

GASTRIC SECRETION OF ACID AND INTRINSIC FACTOR IN PATIENTS WITH HYPER- AND HYPOTHYROIDISM

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Abstract. Fifteen consecutive thyroid disease patients, ten with hyperthyroidism and five with hypothyroidism, have been investigated as far as gastric secretion was concerned. Gastric secretion of acid and intrinsic factor was studied in the patients both basally and with the augmented histamine test. In eight patients with hyperthyroidism and all patients with hypothyroidism, the gastric secretion of acid after histamine stimulation was significantly lowered. The secretion of intrinsic factor correlated with the secretion of acid, and was significantly depressed in four patients with hyperthyroidism and three with hypothyroidism. Further studies showed pernicious anemia in two patients with hypothyroidism.

Disturbances of gastric secretion as related to thyroid gland dysfunction have been noted for many years. After the augmented histamine test normal or low acid output has been registered both in hyperthyroidism and hypothyroidism (3, 4, 11). An association with pernicious anemia has been described in both groups.

In an earlier publication we have noticed a high incidence of achlorhydria, hypochlorhydria and atrophic gastritis in patients with hyper- and hypothyroidism (7). The present paper deals with the findings on gastric secretion of acid and intrinsic factor in these two conditions.

MATERIAL

Fifteen consecutive thyroid disease patients, four men and 11 women, entering either a medical or surgical ward were investigated (Table I). The mean age of the ten patients studied with hyperthyroidism was 42 years and of the five patients with hypothyroidism 59 years. The patients had a typical clinical history of hyper- or hypothyroidism. In all cases except nos. 3, 4 and 10, PBI was taken and the highest value recorded (Table I). In these cases, however, BMR and/or RAI were taken. In cases 3 and 10 subtotal thyroidectomy was performed. Case 3 was later treated with radioactive iodine for recurrency. Case

4 was successfully treated with thyroxin blocking agents only. Five patients were euthyroid at the secretory test. Cases 2 and 9 were studied pre-operatively after having been euthyroid for 2-4 weeks. In cases 3, 4 and 7 the gastric secretory test was performed 3, 20 and 3 years respectively after they were made euthyroid.

METHODS

Gastric secretory studies were performed in the morning after at least 12 hours fasting. A nasogastric tube of 3 mm internal diameter was passed into the stomach. The patient was sitting in a semi-upright position. Continuous draining of the stomach was carried out by suction at subatmospheric pressure of 50 mm Hg. Extra suction and injection of air was applied by means of a syringe. After removal of the residual secretion from the stomach a 60 min collection of basal secretion was made. Midway through this period 100 mg antazoline was given by intramuscular injection. At the end of the basal secretion, histamine HCl was given in doses giving maximal acid output (9). The volume of the gastric juice collected was measured and samples taken from each specimen for determination of HCl and intrinsic factor.

Hydrogen ion activity was determined in an automatic pH-meter (Radiometer, Copenhagen). Gastric juice was titrated with 1/10 NaOH until pH 7.0. Results are given as mEqH⁺/h.

The samples for intrinsic factor assay were neutralized with 10 N NaOH to pH 7.5, centrifuged to remove mucus and stored at -23°C before assay. Intrinsic factor activity was determined as described by Ardeman and Chanarin (1), using ⁵⁷Co vitamin B₁₂ as radioactive isotope. Intrinsic factor was expressed as the difference between total vitamin B₁₂ binding capacity and the vitamin B₁₂ binding capacity after complete blockage of intrinsic factor with excess of antibodies against intrinsic factor. One unit of intrinsic factor was defined as the specific intrinsic factor binding of 1 ng vitamin B₁₂.

Schilling test

The Schilling test was carried out as described by Gräsbeck et al. (8) in some of the patients with achlorhydria or low acid output after histamine stimulation.

