Comment

THE STOMACH IN IRON-DEFICIENCY ANAEMIA

We would like to comment on the interesting papers by Desai, Mehta, Borkar, and Jeejeebhoy (1968) and by Stone (1968) which study gastric acid secretion in iron-deficiency anaemia. In the paper by Desai *et al* there was no rise in acid secretion 72 hours after an infusion of iron, although the authors state that in patients under the age of 30, and in those patients with an acid output between 5 and 15 m-equiv/hr there was some increase but this did not reach significant levels. Of six patients retested six to eight weeks later, three showed a significant rise in acid output. In the paper by Stone (1968) nine out of 21 patients showed an increase in acid secretion on retesting at five to seven months. The findings in these papers confirm and extend previous work on the subject (Delamore and Shearman, 1965; Shearman, Delamore, and Gardner, 1966; Jacobs, Lawrie, Entwistle, and Campbell, 1966). However, the conclusions reached in the two papers are open to other interpretations.

One of the more constant findings in the many studies on iron-deficient patients is the irreversibility of the gastric mucosal lesion. Thus the increased acid secretion in some patients must be due to an improved secretory performance by the remaining parietal cells, and the mechanism for this may be repletion of iron-containing enzyme systems (Delamore and Shearman, 1965). The depletion of these systems has not been demonstrated in human gastric mucosa but it undoubtedly occurs in the severely iron-deficient rat (Shearman, Floch, Herskovic, Levine, and Spiro, 1967). In the paper by Desai *et al* (1968), the absence of acid increase at 72 hours is in itself no evidence for the failure of enzyme repletion. The authors fail to point out that repletion is likely to depend upon the replacement of parietal cells, the turnover of which is thought to be extremely slow (Lipkin, Sherlock,

and Bell, 1963; MacDonald, Trier, and Everett, 1964). It is of importance that repletion of cytochromes in the intestinal mucosa of iron-deficient rats (Dallman and Schwartz, 1965) and children (Dallman, Sunshine, and Leonard, 1967) depends on cell renewal. On the other hand, improvement in acid secretion at a later time obscures the answer to whether the anaemia or the iron deficiency was the operative factor. In this respect the effects of other forms of anaemia on acid secretion may be important. Table I illustrates the gastric secretory findings on two patients who had anaemia and were deficient in folic acid.

PATIENT 1 Male aged 59 at the time of diagnosis. For many years his epilepsy was treated with phenobarbitone 30 mg, tid, and phenytoin 100 mg, tid; Hb was 4.6 g% and MCHC 32%. Marrow was megaloblastic with abundant iron and serum vitamin B₁₂ was at the lower limit of normal for our laboratory. Schilling test showed 13% recovery in 24 hours. Serum folate was 1.9 mμg/ml (normal 4.5 to 18.0 mμg/ml). There was a full haematological response to folic acid. The improvement in acid and intrinsic factor output is shown in Table I. Anti-convulsant treatment has continued.

PATIENT 2 Male aged 43 at the time of diagnosis of sideroblastic anaemia. Hb was 6.3 g%. Serum folate was 2.8 mμg/ml. He was treated with folic acid and pyridoxine and Hb at the time of the second gastric function test was 10.6 g%.

In both patients improvement in acid secretion has occurred after correction of the anaemia, and in case 1 there has been an increased pepsin and intrinsic factor output. In addition, apart from these anaemic states, other patients may show recovery in acid secretion, for example, after treatment in thyrotoxicosis (Bock and Witts, 1963) and tropical sprue (Vaish, Sampathkumar, Jacob, and Baker, 1965) and also the apparently normal patient (Weir, 1967). Thus it is possible that many factors are involved in any one case.

The paper by Stone (1968) again encounters the main

TABLE I
GASTRIC FUNCTION TESTS ON TWO PATIENTS WITH ANAEMIA AND FOLIC ACID DEFICIENCY

	Patient 1				Patient 2		
	Before Treatment	After Treatment			Before Treatment	After Treatment	
Date	15.12.65	31.1.67	7.11.67	5.4.68	16.11.67	3.4.68	
Stimulant	Histamine 0.04 mg/kg	Histamine 0.04 mg/kg	Pentagastrin 6 μg/kg	Histamine 0.04 mg/kg	Pentagastrin 6 μg/kg	Pentagastrin 6 μg/kg	
Volume in post-histamine or post-gastrin hour (ml)	40	42	74	72	308	422	
Minimum pH in any 10-minute sample	5.7	3.0	1.1	1.3	1.1	1.7	
Total acid ¹ (m-equiv)	0.09	0.5	3.6	2.7	19.4	31.6	
Maximum concentration (m-equiv/l)	5	28	88	48	76	92	
Total intrinsic factor in post-histamine or post-gastrin hour (ng) ²	Not done	2,279	Not done	9,655	38,201	29,866	
Total pepsin in post-histamine or post-gastrin hour (mg) ³	Not done	3.0	Not done	16.3	Not done	Not done	

¹Titration to pH 7

²By the method of Ardeman and Chanarin (1963).

