16752 P

Influence of Histamine on Adenosine Triphosphatase.

E. ALBERT ZELLER.* (Introduced by C. F. Code.)

From the Department of Pathology, University of Basel, Basel, Switzerland.

In all snake venoms hitherto investigated a powerful ATP-ase (ophio-ATP-ase) has been found, which is activated by magnesium, calcium and cobalt ions and inhibited by zinc ions.[1,2] Histamine and pyridoxamine act as inhibitors, epinephrine as activator.

The question arose as to whether similar reactions take place in the animal tissues and thus contribute to the understanding of the intimate action of histamine on many organs. Therefore homogenates of different organs were tried on their ability to split ATP. Similar conditions as with ophio-ATP-ase were used (Table I).

Three ATP-ases are known to occur in animal tissues. The ATP-ases from electric tissues of fish[3] and from mammal muscle[4] are activated by magnesium and inhibited by calcium, while the ATP-ase that is inseparable from myosine is influenced by these ions in the opposite way.[5]

In the lung, gastric mucosa, adrenal and kidney of guinea pigs, and in the cortex and medulla of adrenals of cattle an ATP-ase is present which is activated by magnesium, calcium and cobalt ions. The activation by magnesium is the highest and sometimes reaches values which are 10 times higher than the original ones. 0.00001-molar magnesium chloride still caused a rise in ATP-ase activity. By these reactions this ATP-ase differs from the above-mentioned 3 ATP-ases of animal tissues, but resembles the ophio-ATP-ase. The identity is not complete, since zinc ions accelerate the reaction velocity of the new ATP-ase.

The reaction does not stop completely after the liberation of one molecule of phosphoric acid, but the reaction velocity drops after reaching this point. These and other results lead to the assumption that the second molecule of phosphoric acid is split off by other enzymes. This question needs further elucidation.

The new ATP-ase is affected by histamine and epinephrine in a similar way as is ophio-ATP-ase. The highest degree of inhibition is usually reached in the presence of a magnesium concentration that is below the optimum. Under certain conditions calcium exactly counterbalances the influence of histamine (Table I.)

TABLE I.
ATP-ase of the Adrenals of the Guinea Pig.
ATP, 0.0015-molar; glycine buffer, pH 8.3; homogenate corresponding to 1 mg of tissue; volume, 1 ml; incubation period, 15 min.

	Without inorganic ions, Q_P*	With 0.001-molar magnesium, Q_P	With 0.001-molar calcium, Q_P
Without amines	10.4	60.0	25.2
.001-molar histamine	3.6	39.6	11.2
.001-molar epinephrine	20.0	73.6	34.8

* Q_P = μg of inorganic phosphorus per mg of fresh tissue per hr.

* At present research associate, Mayo Clinic, Rochester, Minn.

1 Zeller, E. A., *Experientia*, 1948, **4**, 194.

2 Zeller, E. A., Physiology of Snake Venom Adenosine Triphosphatase. Unpublished data.

3 Greville, G. D., and Lehmann, *Nature*, 1943, **152**, 81.

4 Kielley, W. W., and Meyerhof, Otto, *J. Biol. Chem.*, 1948, **174**, 387.

5 Engelhardt, V. A., Adenosinetriphosphatase Properties of Myosin. In: Advances in Enzymology. New York, Interscience Publishers, Inc., 1946, vol. 6, pp. 147-191.

Pyridoxamine acts like histamine, while aliphatic diamines activate rather than inactivate the tissue-ATP-ase and ophio-ATP-ase.

By these results histamine and ATP, which have been connected with the mechanism of shock production, are brought in a close relationship.

16753

Failure to Produce Lesions or Auto-Antibodies in Rabbits by Injecting Tissue Extracts, Streptococci and Adjuvants.*

JOHN L. PECK† AND LEWIS THOMAS.

From the Department of Pediatrics of the Johns Hopkins University School of Medicine, and the Harriet Lane Home for Invalid Children, Johns Hopkins Hospital, Baltimore, Md.

Schwentker and Comploier[1] demonstrated the formation of complement fixing antibodies for homologous kidney tissue in rabbits which had been inoculated with a mixture of kidney tissue extract and staphylococcal or streptococcal toxin. Cavelti and Cavelti[2] subsequently reported that an antibody for kidney tissue could be demonstrated by the collodion particle-agglutination technic in rabbits and rats which were inoculated with a mixture of homologous tissue and Group A streptococci. The latter workers also reported that rats immunized in this fashion developed acute and chronic glomerulonephritis. Recently, Cavelti[3] described the development of antibody for homologous heart tissue in rats injected with heart extracts and streptococci, and also demonstrated the appearance of inflammatory myocardial lesions in these animals.

Kabat, Wolf and Bezer[4] and Morgan[5] have recently confirmed the earlier observation of Rivers and Schwentker[6] that the immunization of monkeys with extracts of homologous brain tissue leads to the formation of demyelinating lesions of the central nervous system which resemble those seen in multiple sclerosis. These lesions were brought about in greatly accelerated fashion by the use of the adjuvants described by Freund,[7] consisting of "Falba" or "Aquaphor", paraffin oil, and killed tubercle bacilli.

In the present study, the effect of inoculating rabbits with homologous heart and kidney tissue in combination with streptococci and Freund's adjuvants was studied.

Material and methods. Rabbits. Hybrid brown and grey male rabbits, weighing between 1.8 to 2.3 kg each, were used in all experiments.

Tissue Suspensions. Heart and kidney tissue were otained from normal rabbits. The organs were thoroughly perfused with physiological saline under sterile conditions before removal, and were either used immediately or stored whole in a CO_2 ice box. Antigens were prepared by grinding portions of each organ with abrasive, suspending in sufficient physiological saline to make a 10% suspension, and partially clearing by centrifugation for 5 minutes at 1500 R.P.M. Bacteriological cultures were made from samples of each suspension to ascertain sterility.

Streptococci. Several strains of beta hemo-

* This work was supported by a grant from the Life Insurance Medical Research Fund.

† Senior Pediatric Fellow of the National Research Council.

1 Schwentker, F. F., and Comploier, F. C., *J. Exp. Med.*, 1939, **70**, 223.

2 Cavelti, P. A., and Cavelti, E. S., *Arch. Path.*, 1945, **40**, 158.

3 Cavelti, P. A., *Arch. Path.*, 1947, **44**, 1.

4 Kabat, E. A., Wolf, A., and Bezer, A. E., *J. Exp. Med.*, 1947, **85**, 117.

5 Morgan, I. M., *J. Exp. Med.*, 1947, **85**, 131.

6 Rivers, T. M., and Schwentker, F. F., *J. Exp. Med.*, 1935, **61**, 689.

7 Freund, J., and McDermott, K., PROC. SOC. EXP. BIOL. AND MED., 1942, **49**, 548.