13187 P

## New Observation on a Primary Ocular Reaction to Shwartzman Toxins.

CORRADO AJÓ. (Introduced by G. Shwartzman.)
*From the Laboratories, Mount Sinai Hospital, New York City.*

This report deals with a marked reaction in the eye of the rabbit following the intravenous injection of Shwartzman toxins.* It consists of miosis, photophobia, lacrimation, congestion of the iris and conjunctiva with a marked pericorneal ring of dilated capillaries and in some instances with gross conjunctival hemorrhages. Ophthalmoscopical examination is rendered difficult by the turbidity of the dioptic media although a marked congestion of the fundus may be revealed. The ciliary bodies show enhanced permeability to fluorescein injected intravenously. The aqueous humor of the anterior chamber is usually under high pressure and coagulates immediately upon removal. The fluid is clear in appearance although numerous fibrin-threads, crystals, and epithelial cells may be seen microscopically. The reaction reaches its maximal intensity within 2 hours following the intravenous injection of potent toxins but it completely disappears 24 hours later. The toxins may be given intravenously and intraäbdominally, the cutaneous route is only successful when a vascularized area of the skin is used (the upper third of the ear). Microscopically, severe reactions show massive conjunctival hemorrhage with dilatation and engorgement of blood vessels of the recti muscles. No lesions have been seen in the iris, retina, cornea, and ciliary bodies.

Incidentally, other primary toxic effects following the intravenous injection of the Shwartzman filtrates may be noted, *i. e.*, severe diarrhea, enhanced fragility of the capillaries of the skin, serous fibrinous exudation in the joints, some enhanced permeability of the choroid plexus to fluorescein and a high mortality-rate. These effects may be considerably diminished by a previous local preparation of rabbits to the Shwartzman phenomenon (observed on about 50 animals). No similar protection is afforded by local preparation with chemical irritants and inflammatory agents devoid of Shwartzman principles (cantharidin plaster, turpentine, diphtheric toxin, etc.).

Two intravenous injections of 100 reacting units of Shwartzman

* *i.e.*, bacterial factors capable of producing the Shwartzman phenomenon.

toxins 24 hours apart produce very severe ocular reactions as well as enhancement of other toxic effects.

The observations were made on a total of 300 albino male rabbits (average weight 2.5 kg). The ocular reaction was obtained in 95 out of 100 rabbits injected intravenously with "agar-washings" culture-filtrates of meningococcus Type III and *B. typhosus* and their dialysates through cellophane No. 600. It failed to appear in 100 control rabbits injected intravenously with similar or larger doses of bacterial filtrates devoid of Shwartzman reacting potency and various non-bacterial substances, *i. e.,* diphtheric toxin, staphylococcus Type A, *Streptococcus viridans,* sterile "agar-washings" filtrates, human, pig, horse, and ox sera in 1% solution, 2% suspension of silicic acid, etc.

Pooled aqueous humor obtained from 5 rabbits with severe ocular reactions when injected intravenously into normal rabbits produced fever, diarrhea, ocular reactions and in previously locally prepared rabbits—the Shwartzman phenomenon. Neutralization experiments described below were carried out in order to demonstrate the fact that the ocular reactions were due to the toxic principles of the filtrates.

Normal rabbits received typhoid toxin variously diluted in saline. The highest dilution (1:640) of toxin giving only doubtful coagulation of the aqueous humor 2 hours after the intravenous injection was chosen as a toxin-unit.

One cc of an antityphoid horse sera (capable of neutralizing the Shwartzman phenomenon) was mixed with various amounts of typhoid toxin, incubated at 37°C for one hour, and injected intravenously into normal rabbits. One to 10 units of toxin titrated as above failed to produce the ocular reaction or coagulation of the aqueous humor.

To sum up, the experiments demonstrate a severe reaction in the eye of rabbits following the intravenous injection of Shwartzman toxins into the general circulation. It is accompanied by enhanced capillary permeability and other damage. The factors in the toxic filtrates responsible for the eye reaction may be inactivated by immune neutralizing serum.