

# Gastric intrinsic factor secretion after partial gastrectomy

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**EDITORIAL SYNOPSIS** The concentration of intrinsic factor in the gastric juice of patients who have had a partial gastrectomy and are deficient in vitamin B<sub>12</sub> is similar to that found in patients with Addisonian pernicious anaemia.

About 30% of patients after partial gastric resection have an impaired absorption of vitamin B<sub>12</sub> (Lous and Schwartz, 1959) and about 6% develop a megaloblastic anaemia due to vitamin B<sub>12</sub> deficiency (Deller and Witts, 1962). Malabsorption of vitamin B<sub>12</sub> after gastrectomy is usually due to loss of intrinsic factor secretion following both resection of secreting tissue at surgery and atrophy of the gastric remnant.

In Addisonian pernicious anaemia failure of vitamin B<sub>12</sub> absorption can be correlated with the loss of intrinsic factor secretion from the gastric juice as estimated by direct assay of secretion collected over one hour (Ardeman and Chanarin, 1965). Unfortunately collection of gastric juice after partial gastrectomy is often incomplete and our own experience with a radioactive marker put in during the aspiration is that sometimes as little as 20% was recovered in the aspirate.

The purpose of this study was to determine whether the concentration of intrinsic factor in the gastric juice as opposed to the total output in an hour was a useful guide to the amount of intrinsic factor available and whether this could be correlated with the absorption of vitamin B<sub>12</sub>. This paper reports some of our results.

## MATERIALS AND METHODS

Observations were made on 16 patients who had undergone a Polya-type partial gastric resection for either a gastric or duodenal ulcer four to 22 years ago. All but two were studied because of anaemia which was megaloblastic usually with iron deficiency in 11 patients, and due only to iron deficiency in three. Details are shown in Table I. None of these patients had antibodies to intrinsic factor in their sera. In addition, the intrinsic factor

concentration in the gastric juice after an injection of histamine in 68 hospital patients and 42 patients with Addisonian pernicious anaemia is shown.

Gastric juice samples were obtained via a Ryle's tube either by continuous mechanical suction or by frequent aspiration by hand over a period of one hour before an injection of histamine and for one hour after a dose of 40 µg. of histamine per kilogram of body weight. The Ryle's tube was positioned under radiographic control. The assay of intrinsic factor was performed by the method of Ardeman and Chanarin (1963, 1965). One unit of intrinsic factor was that amount that bound 1.0 µmg. of <sup>57</sup>Co-vitamin B<sub>12</sub>.

The absorption of vitamin B<sub>12</sub> was assessed by the urinary excretion method using a 1.0 µg. oral dose of <sup>57</sup>Co-vitamin B<sub>12</sub> (Schilling, 1953).

## RESULTS

The concentration of intrinsic factor in the gastric juice in eight patients with vitamin B<sub>12</sub> deficiency after partial gastrectomy varied from 0 to 6 units per millilitre gastric juice. The absorption of vitamin B<sub>12</sub> was tested in seven of these patients and was impaired in all.

Three patients after partial gastrectomy had a megaloblastic anaemia which was thought to be due to folic-acid deficiency (cases 8, 9 and 10, Table).

**CASE 8** was a tramp on a very poor diet who had undergone a partial gastrectomy four years previously for a duodenal ulcer. The serum vitamin B<sub>12</sub> level was consistently within the normal range. The intrinsic factor concentration was reduced (6 units per ml.) and the urinary excretion of <sup>57</sup>Co-vitamin B<sub>12</sub> was 8%.

**CASE 9** too was thought to be taking an extremely poor diet. He had a normal intrinsic factor concentration and a normal vitamin B<sub>12</sub> absorption.