Table I. Clinical and laboratory data on 15 patients studied with hyper- or hypothyroidism

Pat. no.	Age	Sex	Diagnosis	PBI ($\mu\text{g}\%$)	Thyroid function at the secretory study	Remarks
1	60	♂	Hyperthyr.	11.7	Hyperthyroid	
2	45	♀	Hyperthyr.	9.9	Euthyroid	
3	56	♀	Hyperthyr.	—	Euthyroid	BMR: +56%. RAI 7 h 64%. Schilling test 26%
4	55	♂	Hyperthyr.	—	Euthyroid	BMR: +35% Schilling test 17%
5	59	♀	Hyperthyr.	12.1	Hyperthyroid	Serum Vitamin B ₁₂ 250 pg/ml
6	20	♀	Hyperthyr.	12.3	Hyperthyroid	
7	54	♀	Hyperthyr.	13.8	Euthyroid	
8	26	♀	Hyperthyr.	13.0	Hyperthyroid	
9	19	♀	Hyperthyr.	9.9	Euthyroid	
10	26	♂	Hyperthyr.	—	Hyperthyroid	BMR: +35%
11	67	♂	Hypothy.	1.8	Hypothyroid	Schilling test without intrinsic factor 4%, with intrinsic factor 11%
12	52	♀	Hypothy.	0.9	Hypothyroid	
13	64	♀	Hypothy.	2.5	Hypothyroid	
14	56	♀	Hypothy.	2.0	Hypothyroid	Schilling test without intrinsic factor 8%
15	45	♀	Hypothy.	1.9	Hypothyroid	

RESULTS

Gastric secretion of acid

Basal secretion of acid was significantly lowered in patients with both hyper- and hypothyroidism as compared with controls (Figs. 1 and 2). After histamine stimulation the acid output was within normal limits in two patients with hyperthyroidism (Figs. 3 and 4). For all other patients the secretion of acid was significantly lowered.

Gastric secretion of intrinsic factor

Basal secretion of intrinsic factor was investigated in ten subjects with hyperthyroidism; in four patients the intrinsic factor secretion was lower than the lower range for hospital patients (2) (Fig. 5).

In all patients with hypothyroidism the basal secretion of intrinsic factor was low, in three subjects <100 units/h (Fig. 6).

After histamine stimulation the secretion of in-

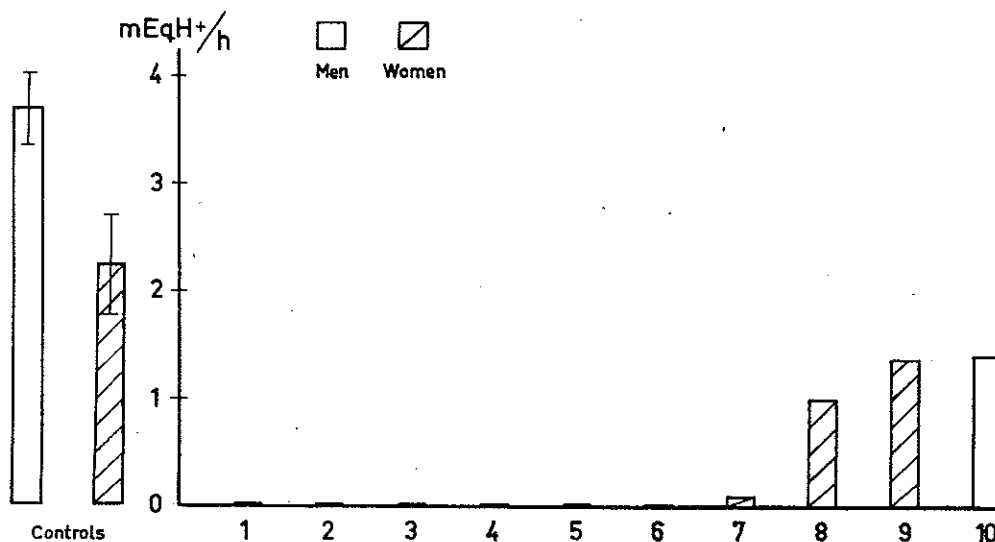


Fig. 1. Basal secretion of acid in mEqH⁺/h in ten patients with hyperthyroidism. Mean and s.e. for controls according to Dotevall (6).

