

talis was 0.060; that between patients was 8.762; that reflecting the interaction (digitalis $\times$ patients) was 2.089; the error within patients was 1.386. It is evident that the clotting times of individual patients differed significantly among themselves regardless of therapy. However, the variance due to treatment with digitalis is considerably less than that due to experimental error. Consequently,

these experiments fail to support the hypothesis that oral digitalization increases the coagulability of the blood as measured by this technic.

Summary. Whole blood coagulation times were determined before and during oral digitalis therapy of 10 patients. No significant alteration of coagulability as so measured was observed.

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The Anti-Histamine Effect of Imidazol.*

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From a study of several compounds (histidine, arginine, cysteine, etc.) which inhibit the action of histamine upon smooth muscle structures, Ackermann and Wasmuth¹ postulated that histamine owes its pharmacological activity to its $=NH$ imine group, and to its NH_2 group, the former acting as an anchoring group with the chemical receptors of the smooth muscle, and the latter as the stimulating agent. The inhibiting compounds, having imine but no amine radicals, bind the chemical receptors, have no pharmacological effects themselves, but block the effects of histamine. Rocha e Silva² confirmed such a view by showing that various histamine compounds in which the amine radicals were masked, were inactive themselves but acted as blocking agents against histamine.

On the basis of this theory one could expect that imidazol (Glyoxalin) would possess anti-histamine properties because it presents a free imine radical.

Imidazol was therefore tested as to its counteracting effect against the stimulating

action of histamine upon the surviving guinea pig intestinal strip and its vaso-depressor action in anesthetized cats. Following Rocha e Silva's technic, histamine was added to the bath in a series of concentrations to determine the dose which produced a marked but sub-maximal contraction. Imidazol (Eastman), neutralized, was then added to the bath in increasing amounts, noting the effect of each increment upon the response to the test dose of histamine. In a series of experiments it was found that imidazol would block the effects of histamine when present in a ratio of 1500 to 1. That the imidazol did not act by damaging the intestinal strip was indicated by the fact that there was prompt recovery of histamine responsiveness on washing. In the cat, the intravenous injection of imidazol (1 to 128 mg per kilo) diminished, but did not obliterate the depressor effect of histamine. Doses of 1 mg per kilo reduced the effect of histamine about 25%, and doses of 128 mg per kilo about 60%. The latter dose approximates the maximally tolerated dose.

Summary. Strong concentrations of imidazol can block the effect of histamine upon the guinea pig intestine, and large doses can decrease the vasodepressor effect of histamine in the cat, but the amounts required are so great as to offer no promise of clinical or laboratory usefulness.

* This investigation has been made with the assistance of a grant from the Clara A. Abbott Fund of Northwestern University.

¹ Ackermann, D., and Wasmuth, W., *Z. f. Physiol. Chem.*, 1939, **258**, 28.

² Rocha e Silva, M., *J. Pharmacol. and Exp. Therap.*, 1944, **80**, 399.