TABLE I

| Sex/<br>Age | Years<br>after<br>Gas-<br>trec-<br>tomy | Hb<br>(g./%) | P.C.V. | M.C.H.C. | LABORATORY FINDINGS IN PRESENT SERIES |               |                                  |                          |                       |                 |   |               |                             |   |               |                |                            |               |                |                       |      |                 |   |
|-------------|---|--------------|--------|----------|---------------------------------------|---------------|----------------------------------|--------------------------|-----------------------|-----------------|---|---------------|-----------------------------|---|---------------|----------------|----------------------------|---------------|----------------|-----------------------|------|-----------------|---|
|             |   |              |        |          | Marrow <sup>1</sup>                   |               |                                  |                          |                       | Serum           |   |               | Figlu <sup>2</sup><br>(mg.) | 57Co-B <sub>12</sub><br>Absorption<br>(% of dose) |               |                | Gastric Juice (60 minutes) |               |                |                       |      |                 |   |
|             |   |              |        |          | Before<br>Iron                        | After<br>Iron | B <sub>12</sub><br>(μg./<br>ml.) | Folate<br>(μmg./<br>ml.) | Iron<br>(μg./<br>ml.) | B <sub>12</sub> | B <sub>12</sub> with<br>Intrinsic<br>Factor | Vol.<br>(ml.) |                             | pH  | Units/<br>ml. | Total<br>Units | Post-histamine             |               |                |                       |      |                 |   |
|             |   |              |        |          |                                       |               |                                  |                          |                       |                 |   |               | Vol.                        |   |               |                | pH                         | Units/<br>ml. | Total<br>Units | Defi-<br>ciency<br>of |      |                 |   |
| 1           | F 61                                    | 7            | 11.4   | 37       | 31                                    | ?M            | M                                | 70                       | 5.0                   | 65              | 168   | 6.1           | 14.7                        | 36  | 7.2           | 4              | 140                        | 75            | 7.6            | 0                     | 0    | B <sub>12</sub> |   |
| 2           | M 69                                    | 15           | 11.4   | 35       | 32                                    | ?M            | M                                | 70                       | 7.0                   | 146             | —   | —             | —                           | 12  | 7.6           | 0              | 0                          | 11            | 7.6            | 0                     | 0    | B <sub>12</sub> |   |
| 3           | M 61                                    | 11           | 9.5    | 33       | 29                                    | M             | —                                | 60,                      | 5.5,                  | 14              | 17  | 1.7           | 19.0                        | 6   | 7.6           | 6              | 40                         | 11            | 7.4            | 0                     | 0    | B <sub>12</sub> |   |
| 4           | F 48                                    | 6            | 6.1    | 23       | 27                                    | N             | M                                | 130,                     | 6.0,                  | 23              | 18,   | 5.9           | 13.6                        | 13  | 6.9           | 5              | 70                         | 29            | 7.1            | 10                    | 290  | B <sub>12</sub> |   |
| 5           | F 65                                    | 19           | 8.2    | 30       | 27                                    | M             | M                                | 110,                     | 4.5                   | —               | 7   | —             | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
| 6           | F 28                                    | 8            | 5.0    | —        | —                                     | M             | —                                | 90,                      | 6.5,                  | 95              | 126,  | 5.6           | 19.9                        | 19  | 7.8           | 10             | 190                        | 20            | 7.9            | 2                     | 40   | B <sub>12</sub> |   |
| 7           | M 65                                    | 17           | 12.8   | 39       | 33                                    | M             | —                                | 60,                      | 7.0                   | —               | 44  | —             | —                           | —   | —             | —              | —                          | 8             | 7.2            | 6                     | 50   | B <sub>12</sub> |   |