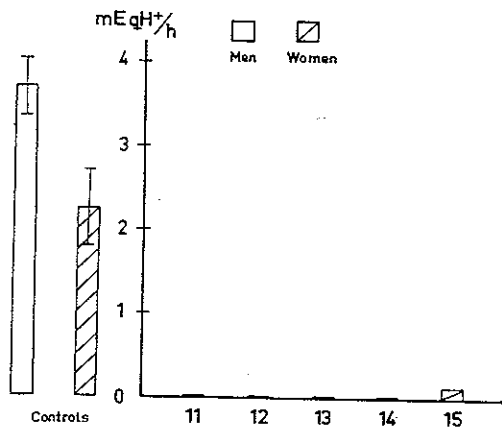


Fig. 2. Basal secretion of acid in five patients with hypothyroidism. Mean and s.e. for controls.

trinsic factor was within normal limits in four patients with hyperthyroidism (Fig. 7). In all other patients the secretion of intrinsic factor was low, (Figs. 7 and 8), in four patients with hyperthyroidism and three patients with hypothyroidism lower than the lower range for hospital patients (2).

DISCUSSION

Our findings of low acid output in patients with hypothyroidism and hyperthyroidism are in agreement with those of others. In an earlier publication (7) we found a good correlation between

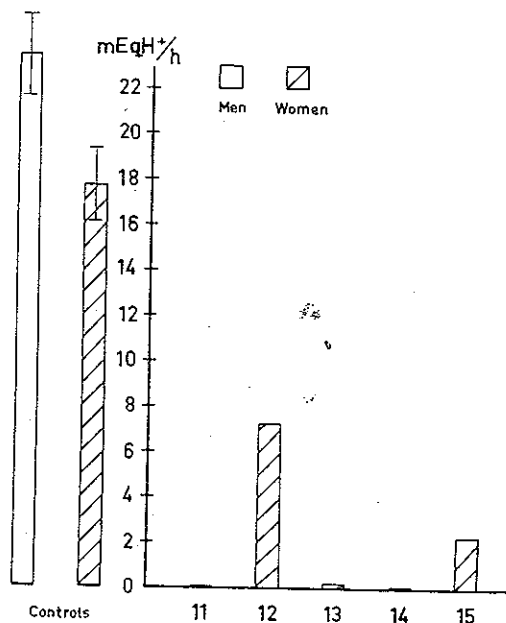


Fig. 4. Gastric secretion of acid in mEqH⁺/h after maximal histamine stimulation in five patients with hypothyroidism. Mean and s.e. for controls.

gastric acid secretion and gastric biopsy findings in patients with thyroid gland disease. Eight of 17 subjects studied with hyperthyroidism had atrophic gastritis and achlorhydria or highly depressed acid secretion after the augmented histamine test. In 15 patients with hypothyroidism,

