The Effect of Antigastric Mucosal Antibodies on Iron Absorption in Experimental Achylia Gastrica (34413)

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We have observed that antibody to rat gastric mucosa depressed absorption of ^{59}Fe by normal and iron deficient rats (1). We had investigated this phenomenon because certain individuals with complete achlorhydria and iron-deficiency anemia had circulating antibodies to parietal cells in their sera (2, 3). We wondered if these antibodies had any influence on iron absorption. Our previous experimental animals showing depression of iron absorption by antibody had normal gastric secretions and did not approximate the human situation of achylia gastrica. Accordingly, we devised a method of producing gastric atrophy in rats (4) and studied the effect of antigastric mucosal antibodies (AGMS) on their absorption of ^{59}Fe.

Materials and Methods. Achylia gastrica was produced in mature female Sprague-Dawley rats by exposing the mobilized stomach to 1750 rads of X-irradiation (4). Antigastric mucosal antibody (AGMS) was prepared in New Zealand white rabbits by injecting them with an extract of rat gastric mucosa (1). Iron-deficient rats were prepared by feeding young rats a low iron diet consisting of evaporated milk supplemented with copper (1). Normal control animals were sham operated by opening the abdomen, mobilizing the stomach and exposing it to the air, but not to X-irradiation for 10 min. Normal rat gastric juice was obtained from normal rats by the 4-hr Shay procedure (5) and kept frozen until used. The following animals were prepared: 14 sham-operated normals, 20 iron-deficient and anemic, 20 with achylia gastrica, used not less than 3 weeks after irradiation and with gastric juice pH values not less than 7.5.

After initial hemoglobin determinations, the percentage absorption of 0.25 μC of ^{59}Fe as ferrous citrate without carrier, but with the test material, was determined in all rats. This was done by total body counting 10 days after dosing in an Armac Packard scintillation counter (6). The ^{59}Fe and test material were given intragastrically as follows: Group 1. 14 normal, sham-operated rats received ^{59}Fe in 1.0 ml of distilled water. Group 2. 10 iron-deficient rats were dosed with ^{59}Fe with 0.5 ml of AGMS. Group 3. 10 iron-deficient rats received ^{59}Fe with 0.5 ml of normal rabbit serum (*i.e.*, containing no antibody). Group 4. 10 rats with achylia gastrica were given ^{59}Fe with 0.5 ml of AGMS. Group 5. 10 rats with achylia were given ^{59}Fe with 0.5 ml AGMS and 1.0 ml normal rat gastric juice.

After the study the rats were killed and the livers were removed for analysis of nonheme iron as a measure of iron stores (7).

Results. All results as means $\pm$ 1 SE are recorded in Table I, while Fig. 1 records the absorption of ^{59}Fe in the groups as a histogram. It is clear that profound depression of iron absorption occurs when animals with achylia gastrica receive their ^{59}Fe with AGMS. This effect however is offset by the concurrent administration of gastric juice with the ^{59}Fe and AGMS. Much less depression of absorption (but still significant) occurs when ^{59}Fe and AGMS are given to iron-deficient animals with normal stomachs.

Discussion. Previously we reported some depression of ^{59}Fe absorption when AGMS was given with the isotope in normal and anemic animals (1). The present study revealed the profound depression of absorption of ^{59}Fe when the AGMS is given in an animal with achylia gastrica. This is all the more revealing as these animals had a degree of iron deficiency as shown by their liver non-

TABLE I.

Groups	No.	Hb (g/100 ml)	Gastric pH	^{59}Fe absorbed (%)	Non-heme liver iron (μg/g)
1. ^{59}Fe in H_2O; normal rats (sham operated)	14	14.3 (0.09)[a]	2.4 (0.1)	5.16 (1.2)	391.7 (35.8)
2. ^{59}Fe in AGMS; iron-deficient rats	10	10.4 (0.69)	2.3 (0.3)	59.04 (4.7)	149.7 (11.67)
3. ^{59}Fe in rabbit serum; iron-deficient rats	10	10.12 (0.54)	2.27 (0.7)	75.12 (5.3)	166.6 (14.84)
4. ^{59}Fe in AGMS; rats with gastric atrophy	10	12.3 (0.17)	7.68 (0.12)	2.06 (0.43)	134.6 (18.2)
5. ^{59}Fe in AGMS & rat gastric juice; rats with gastric atrophy	10	12.6 (0.3)	7.5 (0.09)	42.0 (3.56)	169.4 (11.13)

[a] ($\pm$ 1 SEM).

heme iron levels, calculated to raise their absorption substantially. This absorptive defect was overcome, however, by the addition of normal gastric juice to the test dose. It appears then that antibody is more effective in depressing iron absorption in the absence of gastric secretion. The sequence of events might be as follows: The ^{59}Fe becomes attached to a large antibody–antigen complex which results when AGMS enters the stomach. In a normal stomach most of the complexes are degraded by gastric secretion releasing ^{59}Fe for absorption. In animals with achylia gastrica, however, degradation of the complexes is incomplete so that the ^{59}Fe is held in a form not easily absorbed. If the ^{59}Fe is added to non-immune rabbit serum, absorption is not decreased suggesting no unusual complexing. Finally, the addition of gastric juice to the ^{59}Fe antibody–antigen complex appears to release the ^{59}Fe for easy absorption.

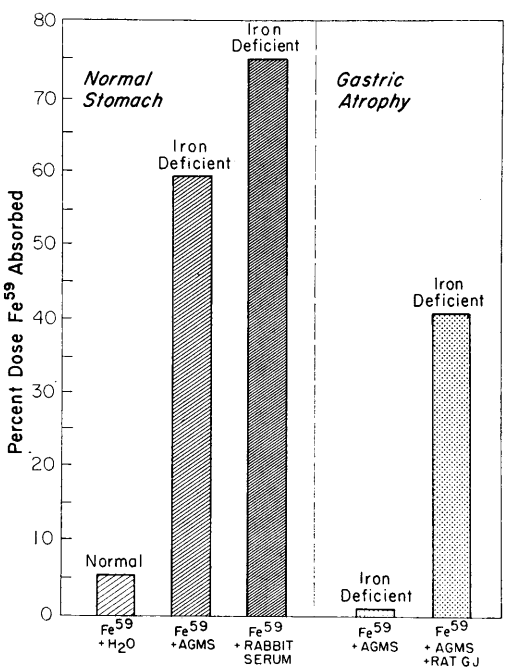

FIG. 1. Histogram of ^{59}Fe absorption.

Extrapolating these observations to the human situation, we could postulate that patients with gastric atrophy and circulating antibodies to parietal cells might find it difficult to assimilate iron from the diet because of this mechanism rather than because of reduction in gastric acid or peptic activity. In patients with pernicious anemia (the human counterpart of rats with achylia gastrica), Cook *et al.* (8) observed reduced absorption of ^{59}Fe from food. This could be corrected by giving gastric juice with the dose and partially corrected by giving neutralized gastric juice. These observations are similar to our own in rats and suggest the possibility that the mechanism we have described may play a part in pernicious anemia and other types of gastric atrophy.

Summary. Absorption of ^{59}Fe given with antibody to gastric mucosa, was studied in rats with and without induced gastric atro-

phy. Whereas mild but significant depression of absorption occurred in rats without gastric atrophy, profound depression occurred in rats with gastric atrophy. This reduction in absorption could be largely corrected by concurrent administration of normal gastric juice.

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