| 8           | M 39                                    | 4            | 10.7   | 32       | 33                                    | M             | —                                | 75,                      | 18.0                  | —               | 10,   | 4.1           | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
| 9           | M 73                                    | 18           | 12.1   | 39       | 31                                    | M             | —                                | 15,                      | —                     | —               | 5   | —             | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
| 10          | F 53                                    | 15           | 11.6   | 36       | 32                                    | M             | —                                | 75,                      | 5.5,                  | 190             | 10,   | 1.4           | 12.6                        | 14  | 7.4           | 0              | 0                          | 10            | 8.5            | 3                     | 30   | B <sub>12</sub> |   |
| 11          | F 62                                    | 11           | 7.0    | 26       | 27                                    | N             | N                                | 85,                      | 7.0                   | —               | 7   | 8.0           | —                           | 52  | 7.2           | 5              | 260                        | 45            | 7.1            | 6                     | 270  | Folate          |   |
| 12          | F 68                                    | 7            | 7.8    | 30       | 26                                    | N             | N                                | 230,                     | 12.0                  | 12              | 7   | —             | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
| 13          | F 34                                    | 5            | 9.2    | 32       | 28                                    | N             | N                                | 220,                     | 12.0                  | 12              | 7   | —             | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
| 14          | F 67                                    | 5            | 13.5   | —        | —                                     | N             | —                                | 180,                     | 6.3,                  | 18              | 0,  | 14.3          | —                           | 15  | 7.0           | 0              | 0                          | 20            | 7.0            | 10                    | 300  | Iron            |   |
| 15          | M 74                                    | 22           | 14.5   | 44       | 33                                    | —             | —                                | 160,                     | 7.0                   | —               | 5   | —             | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
| 16          | M 68                                    | 11           | 9.7    | —        | —                                     | N             | —                                | 265,                     | 3.5                   | 32              | 3,  | 14.4          | 13.9                        | 17  | 7.0           | 34             | 580                        | 12            | 5.1            | 33                    | 400  | Iron            |   |
|             |   |              |        |          |                                       |               |                                  | 310                      | —                     | —               | 7   | —             | —                           | —   | —             | —              | —                          | —             | —              | —                     | —    | —               | — |
|             |   |              |        |          |                                       |               |                                  | 280                      | —                     | —               | 7   | 12.5          | —                           | 4   | 7.5           | 5              | 20                         | 5             | 5.5            | 40                    | 200  | —               | — |
|             |   |              |        |          |                                       |               |                                  | 625                      | 11.0                  | —               | —   | —             | —                           | 31  | 4.3           | 20             | 620                        | 49            | 2.0            | 33                    | 1620 | —               | — |
|             |   |              |        |          |                                       |               |                                  | 25                       | 12.0                  | —               | 51  | 0.5           | 17.5                        | 10  | 7.4           | 0              | 0                          | 30            | 7.0            | 2                     | 60   | B <sub>12</sub> | — |

