8. Nieft, M. L., Deuel, H. J., Jr., *J. Biol. Chem.*, 1949, v177, 143.

9. Swell, L., Byron, J. E., Treadwell, C. R., *ibid.*, 1950, v186, 543.

10. Metzger, E. F., Favarger, P., *Helv. Chim. Acta*, 1952, v35, 1805.

11. Bollman, J. L., Cain, J. C., Grindlay, J. H., *J. Lab. Clin. Med.*, 1948, v33, 1349.

12. Sperry, W. M., Webb, M., *J. Biol. Chem.*, 1950, v187, 97.

Received June 27, 1958. P.S.E.B.M., 1958, v99.

Comparison of Effect of Reserpine and Syrosingopine on Gastric Acid Secretion. (24328)

WILLIAM H. BACHRACH (Introduced by M. I. Grossman)
Vt. Adm. Center, Los Angeles, Calif.

In the search for Rauwolfia derivatives preserving the hypotensive action but free of the undesirable side effects of reserpine, a new alkaloid, carbethoxysyringoyl methylreserpate, (Syrosingopine, Ciba) has been prepared.* The gastric acid-stimulating action of this compound was compared with that of reserpine.

Methods. The effects of oral and parenteral administration of the drugs in humans were tested by measuring volume and acidity of continuously-aspirated gastric contents at hourly intervals. The subjects were known or suspected patients with peptic ulcer, fully ambulated and with no complaints at time of study. Output of acid in meq was calculated by multiplying volume of secretion by concentration of free acid. The control period before administration of drug was one or 2 hours; when a 2 hour control period was obtained, the higher of the 2 hours was taken as the basal secretion. Since average basal secretion varied considerably from one group of patients to another, post-drug output was recorded as increments over basal, as well as absolute values.

Results. Ordinary therapeutic doses of reserpine orally, as used in the management of hypertension (0.25 to 0.5 mg), stimulate secretion of HCl to a mild extent; higher doses, both oral and parenteral, induce a very definite hypersecretion of acid. The excellent absorption on oral administration is indicated by the similarity in acid secretory response after oral and parenteral administration.

Syrosingopine in oral doses of 0.5 to 1 mg stimulates less acid than does reserpine. Intramuscularly, reserpine stimulates more acid secretion than does an equal dose of Syrosingopine by the same route.

TABLE I. HCl Output in Gastric Juice after Reserpine and Syrosingopine.

			HCl, meq/hr				
				Hr after			
	Dose, mg	No. tests	Hr before	1	2	3	4
Oral							
Reserpine	.5	9	1.8	2.9	2.8	2.4	3.1
"	1.0	7	1.2	2.9	4.2	6.1	5.3
Syrosingopine	.5	6	1.4	2.0	1.8	1.0	3.1
"	1.0	10	2.5	4.0	3.2	3.4	3.5
Intramusc.							
Reserpine	1.0	6*	.8	1.8	3.4	7.6	8.2
Syrosingopine	1.0	6*	.8	1.3	1.6	2.5	3.7

* Same subjects.

* Supplied by Ciba Pharmaceutical Co.

TABLE II. Increment of HCl Output over Basal after Reserpine and Syrosingopine.

	Dose, mg	No. tests	HCl, meq/hr (increments over basal) Hr after drug 1	2	3	4
Oral						
Reserpine	.5	9	1.1	1.0	.6	1.3
"	1.0	7	1.7	3.0	4.9	4.1
Syrosingopine	.5	6	.6	.4	.4	1.7
"	1.0	10	1.5	.7	.9	1.0
Intramusc.						
Reserpine	1.0	6	1.0	2.6	6.8	7.4
Syrosingopine	1.0	6	.5	.8	1.7	2.9

Discussion. During these investigations, no observations were made regarding the primary therapeutic purpose of Syrosingopine, namely, reduction of elevated blood pressure. Consequently we do not know from first hand data whether the chemical modification of the reserpine molecule, which yields Syrosingopine, preserves the hypotensive action of reserpine. In our experience, the gastric secretagogue effect of reserpine has not been a significant problem, although it has been so reported by others(1).

Conclusion. Syrosingopine is a less potent stimulant of gastric secretion than is reserpine.

1. Bachrach, W. H., Reserpine, *Am. J. Dig. Dis.*, in press.

Received June 30, 1958. P.S.E.B.M., 1958, v99.

Effect of Cortisone on Connective Tissues of the Rat.* (24329)

HARRY SOBEL,† SABIT GABAY AND CLARENCE JOHNSON

Inst. for Medical Research, Cedars of Lebanon Hospital and Dept. of Biochemistry and Nutrition, University of Southern California, School of Medicine, Los Angeles

Cortisone causes a decrease in the content of the hexosamine-containing mucopolysaccharides of the skin and femurs of the rat (1). However, the collagen content of these organs remains relatively undisturbed. The latter findings are related to the general metabolic inertia of the mature fibrillar components of connective tissue(2,3).

The decrease in ground substance would, of course, lead to an increase in fibrillar density. In this laboratory, the ratio of hexosamine to collagen (H/C) in tissues rich in connective tissue is used to evaluate fibrillar density. Heretofore, it has been assumed that the changes observed with skin and femurs occurred in connective tissues generally following cortisone administration. Since these cortisone-induced changes in connective tissue have certain pathological and gerontological implications, studies were made of several other tissues following cortisone administration. In addition, the changes which took place after withdrawal of cortisone were investigated.

Methods. Male rats of the Wistar or Addis-Slonaker strain were maintained on Rockland Rat Diet. Cortisone acetate (Cortone) was administered subcutaneously at a dose level of 30 mg/kg of body weight. The dose was calculated on the basis of weights obtained on alternate days. Cortisone was injected until a 20% loss occurred in body weight, at which time the animals were either sacrificed or injections were discontinued and recovery permitted to take place. When the original weight was regained, some were then sacrificed and others maintained for biopsy study.

When the response of different tissues was studied, specimens were always taken from a consistent site and in a consistent manner: 1.5 cm^2 of skin was removed from the right hind quarter of the animal and scraped free of visible fat. Approximately 100 mg of lung tissue was taken from the right lower lobe and washed free of blood by intermittent compression in saline. The sternum was cleaned free of all adhering tissue, treated with ace-

* This project was supported by a grant from the U. S. Public Health Service.

† Investigator Howard Hughes Foundation.