

This Week's Citation Classic®

Chanarin I, Anderson B B & Mollin D L. The absorption of folic acid.
Brit. J. Haematol. 4:156-66, 1958.

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The increase in serum folic acid after an oral dose was used as a test of intestinal folate absorption: impaired absorption was present in the majority of patients with gluten-sensitive enteropathy and in untreated, but not in treated, tropical sprue. An altered pattern of absorption was present in normal pregnancy and in achlorhydric patients. [The SCI® indicates that this paper has been cited in over 195 publications.]

the Postgraduate School. Gluten-sensitive enteropathy (termed idiopathic steatorrhea) was the commonest disorder we saw giving rise to folate-deficient megaloblastic anaemia. The assumption was that such patients had impaired folate absorption.

Girdwood had introduced a urinary excretion test as a measure of folate absorption, and the results of this test were abnormal in idiopathic steatorrhea.¹ Others had noted the rise in plasma folate after an oral dose.²

In the test we introduced, we simply measured the serum folate level by microbiological assay before and after 3 mg folic acid by mouth. Subsequently, we gave 40 µg folate/kg. It was, however, applied in a systematic way to controls and to well-investigated groups of patients and established clearly the pattern of abnormal folate absorption in coeliac disease, the occasional malabsorption after partial gastrectomy and in tropical sprue. Subsequently, we showed that, following a gluten-free diet in coeliac disease, folate absorption became normal.

Reproducible results in the absorption test depended entirely on pretreating the patient first with folic acid to overcome any folate deficiency. This, in turn, standardized the rate at which the absorbed folic acid left the plasma to the tissues.

One of the reasons why the study has been cited is that it involved a clear statement that impaired folate absorption was the cause of a folate deficiency state and of megaloblastic anaemia. It led to other studies on the mechanism of absorption of physiological folate analogues³ as well as to more sophisticated methods of assessment of folate absorption.⁴

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April 23, 1986

I was a member of Sir John Dacie's department at the Postgraduate Medical School in London between 1955 and 1960. Although this may be difficult to believe, there were at that time haematologists who had interests outside the treatment of leukaemia. David Mollin headed a small group in the department who were concerned with the investigation of patients with megaloblastic anaemia. My own interest lay in folic acid, deficiency of which also caused megaloblastic anaemia.

At the same time, gastroenterology was developing as a specialty. The Crosby capsule had just been introduced and there was an enthusiastic group concerned with small-gut diseases at

1. Girdwood R H. A folic-acid excretion test in the investigation of intestinal malabsorption. *Lancet* 2:53-60, 1953. (Cited 125 times since 1955.)
2. Clark S L, Jr. Oral folic acid tolerance test in normal subjects and patients with pernicious anaemia. *Proc. Soc. Exp. Biol. Med.* 82:25-8, 1953. (Cited 20 times since 1955.)
3. Chanarin I & Perry J. Evidence for reduction and methylation of folate in the intestine during normal absorption. *Lancet* 2:776-8, 1969. (Cited 45 times.)
4. Halsted C H. Intestinal absorption and malabsorption of folates. *Annu. Rev. Med.* 31:79-87, 1980.