Adrenergic Potentiation, a Pharmacodynamic Effect Associated with Antihistaminic Agents

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Several new compounds capable of nullifying certain pharmacodynamic actions of histamine and allergens have been announced in recent years: Antergan (1), Neoantergan (2), Benadryl (3), Pyribenzamine (4), Antistin (5), and Hetramine (6). Pyribenzamine, like others (1, 2, 3), also has analeptic, local anesthetic and adrenergic potentiation actions which were initially reported last year (7). The present paper extends the study of the last property.

RESULTS

The potentiation by Pyribenzamine of epinephrine's action in the cat has been reported (8) with respect to salivation, retraction of the nictitating membrane and elevation of blood pressure and these effects are illustrated in Figures 1 and 2. Potentiation of the effect of faradic stimulation of the feline cervical sympathetic nerves controlling salivation and retraction of the nictitating membrane is also demonstrated in these figures and thus indicates that adrenergic and sympathetic actions of varied SE effector mechanisms are potentiated by Pyribenzamine. Adrenergic potentiation of epinephrine's relaxing effect through SE effectors mechanisms associated with canine intestinal muscle is illustrated in Figure 3. In canine anaphylaxis (horse serum) Pyribenzamine almost invariably produced a moderate degree of hypertension (Table 1), apparently as a result of adrenergic potentiation, and this feature will be presented in greater detail in a forthcoming paper dealing with certain vascular reactions to Pyribenzamine in normal and anaphylactic experimental subjects. The potentiation of epinephrine's vascular effects has been reported for other antihistaminics: Antergan (9), Benadryl (10, 11), and Neoantergan (2, 12).

DISCUSSION

In many of its actions histamine duplicates those characteristic of acetylcholine; it produces hypotension.
secretion, and contraction of smooth muscle. Actually there is definite evidence available substantiating the contention that histamine produces its effects through the mediation of acetylcholine (13, 14). Whereas atropine is a relatively weak antihistaminic but strong anticholinergic agent, most histamine antagonists are rather weakly anticholinergic but strongly antihistaminic; hence, their chief designation as such in the conventional but not entirely satisfactory system of classifying pharmacologic agents. It is therefore not difficult to appreciate that after inhibition of such cholinergic stimulants as histamine or acetylcholine, as effected either by such antihistaminics as Benadryl or Pyribenzamine, or by such an anticholinergic agent as atropine, the functions of the unopposed sympathetic nervous system come into prominence, thus influencing the observer to attribute to such agents "sympathetic or adrenergic" potentiating properties. Whether this be

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**Figure 1** — 11/28/44, Cat, urethane anesthesia. Pyribenzamine 0.200 mg. elevated the blood pressure, nullified the action of histamine, 10 micrograms, on salivation, lessened the hypotensive effect of histamine and potentiated the vasopressor and salivary effects of epinephrine, 10 micrograms.

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**Figure 2** — 12/8/44, Cat, urethane anesthesia. Pyribenzamine, 0.010 mg. potentiated the effect of epinephrine, 10 micrograms, on the retraction of the nictitating membrane and on the induction of salivation.