Suppression of Prednisone-Induced Gastric Hypersecretion by an Anticholinergic Drug.*† (22925)

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(With technical assistance of Valda Crevling) (Introduced by T. L. Althausen)
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While the stimulatory effects of corticoids on gastric secretion have been well established, the exact mechanism remains unknown (1). The complications of acute perforation and hemorrhage following the activation of peptic ulcers during administration of corticoids(1-4) in many instances have precluded the therapeutic use of these drugs. This study was undertaken to determine whether the anticholinergic drug, oxyphenonium bromide,§ would affect the gastric hypersecretion induced by the synthetic corticoid, prednisone.‖

Methods. Ten normal male medical students, aged 22 to 30 years, were selected as subjects because they showed a definite rise in gastric acidity when given prednisone orally. The experiment was divided as follows: 1) a 7-day period during which 8 subjects received 40 mg of prednisone daily in 4 equally divided oral doses, 2) a 7-day period during which these 8 subjects received 40 mg of prednisone and 40 mg of oxyphenonium bromide daily in 4 equally divided oral doses, 2) a 7-day period during which 5 of the 10 subjects received 40 mg of prednisone and 20 mg of oxyphenonium bromide daily in 4 equally divided oral doses, 3) a 7-day period during which 5 of these subjects received 20 mg of oxyphenonium bromide and 5 received 40 mg of oxyphenonium bromide in 4 equally divided oral doses. The study periods were separated by recovery periods of 2 to 4 weeks. The gastric contents of the fasting subjects were aspirated during 4 consecutive 15-minute intervals before and after administration of the drugs. The volume and the free hydrochloric acid concentration were determined, and the total content of hydrochloric acid was calculated. Twenty-four-hour urine output was collected for uropepsin determinations(5) prior to and on the last day of each period.

Results. As shown in Fig. 1, oxyphenonium bromide significantly suppressed hydrochloric acid secretion when given alone and when given in conjunction with prednisone ($P = .001$). In both cases the suppression was quantitatively similar. The drug was equally effective at the 20 and 40 mg dose level.

Uropepsin excretion rose significantly in 8 subjects following the administration of 40 mg of prednisone ($P = .01$). A significant suppression ($P = .06$) occurred in all subjects when oxyphenonium bromide was administered simultaneously (Fig. 2). The two instances in which the uropepsin level remained above control levels (columns 4 and 6) occurred in individuals whose uropepsin excretion was 19,000 and 24,000 units, respectively, during administration of prednisone.

Discussion. The unresponsiveness of ACTH-induced hypersecretion to anticholinergic drugs has been reported(6). The successful clinical use of such agents in preventing peptic ulceration in patients treated with large doses of prednisone was described recently by Dubois(7). According to our results, the conjunctive use of the anticholinergic drug, oxyphenonium bromide, during administration of prednisone does prevent an increase in gastric hydrochloric acid secretion and uropepsin excretion. The increased gastric secretion induced by corticoids has been

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§ Diethyl (2 hydroxyethyl) methylammonium bromide αphenylcyclohexaneglycolate (Antrenyl®,Ciba).

‖ Δ1cortisone (Meticorten®, Schering).

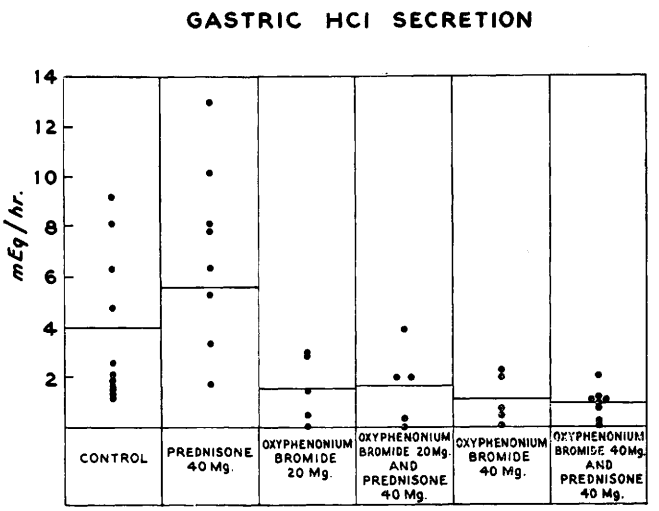

FIG. 1. Effect of oxyphenonium bromide with and without prednisone on gastric secretion.

shown to be independent of vagal innervation (8). Yet, oxyphenonium bromide, which antagonizes acetylcholine, appears to prevent the action of prednisone on gastric secretion.

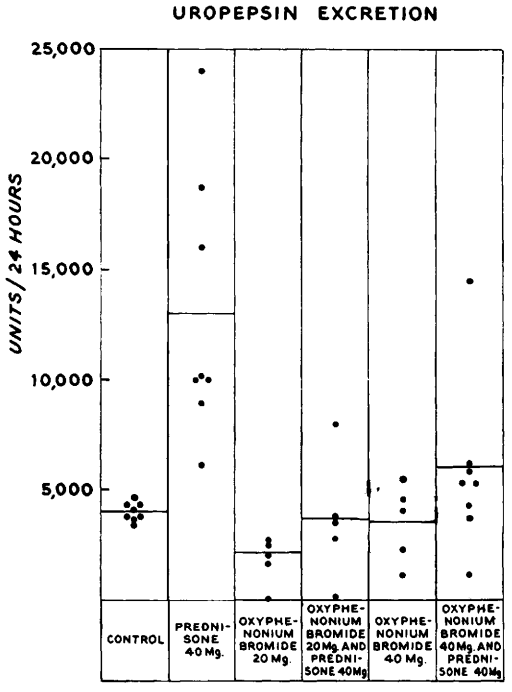

FIG. 2. Effect of oxyphenonium bromide with and without prednisone on uropepsin excretion.

Apparently, prednisone enhances the effect of acetylcholine either by sensitizing the parietal cell to its action or, more directly, by increasing its production or decreasing its destruction.

Summary. The effect of an anticholinergic drug was studied in 10 normal males who showed increased gastric secretory activity during administration of prednisone. It was found that concurrent administration of oxyphenonium bromide (Antrenyl®) suppressed the increase in gastric hydrochloric acid secretion and reduced uropepsin excretion.

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