

## CHAPTER IV

### DISCUSSION

It has been well established that folic acid is essential for the metabolic pathway of the normoblastic blood formation. Determination of serum folate levels could detect the sub-clinical cases of folic acid deficiency. However, the methods for assaying serum folate levels are quite complicated and time-consuming, therefore not so many institutions could establish their own laboratories for this study. It is, therefore, not surprising that no available data of the normal serum folate levels in Thais have been reported. The mean value of serum folate level which was found to be 9.32 ng./ml. from the present study was in the same order of magnitude as those results reported earlier in the other countries (see Table 3). The finding of no relationship between the serum folate levels and age or sex was in accordance with the result reported previously (Magnus, 1967).

The difficulty of defining a normal range is evident from the Table 3 and emphasizes the necessity of each laboratory to assay a normal series before attempting any serious interpretations of a hospital patients series. As a generalization, healthy subjects have a lower level in

excess of 3 ng./ml. and reasonably nourished patients requiring hospitalization have lower levels in excess of 2 ng./ml.

Folic acid absorption was also studied in 12 normal subjects. Mean value of  $49.96 \pm 7.0$  % (range 37.8 - 61.2 %) was found in these subjects. These values were in accordance with data reported earlier by Anderson et al., (1960). They showed that 31 - 43 % (mean 41 %) of the radioactivity was carried into the urine with 2 mg. oral dose and between 28 and 65 % (mean 42 %) with 200  $\mu$ g. dose.

Low serum folate levels with normal folic acid absorption were found in patients with P. falciparum malaria. This result was very similar to the data of Strickland and Kostinas (1970) who found reduced serum folic acid in their patients with P. falciparum malaria. Since the absorption of folic acid in these patients was normal, it should exclude the possibility of the impaired absorption. The cause of the low serum folate level was most likely multiple i.e., inadequate dietary folate, increased utilization of folic acid owing to the haemolysis and fever of malaria and drug inhibition by the antimalaria chemotherapy (Strickland and Kostinas, 1970). It has been shown that haemolysis and fever could cause an increased utilization of folic acid (Lindenbaum and Klipstein, 1963 ; Chanarin et al., 1959). Malaria produced both fever and haemolysis which in turn may

increase utilization of this vitamin. Pyrimethamine, a dihydrofolic acid reductase inhibitor, may cause megaloblastosis in human bone marrow (Myatt et al., 1953 ; Waxman and Herbert, 1969). It was therefore highly probable that these factors may be responsible for the low levels in these patients.

Folic acid absorption was studied in 13 patients with hookworm infection with a mean value  $\pm$  one standard deviation of  $34.9 \pm 18.4$  %. Six out of these 13 patients showed impaired absorption of this vitamin. This result was similar to the results obtained by Layrisse et al. (1959, 1964) who found definite impairment of folic acid absorption in the majority of the 34 patients they studied. Serum folate levels in 5 patients with hookworm infection were found to be  $6.5 \pm 2.8$  ng./ml. (range 2.65 - 9.25 ng./ml.) which was in the normal limit ( $P > 0.05$ ). Low serum folate level has also been observed in heavily infected subjects by Layrisse et al. (1964). The reduction in the serum folate level and the low absorption of some patients could be due to either dietary deficiency or to impairment of absorption or to both. Since hookworm patients are usually agricultural workers, their diet should prevent folic acid deficiency for it contains a large number of vegetables. It was therefore highly probable that the cause of low serum folate level was due to the impaired absorption.

Changes in the duodenal appearance characteristic of ulcer in hookworm patients have been reported previously (Yenikomshian and Shehadi, 1943 ; Krause and Crilly, 1943). The functional and anatomical changes in the mucosa of the intestine may be responsible for the low absorption of folic acid in these patients.

In the present experiments, 5 out of 10 patients with opisthorchis infection showed low absorption of folic acid when compared with 12 control subjects. There was no correlation between the absorption and the number of eggs in the stool, haemoglobin or liver function tests. The reduced intestinal absorption of this vitamin in these patients might be explained in terms of morphological or functional changes in the mucosal membrane of the intestine or in terms of both. As previously mentioned, it is quite common for opisthorchiasis patients to complain of **diarrhea and loose stools** (Harinasuta and Vajrasthira, 1960). Functional changes in the intestine may be responsible for the impaired absorption of folic acid in some of these patients. A study of upper gastro-intestinal tract by X-ray examinations and an autopsy in three cases of retention cysts in the liver due to chronic opisthorchis infection, revealed normal findings in the intestinal tract (Ujjin, 1961). Another report of the autopsy finding on the intestine in the fourth case of retention cysts caused by opisthorchiasis association with

carcinoma of liver, also showed nothing remarkable (Viranuvatti et al., 1961). However, morphological changes in the intestinal mucosal membrane could not be totally excluded. The further indication of the state of intestinal absorption might have been obtained from serum folic acid concentration in these patients. Three patients with opisthorchiasis infection in the present studies showed slightly low serum folate level. These findings probably indicated that the impaired absorption of folic acid was responsible for the low serum folate level in these patients.