Effect of Prolonged Oral Administration of Reserpine (Reserpoid®) on Gastric Secretion.* (22119)

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An increasing number of reports in medical literature testify to the effectiveness of *Rauwolfia serpentina* Bentham and its alkaloid, reserpine, in the treatment of hypertension, psychoses, neuroses and other conditions in which anxieties, tension and aggressions play a prominent role either in symptomatology or etiology. Reserpine might also be useful in the treatment of certain gastrointestinal disorders, such as peptic ulcer, functional bowel distress, including irritable colon syndrome with diarrhea or constipation, and other types of functional digestive disturbances. The work of Bein(1,2) indicates that reserpine acts upon the central autonomic mechanisms and that this action can be explained by a direct depressant effect on the hypothalamus. This produces peripheral effects similar to those resulting from stimulation of the parasympathetic nervous system. For example, Bein(3) and Plummer *et al.*(4) observed increased motor activity of intestinal tract in animals after administration of reserpine. More important, Plummer *et al.*(4) found that an increase in both volume and hydrochloric acid content of the gastric juice of dogs followed intravenous administration of 15 mg/kg of body weight of reserpine. This increased secretion was effectively prevented for several hours by parenteral use of an anticholinergic drug. Beman(5) stated that both oral and intravenous preparations of reserpine have a potent effect on parietal cells of gastric glands in man, as shown by a significant elevation of gastric acidity, not altered by administration of atropine.

Since it is recognized that free hydrochloric acid is one of the essential factors in production of peptic ulcer and that increased gastric acidity is more common in patients with duodenal ulcer than in normal subjects, it is of importance to determine whether prolonged oral administration of reserpine in therapeutic doses produces significant alterations in gastric acidity. It is the purpose of this paper to report effects of daily administration of reserpine orally on gastric secretion of 20 patients with various gastrointestinal disorders, including peptic ulcer.

Materials and methods. Twenty unselected patients from the Gastrointestinal Clinic, diagnosed as having duodenal ulcer, gastric ulcer, functional bowel distress, etc. (Table I), were given 0.25 mg reserpine† orally 4 times daily for 7 to 210 days; 8 were males and 12 females; age ranged 29 to 73 years. Patients with peptic ulcer were maintained on a modified Sippy diet with antacid medication. They received no anticholinergic drugs or other agents known to affect gastric secretion during this study. A one-hour basal gastric analysis was performed on each patient prior to therapy. The technic has been described previously(6). It consists first of collection via a Rehfuss tube of all gastric juice in the stomach after an over-night fast. This is called the residual specimen (R). Continuous aspiration is then carried out by means of hand syringe for 4 consecutive 15-minute periods. The (R) and each 15-minute collection (B1, B2, B3, B4) are titrated for free hydrochloric acid; total volume is measured and output of hydrochloric acid calculated. After the control basal gastric analyses were made, patients were given 0.25 mg of reserpine orally 4 times a day for variable lengths of time, and a second basal gastric analysis obtained. The results were compared with corresponding pre-treatment values.

Results. As shown in Table I, maximum free gastric acidity rose in 6 instances, fell in 13 instances, and was unchanged in one. Patients

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† Supplied as Reserpoid® tablets by The Upjohn Co., Kalamazoo, Mich.

TABLE I. Individual Comparisons of Basal Gastric Analyses before and after Reserpine Therapy in 20 Patients.

