Nervism in Ophthalmology. Experiences of Novocain Blockade of the Ciliary Ganglia.

By P. WEINSTEIN.

A. Pathophysiological Introduction.

In the course of development of medical science, following the cellular and humoral aspects of pathology, the neural comes to the fore. This new point of view is based on researches of *Pavlov*, *Ricker* and *Speransky*. *Ricker*'s pathology of correlation emphasizes the alterations of the circulatory system and nervous terminal organ coordination, while *Speransky*'s theory underlines the superimposed organising part of the nervous system. The cornea, possessing only nerves and no vessels, is an especially important object of *Speranky*'s researches.

Outlining the ophthalmologically important principles of Speransky's views, the following have to be mentioned: Unity of the nervous system. According to this postulate, any pathological excitation of a nerve spreads to the entire nervous system, leaving behind an engramme, and thus a second subsequent common irritation (influenza, trauma, etc.) acts on an already altered nervous system. Late investigations concerning the nervous system (Fr. Kiss, Loewenstein, Bikov, etc.) doubtless prove that the dual division into a spinal and autonomous nervous system cannot be maintained any more. The so-called pupillographic investigations have revealed that the pupillar contraction following exposure to light consists of a primary parasympathetic and a secondary and tertiary sympathetic effect. Later on, we shall point out the part of the principle of unity of the nervous system concerning the structure of the ciliary ganglion. The trophic effect of the nervous system. The nervous system exerts a dominating influence on the cellular and tissue-biochemism, the cellular and humoral relations being coordinated into a unity by this neural predominance. In contrast to previous views, according to which keratitis neuroparalytica is exclusively caused by the lesion of the intracranial part of the trigeminus, Speransky's et al. series of experiments point at the possibility that any other nerve beside the trigeminus (sensitive, motoric, secretory) exerts a trophic effect. Nerve-dystrophia. While atrophy of a nerve signifies its complete exemption, neurodystrophia means complete alterations of an organ. In this regard experiments of the Soviet school are important which reveal that irritation of the central stump following cutting of the ischiadic nerve, causes keratitis. Speransky et al. were able, by compressing peripheral nerves by means of a metal ring, to produce the most various kinds of pathologic alterations (ulcera, inflammation, tumours, etc.).

The essential factor of such alterations is the continuous irritation of the nervous system. This fact is of basic importance, e.g., concerning the origin of iritis (Parade). Iritis is never a primary disease, but always a consequence of some focal infection. But we are frequently unable to find any foci. According to Speransky, the toxin produced by the germ is as much a constant irritation as any other chemical or mechanical one. The constant irritation is apt to cause alterations located even remote from the focus, because the nerve fibers inserted between them are in a state of dystrophia. In this state the decisive factor is not the focus but the nervous system. The removal of the focus is frequently ineffective because the neurodystrophia (engramme of the disease) persists: if the nervous system is disconnected (novocain blockade), the process stops. The importance of the nervous system in connection with the origin of focal infection, also emphasized by Slauck, Spiess (quoted by Denig), recommends exemption of the nervous system as a curative measure. Blockade of the nervous system establishes new nervous associations, which promote healing of the pathologic process (Scheffels, Speransky, Denig).

On the basis of the above detailed points of view we began our therapeutical experiments of various acute and chronic diseases of the eye by novocain blockade of the ciliary and sphenopalatine ganglia (biganglionary blockade) and by perilimbal subconjunctival novocain injection. First we have to discuss the structure of the ciliary ganglion, before attempting an evaluation of results.

B. Structure of the Ciliary Ganglion.

The basic unity of the nervous system is also proved by the structure of the ciliary ganglion. While former researchers (Len-