³By the method of Hunt (1948) as modified by Bitsch (1966).

difficulty that has arisen in many previous communications, namely, the definition of 'idiopathic' because in retrospect it is impossible to assess menstrual loss or dietary deficiency of iron. Many patients who are classified as having primary achlorhydria (Delamore and Shearman, 1965) may have had blood loss, *eg*, menstruation, or may develop a source of blood loss as a secondary factor. Nevertheless, the study of many differing groups of patients by several groups of workers (Coghill, 1960; Shearman *et al*, 1966; Wright, Whitehead, Wangel, Salem, and Schiller, 1966; Cowan, Joseph, and Satija, 1966) lends support to the idea that gastritis may cause the iron deficiency in some cases. Such difficulties in classification make family studies important and these tend to associate pernicious anaemia with idiopathic iron-deficiency anaemia. (MacLachlan and Kline, 1926; Heath, 1933; McFadyen, Goldberg, Dagg, and Anderson, 1967; Wangel, Callender, Spray, and Wright, 1968). It should be noted that iron is less well absorbed in achlorhydria (Goldberg, Lochhead, and Dagg, 1963) as is reflected in the iron deficiency that can accompany pernicious anaemia (Gibson, Kelly, and Wang, 1963).

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REFERENCES

- Ardeman, S., and Chanarin, I. (1963). A method for the assay of human gastric intrinsic factor and for the detection and titration of antibodies against intrinsic factor. *Lancet*, 2, 1350-1354.
- Bitsch, V. (1966). A modification of the Hunt method for estimating peptic activity in gastric juice. *Scand. J. clin. Lab. Invest.*, 18, 357-358.
- Bock, O. A. A., and Witts, L. J. (1963). Gastric acidity and gastric biopsy in thyrotoxicosis. *Brit. med. J.*, 2, 20-24.
- Coghill, N. F. (1960). The significance of gastritis. *Postgrad. med. J.*, 36, 733-742.
- Cowan, B., Joseph, S., and Satija, V. K. (1966). The gastric mucosa in anaemia in Punjabis. *Gut*, 7, 234-243.
- Dallman, P. R., and Schwartz, H. C. (1965). Myoglobin and cytochrome response during repair of iron deficiency in the rat. *J. clin. Invest.*, 44, 1631-1638.
- , Sunshine, P., and Leonard, Y. (1967). Intestinal cytochrome response with repair of iron deficiency. *Pediatrics*, 39, 863-871.
- Delamore, I. W., and Shearman, D. J. C. (1965). Chronic iron deficiency anaemia and atrophic gastritis. *Lancet*, 1, 889-891.
- Desai, H. G., Mehta, B. C., Borkar, A. V., and Jeejeebhoy, K. N. (1968). Effect of intravenous iron therapy on gastric acid secretion in iron-deficiency anaemia. *Gut*, 9, 91-95.
- Gibson, I. I. J., Kelly, A. M., and Wang, I. (1963). The iron deficiency of pernicious anaemia. *Scot. med. J.*, 8, 357-364.
- Goldberg, A., Lochhead, A. C., and Dagg, J. H. (1963). Histamine-fast achlorhydria and iron absorption. *Lancet*, 1, 848-850.
- Heath, C. W. (1933). The interrelation of pernicious anemia and idiopathic hypochromic anemia. *Amer. J. med. Sci.*, 185, 365-381.
- Hunt, J. N. (1948). A method for estimating peptic activity in gastric contents. *Biochem. J.*, 42, 104-109.
- Jacobs, A., Lawrie, J. H., Entwistle, C. C., and Campbell, H. (1966). Gastric acid secretion in chronic iron-deficiency anaemia. *Lancet*, 2, 190-192.
- Lipkin, M., Sherlock, P., and Bell, B. (1963). Cell proliferation kinetics in the gastrointestinal tract of man. II. Cell renewal in stomach, ileum, colon, and rectum. *Gastroenterology*, 45, 721-729.
- MacDonald, W. C., Trier, J. S., and Everett, N. B. (1964). Cell proliferation and migration in the stomach, duodenum, and rectum of man: radio-autographic studies. *Ibid.*, 46, 405-417.
- McFadyen, I. J., Goldberg, A., Dagg, J. H., and Anderson, J. R. (1967). Incidence of gastric parietal cell antibody in families of patients with iron deficiency anaemia. *Clin. exp. Immunol.*, 2, 737-741.
- MacLachlan, W. W. G., and Kline, F. M. (1926). The occurrence of anemia in four generations. *Amer. J. med. Sci.*, 172, 533-543.
- Shearman, D. J. C., Delamore, I. W., and Gardner, D. L. (1966). Gastric function and structure in iron deficiency. *Lancet*, 1, 845-848.
- , Floch, M. H., Herskovic, T., Levine, R. J., and Spiro, H. M. (1967). Alimentary tract lesions in rats born of iron deficient mothers. *Clin. Res.*, 15, 243.
- Stone, W. D. (1968). Gastric secretory response to iron therapy. *Gut*, 9, 99-105.
- Vaish, S. K., Sampathkumar, J., Jacob, R., and Baker, S. J. (1965). The stomach in tropical sprue. *Ibid.*, 6, 458-465.
- Wangel, A. G., Callender, S. T., Spray, G. H., and Wright, R. (1968). A family study of pernicious anaemia. I. Autoantibodies, achlorhydria, serum pepsinogen and vitamin B₁₂. *Brit. J. Haemat.*, 14, 161-181.
- Weir, D. G. (1967). Spontaneous recovery of gastric secretion. *Brit. med. J.*, 2, 681.
- Wright, R., Whitehead, R., Wangel, A. G., Salem, S. N., and Schiller, K. F. R. (1966). Autoantibodies and microscopic appearance of gastric mucosa. *Lancet*, 1, 618-621.