but we have detected bismuth in cerebrospinal fluid and blood 10 months after administration of bismuth and expect to find it in all organs, but especially in the usual organs for storage of heavy metals. We are indebted to Dr. Frederick Proescher of the Agnew State Hospital for assistance in securing a portion of the materials used in the study. The work is being continued.

[1] Leonard, *J. Pharm. Exp. Therap.*, 1926, xxviii, 81.

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Comparative Electrocardiography of Cardiac Drugs With Reference to Emesis from, and Distribution of, Digitalis.

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Electrocardiographic studies of pigeons were made with the idea of comparing the emetic and cardiac actions of digitalis, since emesis is a prominent action of the drug in pigeons, and the emetic assay method appears to predict the therapeutic dosage for slowing of the heart in man. Using tinctures of the drug injected intravenously, one-fourth the minimum emetic dose of digitalis caused a 10% slowing of the rate, and one-half the dose a 20% decrease in auricular rate and an A-V block in some pigeons. A single minimum emetic dose, causing emesis in 10 minutes, produced heart block or marked slowing in 1 to 5 minutes and 3 times the emetic dose produced all the effects in 10 to 15 seconds. The cardiac slowing was always preceded by a short period of acceleration which was due only partly to the injection fluid. On the other hand, veratrum and aconite, which also affect the heart through the vagus mechanism but do not cause emesis in pigeons, caused an immediate but brief slowing followed by tachycardia, either auricular or ventricular in origin, and in the case of veratrum there was, in addition, a curious waxing and waning of electrical complexes in cycles, 20 to 30 beats long. That the cardiac changes after digitalis and the slowing of veratrum were of vagal origin was shown by the fact that the effects were prevented and abolished by atropine and vagotomy. The effects were not altered by previous injection of ergotoxine, which by itself slowed the pulse through paralysis of the accelerator nerves, although epinephrine, in large doses, still caused a marked and pro-

longed acceleration presumably due to muscular stimulation. The electrocardiographic results with the cardiac drugs used corroborate their well known pharmacological actions and indicate practical possibilities of the method for studies of their distribution, accumulation and excretion in different species. An application was attempted in connection with a study of the distribution of digitalis with reference to emesis, with the following results.

Acetone extracts of organs from pigeons injected with digitalis were treated with normal saline solution, filtered and injected intravenously into healthy pigeons which were then observed electrocardiographically. Control injections of saline solution and of blank organ extracts gave only slight and temporary cardiac acceleration, while the addition of a single, minimal emetic dose of digitalis caused the typical effects of digitalis described above, but organ extracts after the injection of a single emetic dose were negative. Liver extracts from pigeons receiving from 1 to 6 minimum fatal doses of digitalis gave definite digitalis effects, while the heart and blood extracts were negative; lung extracts were variable. Hence, it appears that digitalis, even after very large and fatal doses, disappears rapidly from the circulation and is not detectable in the heart where it might be assumed to accumulate on the basis of current conceptions of the mechanism of digitalis emesis.[1]

The tendency to accumulation in the liver was supported by another series of experiments with organ extracts and in which emesis was the index of digitalis action. Here the amount of digitalis needed for positive effects from organ extracts after injection of the drug was 6 to 8 times the M. F. D., showing that the electrocardiogram was more sensitive than emesis as the index of digitalis action.

From these results and also from the facts that previous atropinization did not prevent emesis in pigeons and ergotoxinization and vagotomy together did not prevent nausea, it may be concluded that digitalis emesis is of peripheral origin.

[1] Hatcher and Weiss, *J. Pharm. Exp Therap.*, 1927, xxxii, 37.