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Uveal Tissue Sensitization in Rabbits by Synergic Action of Staphylotoxin.

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Sympathetic ophthalmia is a disease of obscure etiology, characterized by a special type of inflammation of both eyes, involving chiefly the uveal tract, and usually follows a penetrating injury of one eye.

Although this disease is comparatively rare, its pathogenesis has offered fertile ground for speculation among ophthalmologists. Of the several theories proposed to explain its etiology, the so-called allergic theory is one of the most important. The purpose of this report is to summarize the approach to the problem of sensitization with uveal-tissue pigment in laboratory animals. A detailed report covering the methods used, the results obtained, and their relationship to experimental sympathetic ophthalmia will appear in an ophthalmological journal at a later date.

During the last 30 years a considerable amount of evidence has appeared in ophthalmic literature, indicating that hypersensitivity to uveal tissue pigment may play some part, as yet undetermined, in the pathogenesis of the disease. The so-called anaphylactic or allergic theory was first proposed by Elschnig, and it has been strongly supported, with an important qualification, by Woods[1] in this country. These and other authors have shown that uveal tissue possesses antigenic properties; that it can act as an antigen in the homologous animal; that it is organ-specific; and that it materially lacks species-specificity.

In the experimental approach to this problem, the difficulty has been in sensitizing laboratory animals with the insoluble uveal-tissue pigment. For instance, no one has been able to demonstrate in the laboratory animal a hypersensitivity to uveal pigment comparable to the reaction that occurs in the human in cases of sympathetic ophthalmia. This step, the production and demonstration of hypersensitivity to uveal pigment, is manifestly necessary before the relationship of pigment sensitivity to sympathetic ophthalmia can be evaluated experimentally.

[1] Woods, A. C., *Allergy and Immunity in Ophthalmology*, Baltimore, Johns Hopkins Press, 1933, pp. 67 ff.; *N. Y. State J. of Med.*, 1936, **36**, 1.

Burky[2] isolated a strain (Ha) of staphylococcus which produced an exotoxin toxic for adult rabbits. He discovered that by repeated intracutaneous injections of the toxin there was developed in the animal, not only an active immunity, but also a hypersensitive state to the broth in which the toxin had been produced. From this primary observation, Burky concluded that other substances with mild antigenic properties might become activated if combined with the toxin. By this method he succeeded in sensitizing rabbits to low-ragweed extract, lens-protein, and homologous muscle-tissue.

Following Burky's method, a "uveal-tissue-toxin" was prepared by aseptically removing uveal tissue from beef and rabbit eyes. This tissue was dropped into individual tubes containing hormone-bouillon. After a period of incubation, the contaminated tubes were discarded, and the sterile ones were inoculated with Burky's staphylococcus (Ha) and incubated for 2 weeks at 37°C. The contents of the tubes were pooled, enough trikresol was added to make a 0.5% solution and the material was then thoroughly macerated in a mortar and filtered through sterile gauze. An intravenous injection of this filtrate, consisting of 0.1 cc per kilo of body weight, given to an adult rabbit, killed the animal within 24 hours.

Fifty-three adult rabbits were used in the experiment. Twenty-two of these were used for bovine uveal-tissue-toxin sensitizing inoculations, 11 for rabbit uveal-tissue-toxin inoculations, and 20 served as controls for similar inoculations with uveal-tissue suspension without toxin. Preliminary to the sensitizing injections, all the rabbits were tested by an intracutaneous injection of a stock uveal-pigment suspension, and the injected skin was removed 2 weeks later for histologic examination as recommended by Friedenwald.[3] Sensitizing injections, consisting of 0.1 cc of the above preparations respectively, were given intracutaneously at intervals of one week for 4 weeks. Those animals that had received bovine uveal-tissue-toxin were tested with swine or rabbit uveal-pigment suspensions, and those which had received rabbit uveal-tissue-toxin were tested with swine uveal-tissue suspension. The control animals were tested with swine, rabbit, and autogenous uveal pigment. Six of the 22 animals that had received bovine uveal-tissue-toxin sensitizing inoculations proved hypersensitive at the end of this period. None of the 11 rabbits that had received homologous uveal-tissue-toxin proved hypersensitive. None of the 20 control animals showed a positive reaction.

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[2] Burky, E. L., *J. Allergy*, 1934, **5**, 466.

[3] Friedenwald, J. S., *Am. J. Ophth.*, 1934, **17**, 1008.

To determine the reliability of the positive reaction, 2 of the hypersensitive animals were tested simultaneously with rabbit, swine, and autogenous uveal pigment. Both of these animals showed a uniformly positive histologic reaction to all 3 suspensions of pigment, thereby demonstrating once more the organ-specific antigenicity of uveal-tissue pigment. One of these animals was retested 8 months later and was found to be hypersensitive at the end of this period.

Summary. 1. A method of preparation of "uveal-tissue-toxin" is described. 2. Repeated intracutaneous injections with heterologous (bovine) uveal-tissue-toxin produced simultaneous sensitization to heterologous (swine), homologous, and autogenous uveal pigment in 6 out of 22 rabbits. 3. Similar sensitizing injections with homologous uveal-tissue-toxin produced no sensitization to uveal pigment in any of the 11 rabbits used. 4. Repeated injections of uveal-tissue devoid of staphylotoxin produced no sensitization to uveal pigment. 5. The criterion of hypersensitivity was based upon the histologic cellular reaction observed in tissues excised 2 weeks after the injection.

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Cesium in the Mammalian Retina.*

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Fox and Ramage[1] and Sheldon and Ramage[2] reported that they were unable to identify, by spectrographic methods, cesium in the tissues of animals of widely divergent genera. Since it is well recognized that different methods of spectra excitation favor the identification of some elements it occurred to us that by use of the interrupted arc method (McMillen and Scott[3]) we might get the identifying lines. Fox and Ramage and Sheldon and Ramage used flame excited spectra in their studies. An examination of several hundred tissue and fluid samples from various mammals by our method failed to give any positive results.

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1 Fox and Ramage, *Proc. Roy. Soc. Lond.*, 1931, **108**, 157.

2 Sheldon and Ramage, *Biochem. J.*, 1931, **25**, 1608.

3 McMillen and Scott, *Rev. Sci. Inst.*, 1937, **8**, 121.