7. Title: Study of Malabsorption. V. The Effect of Prophylactic Folic Acid in Preventing Tropical Malabsorption Syndromes.

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Objective This study was originally planned to answer this question: Will the administration of folic acid by mouth to normal Americans in Thailand prevent intestinal malabsorption as determined by clinical and biochemical means? This is no longer its objective (see below).

Description Details of the study plan may be found in the preceeding SMRL Annual Report. In brief, a group of 28 volunteers from a Special Forces Unit in Lopburi, Thailand were studied by history, physical examination and biochemical tests (outlined below). They were then randomly divided into two groups, one receiving 5 mgm folic acid by mouth daily, the other receiving one placebo tablet daily in double blind fashion. All subjects were restudied 8 months later in an identical way to the baseline study. During the eight months, their symptoms were noted by one of us, and cases of illness recorded. Baseline data are reported in the last SMRL Annual Report,

The diet of these men is largely American in type, and food stuffs (excluding fruits and vegetables) comes through the PX system. Thai food prepared in the Thai manner is consumed in very small quantities.

Progress At the time of restudy after being followed for 8 months, it was apparent that folic acid and placebo tablets were not taken regularly by many of the study subjects. Since the pills were taken so ~~irregularly~~ it became apparent that any changes in the ~~folic acid~~ treated individuals would be impossible to interpret, so the study was changed to include only those individuals on placebo. Therefore it became, essentially, a study of what happens in 8 months to 13 healthy American troops in Thailand as far as intestinal function is concerned.

The collection of data is now complete. It is summarized in Table 22. During the eight months period there was a significant decrease in xylose absorption and serum cholesterol and carotene concentration for the group as a whole. Lactose absorption for the group as a whole did not change, but those subjects who had the most pronounced fall in xylose absorptive capacity also had the most pronounced fall in lactose absorption. A fall in xylose absorptive capacity was associated with greater falls in serum cholesterol and β-carotene. It is interesting to note that the latter fell in every man. Serum total proteins were decreased in all but one subject, and in every case this fall was specifically due to serum albumin; globulin remained the same. Folic acid levels were generally low normal at both study periods. Anemia did not occur in any subject. There was no change in body weight in the group as a whole, nor could individual changes be correlated with biochemical abnormalities.

Intestinal biopsy specimens (jejunum) showed that over the eight month period, most individuals developed changes including non-specific abnormalities and/or acute inflammatory changes. Three subjects had non-specific abnormalities at the time baseline studies were performed. There was a poor correlation

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between mucosal histology changes and clinical findings. Mucosal disaccharidase assays (maltase, sucrase, lactase and cellobiase) were low compared to persons in North America, and lactase levels were most depressed. This result was the same by both methods of calculation, i.e. enzyme level per gram wet weight or level per gram protein. Disaccharidase assays at the time of initial study were performed at SMRL and are considered unreliable for technical reasons. The assays at the second study period were performed by Dr. Pearl Anderson at Walter Reed Army Institute of Research.

No subject complained of persistent diarrhea, abdominal cramps, steatorrhea, nor was there evidence on physical examination to suggest malabsorption. Frequency of intestinal symptoms did not correlate with biochemical abnormalities (double blind evaluation). Of interest is that two men from this military unit, not in the study group, have been shown to have tropical sprue by SMRL, and both had a brisk response in symptoms and xylose absorption following oral folic acid therapy.

The data described herein will be evaluated statistically and submitted for publication.

Summary In a group of 13 men known to have generally normal intestinal function on arrival in Thailand, distinct changes have occured in an eight month period. Some changes (serum albumin and β-carotene) are characteristic of all members of the group, while others (xylose and lactose absorption; serum cholesterol) seem to occur in some persons but not in others. These changes do not correlate with clinical symptoms or signs. At this time their significance is unknown, as is their cause. Changes in jejunal histology correspond to those seen in normal Thai people.

Table 22. Comparison of Baseline Studies (A) and Studies Eight Months Later (B) in Special Forces Troops in Thailand

Subjects	Body Weight (pounds)		D–Xylose (urine)* grams excretion		Lactose Tolerance Test** maximum rise blood glucose mgm % serum		Cholesterol mgm% serum		β–Carotene μg % serum		Folic Acid*** mμg % serum		Albumin gms %		Globulin gms %	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
1	146	145	6.0	6.0	48	56	235	215	167	85	1.9	8.30	4.7	4.1	2.7	2.9
2	162	164	5.0	1.7	22	8	190	152	133	21	3.3	2.50	4.3	3.7	2.6	2.9
3	170	167	9.2	8.1	19	2	243	199	154	106	3.8	6.56	4.5	4.2	2.6	2.8
4	162	160.5	8.0	3.8	38	10	246	181	198	96	2.1	28.75	4.2	3.8	2.6	1.9
5	161	164	7.4	7.3	2	47	255	266	233	227	2.9	5.12	4.2	4.1	2.5	2.5
6	107	107	3.2	5.0	34	58	116	137	68	46	1.7	3.87	4.1	3.9	2.5	2.6
7	153	147	8.1	5.8	26	8	261	199	239	135	4.1	1.00	4.4	3.8	2.8	2.7
8	141	152	11.8	8.2	16	14	200	184	212	119	1.4	7.50	4.4	3.9	3.0	2.8
9	175	179	6.7	7.3	23	39	182	176	133	60	2.1	2.48	4.5	3.8	2.7	2.7
10	149	143	8.9	4.5	46	28	200	144	137	62	5.9	2.64	4.3	3.8	2.8	2.4
11	174	181	10.1	7.5	88	55	271	247	236	98	3.3	3.28	4.5	4.1	2.9	3.0
12	172	176	4.9	4.7	35	59	166	156	130	99	2.6	—	3.9	4.0	2.9	2.8
13	132	123.5	7.7	3.6	27	2	176	129	147	60	3.9	2.80	4.3	3.9	2.8	3.0
Mean (and S.E.)	154.2	154.6	7.46 (2.33)	5.65 (2.00)	33 (21)	30 (23)	210 (49)	183 (39)	168 (51)	93 (51)	3.0	4.2****	4.3 (.2)	3.9 (.2)	2.7 (.2)	2.7 (.3)

* 25 gram oral dose D–Xylose

** 1.5 grams Lactose per Kg body weight

*** Normal range 1966: 3.1–14.1 mug%
Normal range 1967: 2.0–10.6 mug%
Performed by Dr. C.E. Butterworth; Birmingham, Alabama

**** Excluding value 28.75