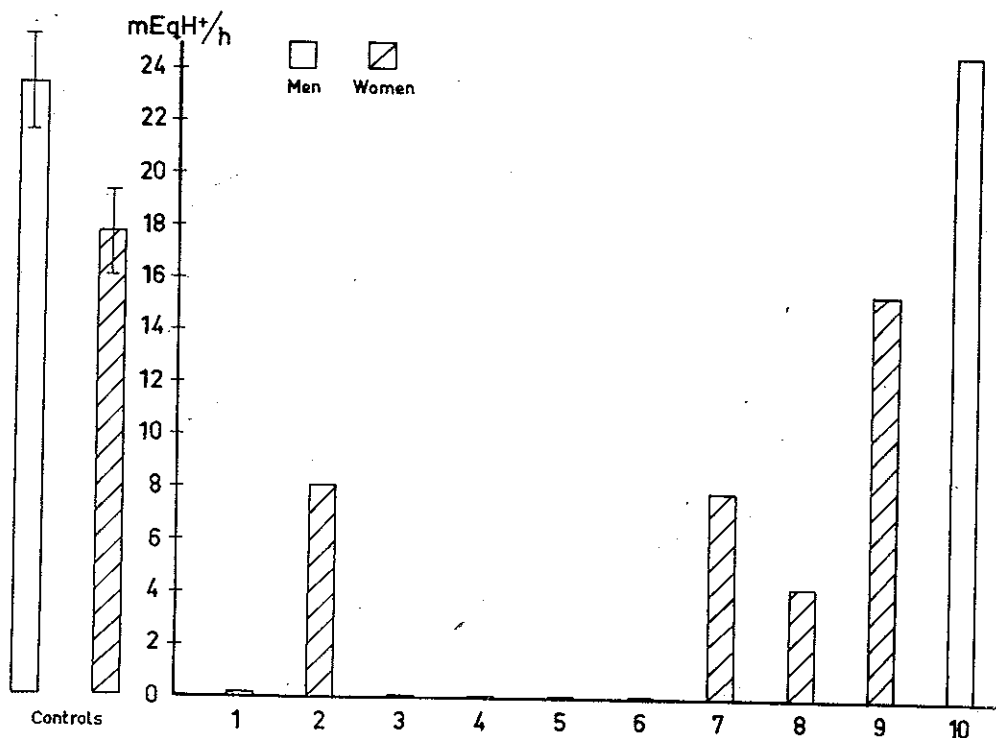


Fig. 3. Gastric secretion of acid in mEqH⁺/h after maximal histamine stimulation in ten patients with hyperthyroidism. Mean and s.e. for controls according to Dotevall (6).

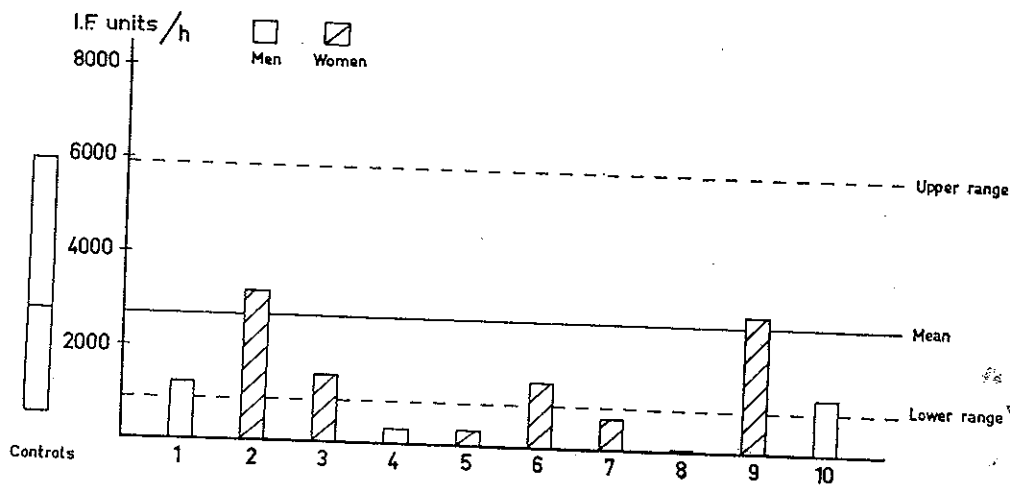


Fig. 5. Basal secretion of intrinsic factor in units/h in ten patients with hyperthyroidism. Mean \pm range for controls according to Ardeman et al. (2).

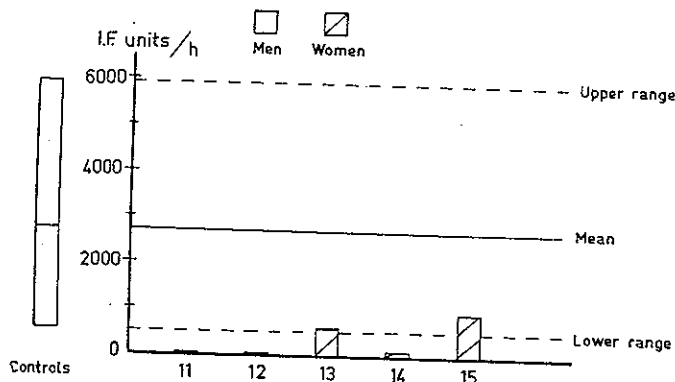


Fig. 6. Basal secretion of intrinsic factor in units/h in five patients with hypothyroidism. Mean \pm range for controls.

atrophic gastritis was seen in eight subjects, who had achlorhydria or low acid output after the augmented histamine test.

