

(one animal in each experiment), the low-speed sediment and the high-speed supernatant and sediment were examined. The experiments clearly showed that to a high extent reserpine may prevent the newly formed DA and NA from becoming 'particle-bound'. This result thus further supports the conclusion that these amines – after dopa administration to normal animals – are incorporated in the specific storage granules.

The findings in the present study, together with those in a previous work², seem to admit of the following general conclusions.

(1) The incorporation of newly formed amines in the storage granules is a rapid process.

(2) The storage mechanism is highly efficient since the newly formed amines are rapidly taken up by the granules, even at very high rates of synthesis.

(3) The storage mechanism is non-specific in the sense that it cannot choose between DA, NA, and A.

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Zusammenfassung

Die intrazelluläre Lokalisation des Dopamins und Noradrenalins, die schnell nach einer intravenösen Injektion von L-DOPA in die Adrenalinzellen des Nebennierenmarks gebildet werden, ist bei normalen und reserpinbehandelten Kaninchen untersucht worden. Die Versuche sprechen dafür, dass die neugebildeten Amine sehr schnell den spezifischen Granula, die gewöhnlich nur Adrenalin enthalten, einverleibt werden. Der Einlagerungsmechanismus der Amine scheint sehr wirkungsvoll zu sein, aber unspezifisch in dem Sinn, dass er nicht zwischen Dopamin, Noradrenalin und Adrenalin unterscheidet.

Immunological Tolerance in Chickens Induced by Blood Group Substance

Since the classical work of BILLINGHAM *et al.*¹, numerous investigators have found that the treatment of embryos, and newborn or newly hatched animals, with foreign red blood cells or proteins may be followed by immunological tolerance. Some workers² have succeeded in producing in chickens an immunological tolerance to erythrocytes. On the other hand, BAER *et al.*³ have shown that chickens injected with hog blood group substance are able to produce the agglutinins which react with human red cells. However, there are no data in the literature concerning the induction in animals of immunological tolerance to human erythrocytes by means of blood group substances. This is the subject of this preliminary communication, which represents only a part of a larger work.

The 12-day old Rhode Island Red embryos and infant chickens from the 2nd to the 32nd day of age were injected with hog O(H) blood group substance (kindly provided by Dr. E. A. KABAT, Department of Microbiology, Columbia University, N. Y.). The embryos received intravenously 0.08 mg of blood group substance, and the treatment was followed during posthatched life until the 32nd day of age (subcutaneous injections of 0.08 mg of substance each in three-day intervals). The challenging injections of

human group O red cells were performed on the 42nd and 62nd day of postembryonic life. The control group of chickens was not preliminarily treated with hog O(H) substance, and received two provocative injections of O red cells at the age of 42 and 62 days. The treated and control chickens were bled on the 50th and 70th day of age. The haemagglutination reaction was performed in small 7 × 45 mm tubes, using serial doubling dilutions of chicken sera starting from 1:10, and 1% suspension of human O erythrocytes. The incubation lasted 2 h at room temperature and the reactions were read microscopically. The hemagglutinin titers were expressed in the term of logarithms to the base 2.

The first and second antibody responses of chickens to the injected human group O red cells are presented in the Table. The data clearly show that hog O(H) blood group substance, used for the treatment of chickens in early life, may elicit the depression in the formation of agglutinins reacting with human O red cells. It is of interest to note that an antigen which is chemically a muco-polysaccharide, mainly composed of non-reducing and reducing carbohydrates, represents an active substance able to produce the immunological tolerance in chickens to human erythrocytes. Furthermore, the foregoing data indicate that an antigen from one animal species (hog), when injected into another species (chicken), may cause immunological tolerance of red cells belonging to a third animal species (man). This phenomenon is based upon the same serological specificity of hog O(H) substance and human group O red cells.

Chicken	Normal haemagglutinins 10 chickens Age: 42 days MPT ± SD	First response 10 chickens Age: 50 days MPT ± SD	Second response 10 chickens Age: 70 days MPT ± SD
Treated with hog O (H) substance	4.02 ± 0.69	6.52 ± 1.11	7.98 ± 0.81
Control	3.62 ± 0.45	8.42 ± 0.94	10.72 ± 0.49

MPT: geometric mean peak agglutinin titer (log₂).
SD: standard deviation.

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Résumé

L'injection de substance O(H) du porc à des embryons et à des poussins récemment éclos a comme résultat un abaissement de leur capacité de produire dorénavant l'immunisation active d'agglutinines spécifiques pour les globules rouges humains du groupe O.

¹ R. E. BILLINGHAM, L. BRENT, and P. B. MEDAWAR, *Nature* 172, 603 (1953).

² M. SIMONSEN, *Nature* 175, 763 (1955); *Acta path. microbiol. scand.* 39, 21 (1956). – R. E. BILLINGHAM, L. BRENT, and P. B. MEDAWAR, *Exper.* 11, 444 (1955).

³ H. BAER, J. K. BRINGAZZ, and M. MCNAMEE, *J. Immunol.* 73, 67 (1954).