which serves to illustrate the biochemical lesions or changes, is of considerable importance, for these are bound to precede clinical signs of malnutrition. As these tests become more applicable in the field, they may eventually assist in the prevention of protein-calorie malnutrition in pre-school children.

**GASTRIC FUNCTION AND STRUCTURE IN IRON DEFICIENCY**

Investigation of gastric function and structure in a group of patients with iron deficiency anemia has led to the suggestion of an auto-immune basis for some cases of iron deficiency anemia.

Achlorhydria or hypochlorhydria, gastritis, and gastric atrophy have long been known to be associated in many patients with chronic iron deficiency anemia. In a recent communication, D. J. C. Shearman, I. W. Delamore, and D. L. Gardner (Lancet 1, 845 (1966)) have investigated the relationship between iron deficiency and the structure and function of the gastric mucosa, as well as the relationship of the gastric changes to disorders of immune tolerance to gastric mucosa.

Seventeen patients with moderate to severe iron deficiency anemia were studied. The diagnosis was based on complete blood counts and examinations of stained films of peripheral blood and, in most patients, by the demonstration of a low serum iron and the absence of stainable iron in the bone marrow. In each patient, gastric acid secretion was measured after histamine stimulation. Whenever possible, a biopsy specimen of mucosa from the body of the stomach was taken with a Crosby capsule. Serum vitamin B12 levels and vitamin B12 absorption tests were carried out when possible, and each patient was tested for parietal cell antibodies by an indirect fluorescent antibody technique and for antibodies to intrinsic factor.

In this group of 17 patients, eight demonstrated complete achlorhydria even after histamine stimulation, and in the nine other patients secretion of hydrochloric acid was significantly depressed. After treatment with oral iron therapy and correction of the anemia (hemoglobin levels in excess of 12.5 g. per 100 ml. of blood) augmented histamine secretion tests were repeated. In the majority of patients in whom some acid was originally present in the stomach there was an increase in acid production after iron therapy. The achlorhydric patients showed no such rise.

Antibodies to gastric parietal cells were demonstrated in the sera of seven of the eight achlorhydric patients, but in none of those who secreted acid. None of the patients exhibited antibodies to intrinsic factor, but three of the achlorhydric patients had an abnormal Schilling test, which was corrected by intrinsic factor. Two patients had low concentrations of vitamin B12 in the serum.

Gastric biopsy was carried out before treatment in 11 patients. In all achlorhydric patients subjected to gastric biopsy parietal cells were absent, and chronic atrophic gastritis was demonstrated. In the five patients subjected to gastric biopsy in whom gastric acid was present, one showed a normal gastric mucosa and four showed varying degrees of chronic gastritis with some preservation of chief and parietal cells.

In an attempt to determine whether correction of the chronic anemia or replenishment of the body’s iron supply was of primary importance in producing the increase in acid secretion seen in the treated hypochlorhydric individuals, two patients with some degree of acid secretion in response to histamine were selected. One was trans-
fused with seven units of packed red blood cells over a period of 48 hours and the histamine infusion test repeated a few days later. The other was given 0.85 g. of saccharated iron oxide intravenously over a period of five days, and histamine infusion tests repeated on the fifth day. In neither patient was a significant increase in acid production noted. However, six months after this experiment, when both patients had normal hemoglobin levels, both had significantly increased acid production in response to histamine.

The authors suggest the recognition of two distinct groups of patients with iron deficiency anemia. In the first group would be included those patients in whom there is sufficient chronic blood loss or deficient iron intake to account for the development of hypochromic anemia. These patients would not exhibit achlorhydria or severe chronic atrophic gastritis. They would not have antibodies directed against the cells of the gastric mucosa, nor would they necessarily show gastric mucosal changes due to iron deficiency itself.

The second group consists of patients whose chronic blood loss and dietary deficiency of iron would not ordinarily be sufficient to produce iron deficiency anemia. In these patients, gastric mucosal changes would precede iron deficiency and would be due to the presence of parietal cell and intrinsic factor antibodies, or to disease elsewhere in the alimentary tract.

The results of the immunological studies presented in this investigation do indeed seem to divide this sample of iron deficient patients into two distinct groups. The differences between the two groups in gastric acid secretion in response to histamine stimulation seem to confirm such a division. Just what is cause and what is effect is less clear. In infants with iron deficiency anemia a high incidence of functional and structural gastrointestinal abnormalities has been described where cause and effect are similarly hard to separate (Nutrition Reviews 22, 323 (1964)).