hossék, etc.) believed it to be a special parasympathetic ganglion, Kiss, by his new method of investigation (prolonged osmium staining), considers it rather as a sympathetic one. In the literature it is generally described as a mixed ganglion. According to Kiss, two sorts of cells are to be distinguished, sympathetic elements staining black, and white sensitive cells. A peculiarity of the ganglion is the property of the postganglionary fibres of being myelated, while all other postganglionary fibres of the system lack a myelin sheet. The ciliary nerves are composed of thin myelated fibres (sensitive or parasympathetic fibres), and fibres without myelin (sympathetic ones). We regard it as of peculiar significance that the structure of the sphenopalatine ganglion is the same as that of the ciliary. According to researches of Axenfeld, Givner, etc., cells of the ciliary ganglion are to be found within every eye as episcleral ganglionary cells, and therefore should be regarded as accessory ganglia of the ggl. ciliare. The cells of different morphological types of the ganglia possess, according to Kiss, Sávai, and Szegvári (quoted by Kiss), Temesváry (quoted by Kiss), and Farkas, different physiological functions. These authors have proved that experimental alterations of the multipolar dark ganglionar cells cause corresponding changes of the blood-pressure of the experimental animals. In cases of Raynaud's disease, the multipolar cells of the thoracal ganglia appeared to be paler after osmium treatment. According to Kiss, this shows at an increased function. The dark cells of the spinal ganglia seem to be somehow connected with the blood-vessels. Concerning the ciliary ganglion, some investigations of Ruttner seem to be of peculiar importance, according to which some cases of Adie's tonic pupil, observed and autopsied by him. did not reveal any other post-mortem changes than such of the ciliary ganglion, the cells of which showed grave alterations. Duke-Elder emphasizes that the eye has autonomous pupillomotoric and vasomotor fibres. These circumstances seem to suggest that the different cells of the ciliary ganglion exert different physiological activities. Marchesani, basing on clinical experiences, assumes that within the superficial part of the conjunctiva, the cornea and the tear-glands, trophical effects become active which are transmitted by the sphenopalatine ganglia and the superior major petrosus nerve. The deeper layers of the cornea and the uvea are provided trophically by the first branches of the trigeminus nerve. Pau's observations indicate that typical neuroparalytic keratitis may affect an entirely sound trigeminus nerve. He quotes investigations of *Reiser*, according to which the nerve fibres of the peripheral parts of the cornea originate in the conjunctiva and proceed by way of the pterygopalatine and facial nerves. The nerve fibres of the central cornea derive from scleral plexus of fibres (Gasser's ganglion). If they are destroyed, the fibres of the perimarginal plexus are restored by anastomosis. But if these anastomoses are deficient (*Reiser*), neuroparalytic keratitis ensues. If chronic irritation (*Speransky*) influences the sympathetic trophic fibres, the results are the same (*Behr*, *Pau*).

C. Therapeutic Experiments by Novocain-Blockade of the Ciliary Ganglion.

The first so-called neuraltherapeutic treatments of various ophthalmologic diseases were applied by co-workers of Speransky through lumbar blockade of sympathetic bundles. Satisfactory results were achieved in 10 cases of corneal herpes and 17 of suppurative keratitis by Višnevsky, Dymschitz, Mikeljan, and Cirkovsky. Višnevsky and Gluskov treated cases of associated keratitis and alveolar pyorrhoea. Gajewitsch reports good results especially with cases in which the trophic factor was dominant (disciform keratitis, neuroparalytic keratitis). Lumbar blockade as a means of therapy is somewhat far-fetched in the armatory of the ophthalmologist. So it can be understood that subsequently blockade of the ciliary ganglion came to the fore by way of retrobulbar injection of novocaine. Retrobulbar injection of novocain and alcohol was formerly used exclusively to overcome pain in case of absolute glaucoma and for avoiding enucleation (Grüter, Magitot, Vojgodkaja, etc.). But lately quite a number of authors apply the novocain blockade of the ciliary ganglion as a means of neural therapy (Behr, Velhagen, Marchesani, Schmelzer, Paneva). The technique is the same as that of the customary retrobulbar injection of 1 to 2 ml. of 2% tonogen free novocain solution. Kmoniček and Velhagen report extremely favourable results after treating cases of eczematous keratitis and hypopyon keratitis by so-called perilimbal subconjunctival novocain injection. Marchesani, Ruskin, Offret, and Chauvat applied blockade of the sphenopalatine ganglion curing keratitis rosacea and superficial keratitis. Pinto applied blockade of the ganglion stellatum in cases of corneal ulcers in animals with doubtful results. Marchesani emphasizes

the importance of the cervical sympathetic regarding origin of the acute iritis, especially in cases which do not reveal any focus. The most various foci along the course of the sympathetic bundle may play a part as factors of chronic irritation. The parts detailed in figure 1 (after Marchesani), namely tonsils, sinuses, ear, lymphatic glands, alterations of the vertebrae, pleura, etc., may act as factors causing dystrophia and thus the curing effect of the blockade of the sympathetic ganglia may be understood. The same figure may explain mechanism of unilateral and bilateral iritis. Fuchs' so-called biganglionary method may be mentioned (Marchesani, Velhagen, Schmelzer), consisting of an alternating blockade of the ciliary and sphenopalatine ganglia in cases of various eye-diseases. Anesthesia of the sphenopalatine ganglion is simple enough: at 1 to 1½ cm. back of the last molar a long thin needle is inserted medially into the pterygopalatine canal, injecting 1 to 2 ml. of 2% novocain solution.

TABLE I.

