only factor involved, our observations suggest that renal hyperemia may exist during a phase of acute glomerular nephritis.

Evidences of reversible renal ischemia have been obtained in an exacerbation of chronic disease during the period of subsidence. Further discussion of this and other aspects of the problem are postponed in the hope that information may be gained on the relative importance of reversible functional as compared to irreversible structural changes in renal activity at various stages of the disease.

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Further Investigations of the Effect of Tissues on Autonomic Drugs.

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In previous papers[1, 2] it was established that epinephrine and acetylcholine are destroyed by tissues (in this case the scales of *Fundulus heteroclitus*); it was found also that 50% deuterium oxide inhibits this destruction. Using the same technique and method of recording as previously, the destructive effect of the same tissues has now been investigated on atropine, pilocarpine, physostigmine and mecholyl.

Three kinds of solutions were made in each case: (1) solution of the drugs used, (2) the same solution + fish scales, and (3) the same solution + fish scales + 50% deuterium oxide. All solutions were tested 4 times: immediately after they had been made, 12 hours later, 24 hours later, and 48 hours later. The test objects were melanophores of isolated scales of *Fundulus heteroclitus* freshly removed from the fish.

A. Atropine. One-half percent solution of atropine sulphate was used; in this concentration, atropine fully expands the melanophores. The solutions of atropine sulphate to which fish scales were added showed a much slighter effect after 12 hours. After 24 and 48 hours the same solutions were ineffective. If, however, 50% deuterium oxide were added together with the scales, the atropine solu-

1 Barbour, H. G., and Bogdanovitch, S. B., *J. Pharm. and Exp. Therap.*, 1937. In press.

2 Bogdanovitch, S. B., and Barbour, H. G., *J. Pharm. and Exp. Therap.*, 1937. In press.

tion showed practically no change in effect on the melanophores after 12, 24, or 48 hours. Control solutions (pure one-half percent atropine sulphate) also showed no difference in effect during the whole experiment.

B. Pilocarpine. One-half percent solution of pilocarpine chloride was used; in this concentration pilocarpine fully expands the melanophores. There was no difference in the effect on fish melanophores between the solutions of pilocarpine without and with scales, even 48 hours after the scales had been added.

C. Physostigmine. One-half percent solution of physostigmine sulphate was used; in this concentration, physostigmine, too, expands the melanophores well. As with pilocarpine, there was no difference in effect between the solutions without and with scales, even 48 hours after the scales had been added.

D. Mecholyl. (Acetyl-beta-methylcholine chloride) 0.02% solution of mecholyl was used. In this concentration, mecholyl well contracts the melanophores. Mecholyl solutions also did not show significant differences in effect on the melanophores between the solutions with and without scales, even after 48 hours.

From these results it may be concluded that: (1) atropine was also destroyed by fish scales as had been epinephrine and acetylcholine. Deuterium oxide inhibits this destruction. (2) Pilocarpine, physostigmine and mecholyl resist the destructive influence of fish scales.

Effect of boiling the destructive tissues. In connection with the earlier work it was suggested that this destruction of epinephrine and acetylcholine might be due to the action of certain enzymes, and that deuterium oxide by inhibiting such enzymes protects epinephrine and acetylcholine from the destruction. To investigate further this possibility, the following experiments have been done: besides the previously used 3 kinds of solution (drug alone, drug + scales, drug + scales + deuterium oxide), a fourth kind of solution was used: drug + scales which have been previously boiled in balanced salt solution for 10 minutes at 100°C.

These experiments have been made with acetylcholine, epinephrine and atropine. The results were: scales thus boiled do not destroy any one of the 3 mentioned drugs even after 48 hours. This thermolability of the "destructive" principle in fish scales for these 3 substances is consistent with enzyme hypothesis.