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Resistance of the Eye to Bacterial Infection Following Neuroparalytic Keratitis.

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Neuroparalytic keratitis is regarded as a trophoneurosis caused by injury of the Gasserian ganglion or nerves emanating from it or of the ciliary ganglion. Recently we succeeded in the experimental production of neuroparalytic keratitis through the injection of one cc. of 80% alcohol into the rabbit's orbita.[1] Immediately after the retrobulbar injection of alcohol the cornea loses its sensitivity and in 24 hours the corneal epithelium begins to exfoliate. This usually is associated with more or less profuse discharge from the cul-de-sac and chemosis of the bulbar conjunctiva. Keratitis of various degrees develops in the course of 3-7 days after the injection. In some cases this process is aggravated by the ulceration of the cornea characteristic of neuroparalytic keratitis. Out of 34 experiments done in connection with this study, neuroparalytic keratitis failed to develop only in 4 instances.

Among the hypotheses on the pathogenesis of this disease, one supports the bacterial origin of the affection. Davies and Hall[2] found a pseudo-diphtheritic type of bacillus in human eyes affected with neuroparalytic keratitis to which they attributed the specific etiological rôle. Other authorities are of opinion that neuroparalytic keratitis is due to a secondary infection of the eye, the resistance of which has been diminished by the trophic disturbance of the nervous supply of the organ.

The readiness with which neuroparalytic keratitis can experimentally be produced in the rabbit's eye has offered means of investigating the question of the bacterial origin of this disease and the probable diminution of the resistance of the injured eye to bacterial infection. We at first determined the normal bacterial flora of the rabbit eyes using blood agar plates for culturing the content of the cul-de-sac. It was found that the cultures were constantly negative.

A series of rabbits were then treated with the retrobulbar injection of alcohol and the bacterial flora of the eyes was studied. Daily cultural examination of the material from the eyes has shown that

[1] Soudakoff, P. S., An experimental study on neuroparalytic keratitis, in press.

[2] Davies, H. M., and Hall, G., *Brit. Med. J.*, 1908, **1**, 71.

the development of neuroparalytic keratitis was regularly associated with the appearance of *Staphylococcus albus* or *flavus* or, sometimes *Micrococcus catarrhalis*. The pseudo-diphtheretic type of bacilli was never isolated. This finding suggested that the activity of these microorganisms may be responsible for the morbid process. To elucidate this point a group of 6 rabbits was treated with alcohol in the same manner after which the animals received daily instillation of 25% argyrol. The content of the cul-de-sac, taken every day before instillation of the drug, showed no growth, but nevertheless 5 rabbits in this group of animals developed neuroparalytic keratitis. In 2 cases which at first were culturally negative, staphylococci appeared in the later course of the disease. In these 2 instances, the condition was complicated by hypopyon and extensive ulceration of the cornea. From this observation it may be concluded that the development of the neuroparalytic keratitis in rabbits is independent of the activity of the bacteria spontaneously present in the injured eye. It cannot be excluded, however, that the ulceration of the cornea may be due to a secondary infection by pyogenic microorganisms. Though it is clear that the microorganisms found are not connected etiologically with the disease, their regular presence in the experimental eye may indicate that their development is due to the lowered resistance of the eye. If such a reasoning was correct, it would be logical to expect that other pathogenic organisms could be easily inoculated into the injured eye. To verify this point the following experiment has been conducted.

One cc. of 80% alcohol was injected into the right orbita of 5 series of rabbits. On the second day after the injection a 24-hour broth or blood agar culture of different microorganisms was gently rubbed into the conjunctiva and cornea of both eyes, the fellow eye being used as a control. To assure "intake" 3 inoculations were given at 2 or 3 days' interval. For the experiment we selected the microorganisms which might under certain conditions be pathogenic for human eye, namely, *Streptococcus hemolyticus,* Pneumococcus type III, *B. diphtheriae, B. pyocyaneus* and *B. subtilis.*

A group of 3 rabbits received repeated inoculations of *Streptococcus hemolyticus.* The cultural examination showed that no organism could be isolated from normal eye even 20 hours after the inoculation. The affected eye was usually positive for *Streptococcus hemolyticus* cultures only during the first 24-36 hours after each inoculation. It seems that *Streptococcus hemolyticus* remained viable in the injured eye for somewhat longer time than in a normal eye. This, however, has not modified the usual course of the neuro-

paralytic keratitis in rabbits. A second group of 3 rabbits was inoculated with pneumococcus type III. These animals also showed no apparent variation in the course of the neuroparalytic keratitis. Likewise positive cultures for pneumococcus were secured only 24-36 hours after inoculation, while from normal eye the microorganism was eliminated within few hours. A third group of 6 rabbits received the inoculations of *B. diphtheriae*. Two rabbits developed marked pseudo-membranes upon the conjunctiva of both eyelids. One of these rabbits died in a few days of apparently general toxemia, another animal recovered. In both cases the cultures gave rich growth to *B. diphtheriae*. In those instances in which no formation of pseudo-membranes was noticed, the cultures made within 24 hours after inoculation usually showed no growth of *B. diphtheriae*.

From the data presented above, it follows that the development of experimental neuroparalytic keratitis in rabbits following retrobulbar injection of alcohol is not determined by pathogenic bacterial activity. Though such injections result in a severe reaction manifested by various pathological processes in the eye tissue, no evidence has been found to support the hypothesis that trophoneurotic changes in the eye may alter the normal resistance of this organ.

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The Toxicity of Gelsemium.

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The rhizome and root of *Gelsemium sempervirens*, Linne, indigenous to North America, have long been used in medicine for their analgesic and antispasmodic properties and are actively poisonous. It is recorded that 0.8 cc. of the fluid extract proved fatal to a child of 3 years and many other cases of gelsemium poisoning are studied by Wormley,[1] Witthaus,[2] and others. Gelsemine, the principal alkaloid of gelsemium, was first investigated by Wormley,[3] Sonnenschein,[4] and Gerrard,[5] and by Moore,[6] who isolated it in its pure state. Thompson, in 1887,[7] obtained from the plant a second amorphous alkaloid, gelseminine, which was found by Cushny[8] to

[1] Wormley, *Am. J. Pharm.*, 1882, **54**, 337.

[2] Witthaus, *Medical Jurisprudence, Forensic Med. and Toxicology*, 1911, **4**, 937.