Patient, sex, age and diagnosis		Before reserpine Res.	B1	B2	B3	B4	No. days on drug	During reserpine Res.	B1	B2	B3	B4
P.P. ♀ 72	HCl*	13	20	34	23	16	7	18	52	74	45	63
Duodenal ulcer	Vol.†	10	24	20	17	14		8	8	7	3	6
J.S. ♂ 73	HCl	0	19	38	30	8	9	0	20	20	8	0
Hiatus hernia	Vol.	32	13	11	3	8		4	15	14	5	8
K.B. ♀ 52	HCl	14	0	2	1	0	14	2	0	21	27	12
Gastric ulcer	Vol.	17	10	8	9	7		57	16	13	10	14
M.H. ♂ 70	HCl	4	42	44	44	36	14	19	40	20	26	24
Duodenal ulcer	Vol.	10	5	7	5	4		14	7	5	8	19
W.M. ♀ 56	HCl	60	43	70	85	85	14	34	75	72	72	63
FBD‡	Vol.	58	40	37	28	33		15	70	23	23	23
J.D. ♂ 54	HCl	1	0	7	10	7	17	0	0	0	0	0
Duodenal ulcer	Vol.	26	24	16	10	14		26	30	23	27	12
S.C. ♂ 40	HCl	18	21	40	10	4	24	12	18	26	38	28
FBD	Vol.	49	20	12	20	20		30	16	23	12	20
D.A. ♀ 62	HCl	0	26	17	17	16	28	0	30	28	30	14
FBD	Vol.	24	24	16	23	20		32	30	15	13	18
P.Mc. ♀ 71	HCl	0	0	0	0	4	31	0	0	3	3	0
FBD	Vol.	6	2	12	13	11		69	34	17	21	11
E.B. ♀ 54	HCl	0	9	19	48	48	31	0	0	6	16	10
FBD	Vol.	34	16	15	11	15		9	16	8	8	5
R.M. ♀ 63	HCl	0	35	50	70	45	35	0	2	37	56	34
FBD	Vol.	2	9	5	10	3		16	7	12	8	13
G.G. ♂ 60	HCl	25	20	25	35	40	37	0	0	0	0	12
Gastric resection	Vol.	4	10	20	22	20		5	18	11	13	13
P.E. ♂ 29	HCl	0	6	24	18	26	42	0	0	0	0	0
Gastric resection	Vol.	14	8	7	6	6		10	5	3	9	9
A.D. ♂ 57	HCl	0	41	65	47	84	42	48	67	69	29	70
FBD	Vol.	14	26	23	23	13		9	11	27	49	23
M.S. ♀ 43	HCl	8	0	0	0	0	46	10	0	18	4	15
Hiatus hernia	Vol.	24	38	16	15	18		24	30	32	21	22
C.G. ♂ 67	HCl	0	14	5	0	3	80	11	5	9	16	6
Duodenal ulcer	Vol.	10	6	6	6	4		10	8	7	7	3
M.A. ♀ 65	HCl	17	30	28	32	30	175	0	19	19	24	22
FBD	Vol.	20	25	32	18	43		6	17	10	19	16
M.O. ♀ 65	HCl	15	24	18	17	26	210	0	45	26	20	14
FBD	Vol.	27	15	17	30	25		14	15	12	5	5
M.Mc. ♀ 63	HCl	0	12	20	12	15	52	0	0	0	6	20
FBD	Vol.	33	22	17	8	5		21	43	28	25	22
O.W. ♀ 46	HCl	16	0	15	0	13	25	10	15	6	1	9
Pylorospasm	Vol.	40	10	28	12	47		42	17	15	15	12

* Conc. in mEq/L. † In ml. ‡ FBD = Functional bowel distress.

with peptic ulcer did not appear to react differently from those with other digestive disturbances or diseases. It is apparent that reserpine does not produce a consistent gastric secretory change in either direction. The average volume, free acidity and output of hydrochloric acid of residual specimens and of the four 15-minute basal specimens during reserpine administration showed no significant change from control values.

None of these patients experienced any significant side effects. An occasional patient complained of a slight "stuffy" feeling in the nose.

Discussion. Prior to clinical trial of reserpine in peptic ulcer and other gastrointestinal disorders, we investigated the effect on gastric acidity of prolonged oral administra-

tion of the drug in average therapeutic amounts. Although animal experiments, theoretical considerations, and one report on human volunteers have indicated that reserpine can increase gastric acidity, under conditions of this study, no significant change of volume, free hydrochloric acid or output of hydrochloric acid was observed during reserpine administration.

It is possible that large doses of reserpine taken orally or parenterally over a short period of time may increase gastric acidity, since they have been shown to cause other severe side effects, as indicated by Noce *et al.* (7). It is also possible, however, that tranquilizing effect of well-tolerated doses of reserpine may bring about a secondary decrease in gastric acidity and may therefore be helpful in the management of the peptic ulcer patient.

Conclusions. 1. Basal gastric analyses were made in 20 patients with various gastrointestinal disorders, including peptic ulcer, before and during therapy with reserpine. 2. No consistent change in volume, free hydrochloric acid concentration or output of hydrochloric acid was observed after prolonged oral administration of 0.25 mg of reserpine 4 times daily.

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Effects of Liver Fractions on Thyroid Function of the Rat.*† (22120)

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Several investigators have reported that diets containing liver produced thyroid enlargement in different laboratory animals (1-5). Hou(5) was able to demonstrate that goitrogenic activity was present in the ethanol soluble portion of ox liver. Although substantial thyroid enlargement was obtained in the latter investigation, a search of the literature has failed to yield any further information concerning the substance(s) responsible for the goitrogenicity. Anselmino and Hoffman(6) found fetal blood and other animal tissues to contain an "antithyroid protective" substance capable of overcoming the increase in basal metabolic rate caused by thyroxine injection. More recently Ershoff (7-10) has studied the "antithyrotoxic" effect of liver in overcoming the growth retardation of rats fed thyroidactive materials.

The present investigation is part of a study designed to identify the substance(s) responsible for the goitrogenicity of liver and to determine whether its goitrogenicity is related to the "antithyroid protective" substance or the "antithyrotoxic" factor.

Experimental. Sixty male and 60 female rats of the Wistar strain (housed in individual wire cages) were divided equally into 12 groups of 10 each and treated as indicated in Table I. Pork liver fractions‡ were incorporated into an iodine deficient ration (Table II) and into the same ration containing adequate iodine. The liver fractions replaced

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