In those patients exhibiting total achlorhydria it is suggested that the gastric mucosal lesion precedes the iron deficiency anemia and presumably is responsible for it. In this group, the gastric mucosal lesion would be the result of a genetically determined or auto-immune disorder. This would explain the failure in this group of patients to exhibit increased gastric acid secretion after correction of their anemia.

It is not clear why the marked hypochlorhydria may be seen in the other group of patients, or why there is an increase of acid production after iron therapy in the hypochlorhydric patient. The authors speculate that the anemia itself may result in a reduced secretion of hydrochloric acid. The failure of the one patient who was transfused to normal hemoglobin levels over a short period of time to demonstrate increased acid secretion might simply reflect the fact that improved acid secretion may be dependent upon production of new parietal cells, and that insufficient time for such new cell formation was allowed. It is also possible that some of the enzymes or other compounds necessary for acid production may themselves contain iron, and prolonged iron therapy might be necessary to correct such a functional defect.

The suggestion made in this communication of a possible auto-immune basis for certain cases of iron deficiency anemia is certain to stimulate much more work in this important field. The similarity to proposed mechanisms for the pathogenesis of pernicious anemia is obvious.

The presence of parietal cell antibodies and the disturbances in vitamin B12 metabolism in patients the authors would include in the “auto-immune” group suggest that there may be a relationship between iron deficiency anemia of this type and pernicious anemia. However, none of these
patients had antibodies to intrinsic factor, and iron deficiency is not common in patients with pernicious anemia. It is clear that further elucidation of some very difficult questions remains for future investigation.

GASTRIC SECRETIONS BEFORE AND AFTER VAGOTOMY

The responses of various components of gastric secretions to insulin and histamine stimulation, although differing in pattern, are uniformly altered by vagotomy.

In recent years, operative procedures for the treatment of duodenal ulcer in which major portions of the stomach are removed have given way to less radical surgical procedures. At the present time total vagotomy combined with relatively minor modification of the duodenum is becoming increasingly popular in the surgical treatment of chronic duodenal ulcer.

V. Bitsch, P. M. Christiansen, V. Faber, and P. Rødbro (Lancet 1, 1288 (1966)) have now reported the results of an investigation into the characteristics of gastric secretions before and after vagotomy in a series of male patients with chronic duodenal ulcers. Ten patients were studied, ranging in age from 20 to 64 years. In all patients the diagnosis of duodenal ulcer was verified at operation, at which time truncal vagotomy was performed combined with pyloroplasty or, in one case, a gastrojejunostomy. In all patients, gastric secretions were studied for their content of acid, pepsin, and intrinsic factor before and after injection of histamine and insulin on separate occasions. The effects of both histamine and insulin on gastric secretions were studied before and after operation in each patient.

Gastric secretions were collected through a nasal gastric tube which was positioned under fluoroscopy. In the augmented histamine tests basal secretions were collected for one hour and then, following injection of histamine, four 15-minute samples of stimulated juice were collected. For the insulin test, two 15-minute basal portions of gastric secretions and eight 15-minute volumes following intravenous injections of insulin (0.4 units per kilogram body weight) were collected. In each patient blood sugar determinations obtained 30 and 45 minutes after the insulin injection confirmed that hypoglycemia had been produced.

The volume of gastric secretion was measured for each sample, and aliquots were stored in appropriate forms for determinations of acid, pepsin, and intrinsic factor content. Hydrogen ion concentration was determined by pH measurement and by titration to a pH of 3.3. Intrinsic factor was determined radioimmunologically by measuring the capacity of the gastric secretions to bind radioactive vitamin B12 before and after complete blockage of intrinsic factor with intrinsic factor antiserum. Proteolytic activity of the gastric secretions, using freeze-dried bovine plasma as substrate, was compared with a standard reference crystalline pepsin preparation.

Before vagotomy, the volume of gastric secretion rises promptly following injection of histamine and reaches a plateau in the second 15-minute volume. After injection of insulin, the volume of gastric secretion was reduced in the first 30 minutes, but then rose significantly to a plateau slightly lower than that seen after histamine injection. After vagotomy the volume of gastric secretion was reduced in the basal state and also responded differently to histamine and insulin.

In the vagotomized patient, histamine injection was followed by a rise in the volume of gastric secretions to a level lower than that seen following histamine injection before vagotomy, but the pattern of response