<sup>1</sup>M = megaloblastic; N = normoblastic<sup>2</sup>After 15 g. of histidine-mono-hydrochloride

CASE 10 was an alcoholic. Although the concentration of intrinsic factor was low we were unable to check the position of the tube radiographically. The absorption of vitamin B<sub>12</sub> was normal and was not altered significantly by repeating the test with additional intrinsic factor.

The remaining five patients (cases 11, 12, 13, 14, and 15) had intrinsic factor concentrations which ranged from 10 to 46 units per ml. All absorbed vitamin B<sub>12</sub> normally. The concentration of intrinsic factor in the post-gastrectomy group (Fig. 1) was generally in the range found in Addisonian pernicious anaemia in those patients with impaired vitamin B<sub>12</sub> absorption and in the normal range in those who were able to absorb vitamin B<sub>12</sub>. A comparison of the concentration of intrinsic factor with the results of the vitamin B<sub>12</sub> absorption test is shown in Figure 2.

## COMMENT

There appeared to be a good correlation between the concentration of intrinsic factor in the gastric juice after partial gastrectomy and the results of the vitamin B<sub>12</sub> absorption test. Malabsorption of vitamin B<sub>12</sub> was found in all but one of the patients with an intrinsic factor concentration of less than 6 units

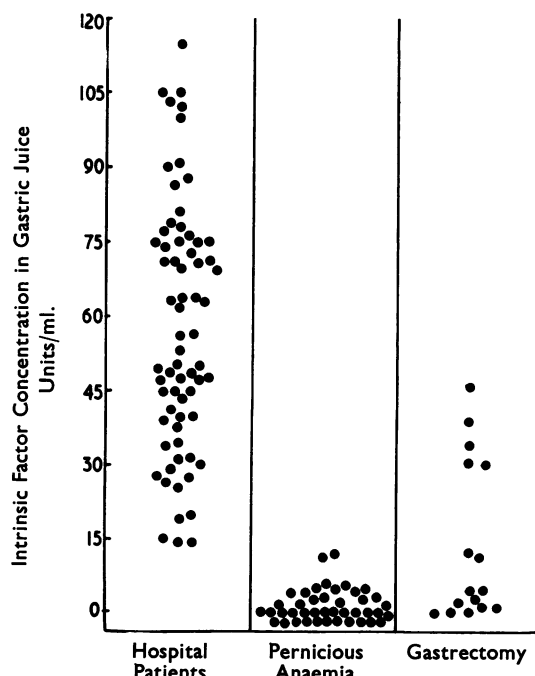


FIG. 1. The concentration of intrinsic factor in the gastric juice in 68 patients with normal serum vitamin B<sub>12</sub> levels.

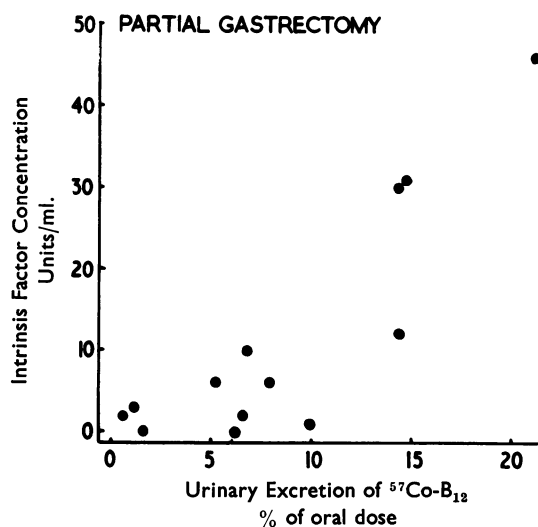


FIG. 2. A comparison of the concentration of intrinsic factor in the gastric juice after partial gastrectomy with the results of the urinary excretion of vitamin B<sub>12</sub> as a test of vitamin B<sub>12</sub> absorption.

per ml. gastric juice. The one exception was a patient with a low intrinsic factor concentration and normal vitamin B<sub>12</sub> absorption and this was probably due to incorrect positioning of the Ryle's tube.

The concentration of intrinsic factor in the patients deficient in vitamin B<sub>12</sub> after partial gastrectomy was similar to that found in Addisonian pernicious anaemia where the highest intrinsic factor concentration we have found was 13 units per ml. of gastric juice and all but two patients had concentrations of less than 7 units per ml. We have been unable to confirm our earlier report of an intrinsic factor concentration of 28 units per ml. in one patient with proven Addisonian pernicious anaemia (Ardeman and Chanarin, 1965). The intrinsic factor concentration in 68 hospital patients with normal vitamin B<sub>12</sub> status ranged from 14 to 114 units per ml.

Direct assay of the intrinsic factor concentration after partial gastrectomy therefore should prove of value in determining the nature of the deficiency in

these patients. Although about 30% of patients will have low serum vitamin B<sub>12</sub> levels six years after partial gastrectomy (Deller and Witts, 1962), this can be the result not only of vitamin B<sub>12</sub> deficiency but also of iron deficiency (Cox, Meynell, Gaddie, and Cooke, 1959) and of folic-acid deficiency (cases 9 and 10). In the last two groups of patients the vitamin B<sub>12</sub> level will return to within the normal range on treatment with iron or with folic acid alone unless a true vitamin B<sub>12</sub> deficiency is also present. Thus estimation of the serum vitamin B<sub>12</sub> level, especially if the level is greater than 80 μg. per ml., is inadequate evidence upon which to base a diagnosis of vitamin B<sub>12</sub> deficiency. Corroborative evidence, such as impaired absorption of vitamin B<sub>12</sub> is required, and the data presented in this paper suggest that a low concentration of intrinsic factor in the gastric juice may also provide helpful information.

#### SUMMARY

The concentration of intrinsic factor in the gastric juice was measured in 16 patients after partial gastrectomy. Patients with a concentration of less than 6 units of intrinsic factor per millilitre of gastric juice generally had impaired absorption of vitamin B<sub>12</sub>. The only exception was thought to be due to incorrect positioning of the Ryle's tube.

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