 had anxiety neuroses. The vitamin B_1 excretion ranged from 58 to 289 µgm./24 hours with a mean of 142 µgm., and showed no significant difference between the two groups (Table I). Subjects showing clinical signs of vitamin B_1 deficiency generally show a much lower excretion than this, of the order of 30 µgm./24 hour or less. The vitamin B_1 saturation test also gave a mean excretion of 115 µgm. or 11·5 per cent. of the test dose in the 4½ hour period after administration. These figures are well above the level commonly found in deficiency disease, and they gave evidence that in neither of the groups were the symptoms attributable to vitamin B_1 deficiency.

Table I.—*Vitamin B_1 Excretion and Saturation Test.*

Group 1.—Constitutional Type.

No.	Vitamin B_1 excretion (µgm./24 hr.).	Vitamin B_1 saturation (µgm./4½ hr.).
1	163	139
2	245	164
3	142	84
4	149	159
5	131	39
6	154	77
7	225	106
8	126	171
9	76	115
10	58	69
11	289	126
	Mean 160	Mean 114

Group 2.—Neurotic Type.

12	116	135
13	83	59
14	117	73
15	81	87
16	130	81
17	155	115
18	154	152
19	89	175
20	224	171
21	76	117
	Mean 122	Mean 116
	Mean of both groups 142	Mean of both groups 115

The vitamin B_1 saturation is expressed as the urinary excretion in 4½ hrs. after a test dose of 1 mgm. vitamin B_1 (1 µgm.=1γ).

This finding was confirmed by testing the effect of vitamin B_1 administration. A group of 6 patients with effort syndrome who were given 15 mgm./day vitamin B_1 by mouth for one week gave no evidence of any subjective or objective improvement.

Vitamin C.—Estimation of the blood vitamin C concentration in 17 patients with effort syndrome gave figures ranging from 0·20 to 0·37 mgm./100 ml. with a

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mean of 0·30 (Table II). These figures indicated a relatively low level of vitamin C nutrition, and this was confirmed by the urinary excretion and saturation tests. The mean resting level of vitamin C excretion was 14 mgm./24 hours, and of 12 patients who were given the saturation test only 2 were saturated in less than 7 days. These figures were obtained in the month of April, 1943, in the fourth year of the war. Administration of 100 mgm. vitamin C per diem for a period of 4 weeks (2·8 gm. ascorbic acid) was sufficient to raise (*a*) the mean blood level to 0·52 mgm./100 ml., and (*b*) the degree of saturation to a mean of 2 days in a small group of 6 patients. Out of 18 patients who were saturated with vitamin C, 2 stated that they felt better, but in none of them was the effort syndrome removed by this treatment.

TABLE II.—*Vitamin C Excretion and Blood Levels.*

Group 1.—*Constitutional Type.*

No.	Blood vit. C (mgm./100 ml.).	Urinary vit. C excretion (mgm./day). Day 1.	Urinary vit. C excretion (mgm./day). Day 2.	Days to reach saturation.
1	0·29	18	11	—
2	0·24	8	7	—
3	0·20	11	13	—
4	0·28	14	9	—
5	0·28	31	22	—
6	0·37	28	31	>6
7	0·32	5	8	>6
8	0·30	10	11	>6
9	0·28	8	10	5
10	0·34	18	5	3
Mean	0·29	16	13	—

Group 2.—*Neurotic Type.*

11	0·27	16	18	>6
12	0·36	15	15	>6
13	0·35	—	24	>6
14	0·30	7	10	>6
15	0·27	12	7	>6
16	0·34	5	8	>6
17	0·32	14	17	>6
Mean	0·31	11	14	>6
Mean of both groups	0·30	14	13	

The urinary excretion figures were calculated from 3-hour samples.

DISCUSSION.

Recent work on Wernicke's syndrome has emphasized the relationship between vitamin deficiency and symptoms, such as lassitude, fatigue, dyspnoea on exertion and the cardio-vascular symptoms, which are prominent in effort syndrome.

In the present investigation the vitamin B_1 and C nutrition was assessed by several different methods in a group of army patients with effort syndrome. Standards vary a good deal as to what should be regarded as an optimal, adequate or deficient level of vitamin nutrition, and figures are given by certain American authors which are higher than those commonly obtaining in this country. In considering the vitamin C level it should be remembered that this shows a considerable seasonal variation, being lowest in spring, when the present investigation was carried out. This is due to the scarcity of green vegetables at this time of year

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and the disappearance of vitamin C from potatoes, which are one of the main sources of vitamin C in the war-time diet. The vitamin C nutrition of these patients was low by most standards, but it was not lower than we have found in other groups of patients and in normal subjects at the same time of year. A group of 30 senile male patients at the Tooting Bec Hospital gave a mean blood level of 0·30 mgm./100 ml., and a group of 348 factory workers a mean level of 0·25 mgm./100 ml. during the spring of 1943. Macbeth (1943) has pointed out that there has been a progressive falling off in the vitamin C nutrition in this country since the war, and his figures for 1943 for other types of patients agree with our own. It is therefore unlikely that the symptoms of the patients with effort syndrome could be attributed to vitamin C deficiency.

The onset of lassitude and fatigue in vitamin B_1 deficiency is observed at excretion levels of the order of 30 mgm./day or less (Williams, Mason and Smith, 1939; Williams and Mason, 1941), and the mean level of 142 μgm. found by us is similar to the figures of 146 μgm., 198 μgm. and 93 μgm./24 hours found for normal individuals by other investigators (Melnick, Field and Robinson, 1939; Najjar and Holt, 1940). These figures therefore give clear evidence that vitamin B_1 deficiency was not a significant factor in producing the fatigue and other symptoms observed in the patients with effort syndrome at the Mill Hill Emergency Hospital.

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References.

Guttmann, E., and Jones, M. S. (1940), *Brit. Med. J.*, ii, 736.
Harris, L. J. (1942), *Lancet*, i, 642.
Idem and Wang, Y. L. (1941), *Biochem. J.*, **35**, 1068.
Jolliffe, N., Goodhart, R., Gennis, J., and Cline, J. K. (1939), *Amer. J. Med. Sci.*, **198**, 198.
Jones, M. S., and Lewis, A. (1941), *Lancet*, i, 813.
Jones, M. S., and Scarisbrick, R. (1941), *Proc. R. Soc. Med.*, **34**, 549.
Idem (1942), *War Med.*, **2**, 901.
Idem (1943), *Lancet*, ii, 331.
Lewis, A. (1941), *Proc. R. Soc. Med.*, **34**, 533.
McAlpine, D., and Hills, G. M. (1941), *Quart. J. Med.*, **10**, 31.
Macbeth, R. G. (1943), *Proc. R. Soc. Med.*, **36**, 625.
Melnick, D., Field, H., and Robinson, W. D. (1939), *J. Nutrit.*, **18**, 593.
Najjar, V. A., and Holt, L. E. (1940), *Johns Hopk. Hosp. Bull.*, **67**, 107.
Richter, D., and Croft, P. G. (1943), *Lancet*, i, 802.
Idem (1944), *Biochem. J.*, in press.
Williams, R. D., and Mason, H. L. (1941), *Proc. Staff Meetings Mayo Clinic*, **16**, 433.
Idem and Smith, B. F. (1939), *ibid.*, **14**, 787.
Wood, P. (1941), *Brit. Med. J.*, i, 767, 805, 845.

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