			TADEL	1.			
Result	Keratitis parench., rosac., e lagophth.	Herpes corn.	Ulcus serp.	Keratoconj. Infiltr. corn.	Kerato- iritis	Iritis, irido- cycl. uveitis	
Healed: +	мдоричи						
Improved: ± Unchanged: 0 Worse: —	8	2	2	per of cases:	12	26 (60)	
+	5		2	10	7	14	
±	3	2			2	10	
0					2	2	
_					1		

In the course of our own therapeutic experiments, about 300 blockade administered to 60 cases were applied (s. table I). Mostly cases of iritis and keratitis, otherwise resistant to treatment, were selected. Blockade of ciliary ganglion of the sphenopalatine and biganglionary blockade and perilimbal anesthesia were administered. Especially favourable were the results of ciliary ganglion blockade in cases of painful uveitis of blind eyes free of glaucoma, diminishing pains and curing the disease, moreover treating plastic iritis. Conspicuously satisfactory results were achieved by perilimbal injection in case of suppurant iritis and lymphatic inflammation. In case of failure of ciliary ganglion blockade, that of the sphenopalatine ganglion is to be tried (keratitis rosacea, corneal

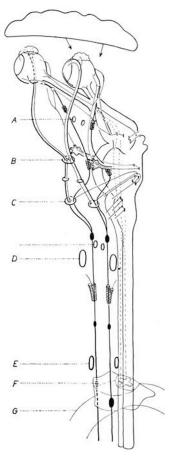


Fig. 1 (after Marchesani), A: Sinus paranasales, B: Tonsilla, C: Cavum tympani, D: Lymphoglandula cervicalis, E: Lymphoglandula clavicularis, F: M. vertebralis, G: Pleura.

infiltration, marginal ulcers). The case of a man aged 60, for decades suffering from iritis alternately of the left and right eye, of uncertain etiology, resistant to all permanent attempts of therapy (fever, own blood, autoserum, microtransfusion, Filatov's tissue-implantation, etc.). Retrobulbar novocain injection was also only of temporary benefit; retrobulbar alcohol injection repeated twice resulted in absence of symptom for 10 days, followed by recurrence. The alcohol injection was performed on a seeing eye without any harm. (According to Weekers, Saint-Martin, Matteucci, Maumenee, good visual acuity is no contraindication of alcohol retrobulbar injection.) Consequently, perilimbal anesthesia and biganglionary blockade were applied; after 8 blockades the patient has been well for months.

The ophthalmologic consequences of blockade of the cervical sympathetic were first investigated by *Angelucci*. Lately *Itakura* performed some physiologic experiments. We tried the blockade of the stellate ganglion in one case of embolia of the art. c. retinae. Acuity reduced to 5/70 did not react on energetic vasodilatatory therapy (priscol, nitrous sodium, inhalation of amylnitrate, etc.). After homologous blockade of the ggl. stellatum, visual acuity improved to 5/10.

D. Pharmacology of the Pupil after Blockade of the Ciliary Ganglion.

Following the novocain blockade of the ciliary ganglion, the function of the pupil reveals extremely interesting pharmacodynamical peculiarities, important also from the clinical point of view. Our observations are in conformity to those of Scheie and Gaylord, Roussel and Weekers, Weekers and Bacq, Hoorens and Heymans, Morpurgo, Persichetti, Jayle and Ourgand, Shenderev and Leontyeva. Within seconds following retrobulbar novocain injection, the pupil dilates to middle size and accommodation stops. Pilocarpin or some cholinderivative dropped into the eye, the blockaded pupil contracts in considerably accelerated time compared to that of control. If after the blockade prostigmine, DFP, or p-nitrophenyl-diethylphosphate (Mintacol) is administered, the pupil of the control eye contracts more rapidly and to a larger extent than that of the blockaded eye. If both eyes are blockaded, both pupils dilate (Fig. 2). If eserin is instilled into the one, pilocarpin into the other eye, the different effects become clearly visible. Pilocarpin acts directly on the nervous terminals of the iridial sphincter (myoneural effect). Eserin, on the other hand, acts by its antagonistic influence on cholinesterase and thereby contracts indirectly. After novocain blockade production of acetylcholin stops, and thus eserin becomes ineffective.

The following practical conclusions have to be drawn from these experiments: following an operation of cataracta done by retrobulbar injection, pilocarpin must be applied to obtain contraction of the pupil, because the mydriatic effect of the novocain blockade is counteracted, whereas eserin und DFP are much less effective. Preceding glaucoma operation, the pupil shall be contracted by the use of pilocarpin, as following retrobulbar novocain blockade the pupil of the eye previously treated with eserin dilates,

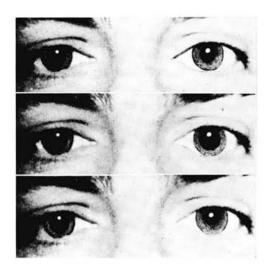


Fig. 2.