As far as hyperthyroidism is concerned a high

incidence of circulating antibodies to the gastric mucosa has been found (5). The report from Bock and Witts (3) of the connection between latent pernicious anemia, hypochlorhydria and achlorhydria in patients who had recovered from hyperthyroidism is of interest. In the present study three of the patients had had their hyperthyroidism some years before the gastric study and were euthyroid at the examination. Two of them (nos. 3 and 4) had achlorhydria after the augmented histamine test and low values for intrinsic factor, 1386 μ /h and 209 μ /h respectively. The Schilling test was, however, normal in both cases. All other patients had their hyperthyroidism diagnosed at the time of the study. Two patients were made euthyroid by thyroxin blocking drugs before the secretory test. They had a normal acid secretive response after histamine stimulation and the secretion of intrinsic

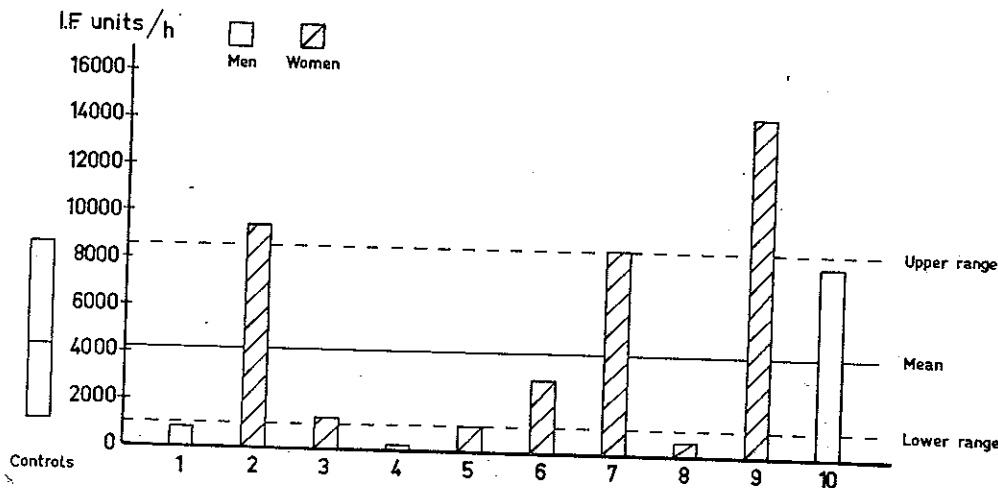


Fig. 7. Gastric secretion of intrinsic factor in units/h after maximal histamine stimulation in ten patients with hyperthyroidism. Mean \pm range for controls according to Ardeman et al. (2).

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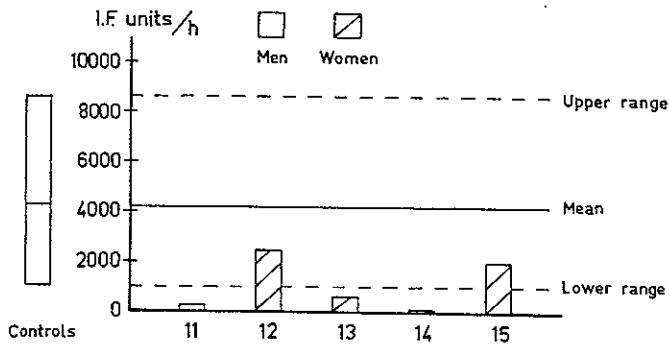


Fig. 8. Gastric secretion of intrinsic factor in units/h after maximal histamine stimulation in five patients with hypothyroidism. Mean \pm range for controls.

factor was within normal limits. Among the five subjects who were thyrotoxic at the study four had achlorhydria or highly depressed acid output after histamine stimulation. Three of the patients had a secretion of intrinsic factor of <1000 units/h. These values are abnormally low according to the data for controls and hospitalized patients presented by Ardeman et al. (2). Further studies did not reveal any manifest pernicious anemia.

Five patients with hypothyroidism were studied as far as gastric acid secretion was concerned. Three of them had achlorhydria or highly depressed acid secretion, two had low acid output. The secretion of intrinsic factor was <1000 in three and within normal limits in two patients. Further studies showed pernicious anemia in one case (no. 11) and the latent pernicious anemia in another (no. 14). Our results support the observations of a connection between hypothyroidism and pernicious anemia. As in hyperthyroidism a high incidence of parietal cell cytoplasmic antibodies has been found in patients with Hashimoto's disease and hypothyroidism (5, 10).

CONCLUSION

The material of hyper- and hypothyroidism presented here is small, but the results confirm earlier findings of a low acid output in these conditions. The secretion of intrinsic factor correlates with the secretion of acid and is low in hypochlorhydria and achlorhydria. This is in agreement with the clinical association between thyroid gland disease and pernicious anemia.