- A: Pupils prior to retrobulbar injection.
- B: Mydriasis immediately following retrobulbar injection of 2% novocaine.
- C: Pupils 20 minutes later, following instillation of eserin O.D., pilocarpin O.S. (Almost unchanged pupil after eserin, marked miosis after pilocarpin.)

while the pilocarpin-treated pupil remains contracted (Scheie). An observation of Leopold should not be omitted: prostigmin counteracts the effects of subsequently administered DFP, but DFP administered first and prostigmin afterwards, the effects of both unite.

Similar were Weekers' statements concerning retrobulbar alcohol blockade. He, Persichetti, Shenderev and Leontyeva describe pupillary reactions similar to Adie's pupillotony following blockade of the ciliary ganglion, and therefore locate the latter in that organ, a fact already proved by Ruttner's pathoanatomic observations mentioned above. Adler, Scheie, Franceschetti and Bischler state that mecholyl (acetyl- β -methylcholin) solution of $2\frac{1}{2}$ % promptly contracts the tonic pupil, while a normal one reacts only to a 20% solution. This corresponds to the experiments described above, considering that following the postganglionary paresis of the parasympathetic (blockade of the ciliary ganglion) an increased sensitivity to cholin and pilocarpin prevails.

E. Ocular Tension. Permeability. TEAB Effect.

We undertook a series of experiments to determine the influence of the novocain blockade exerted on ocular tension, bloodaqueous barrier permeability, etc. The results of these experiments and the ophthalmologic effect of TEAB we intend to publish separately later on. Here only the most essential points should be mentioned. So far the preglaucomatous provocative tests in the dark room act in such a way, that the pupil dilates and, compressing the chamberangle of predisposed individuals, increase ocular tension. Systematic experiments revealed that despite the provocative dark room test, the chamber-angle remains totally uninfluenced within the gonioscopic picture, consequently no purely local mechanism can be held responsible. The fact that we succeeded in neutralising the dark room test tension increasing effect by novocain blockade of the ciliary ganglion, suggests that the provocative dark room test effect is a consequence of a retino-pituitary reflex which is produced by the influence of darkness and which is eliminated if the ciliary ganglion is exempt, the ocular tension remaining then unaltered.

For investigation of the blood-aqueous barrier we used Amsler-Huber's electric 0-point method (published elsewhere). According to our results (in collaboration with my co-worker *J. Forgács*) neither blockade of the ciliary ganglion nor that of the stellate ganglion following immediately cause alteration (within an hour) of the blood-aqueous barrier.

TEAB (tetraethyl-ammonium-bromid) is a drug which paralyses sympathetic and parasympathetic ganglia and which acts on the eye, according to data in the literature, like the disconnection of the ciliary ganglion. General blood pressure and ocular tension decreased immediately following i.v. injection. The effect was even more pronounced after use of TEAB and Hydergin "Sandoz". Heymans and Hoorens have investigated the pupillary action of TEAB. Our experiments reveal expressed mydriasis following the i.v. injection. (We could not elicit this effect by our own preparation.) It instantly stops miosis caused by DFP or physostigmin. Miosis caused by pilocarpin or acetylcholin remains uninfluenced.

Autenrieth (quoted by Hoff) compares medical theories to the tangent of a circle: it touches at a single point and then deviates, or changes, or breaks. The multiplicity of life is comparable to the increasing number of tangents arising from new points of view. Thus it seems that, despite Hallermann being unable to protect the eyes of animals in the course of his experiments against allergic inflammation by blockade of the nervous system. Speransky's neuralpathologic theory enlarges the scope of medicine and perhaps may further the development of ophthalmology.

Summary.

Referring to the teachings of nervism (neuralpathology), therapeutic results in cases of various ophthalmologic troubles (keratitis, plastic iritis, chronic uveitis) achieved by novocain blockade of the ciliary ganglion are described. Satisfactory results are reported in cases of keratitis rosacea, marginal ulcus and corneal infiltration by way of biganglionary blockade (blockade of ggl. ciliare and sphenopalatinum). The combination of the blockade with perilimbal subconjunctival novocain injection proved to be beneficial in treating cases of lymphatic ocular inflammation and suppurative iritis. Pharmacologic and practical experiences concerning contraction of the pupil after various miotica following blockade of the ciliary ganglion are detailed (pilocarpin effective, eserin not effective). Changes of ocular tension, permeability of the blood-aqueous barrier owing to the blockade are dealt with, and experiments with TEAB are described. Later on, a detailed publication of the latest results is intended.

Zusammenfassung.

Nach Besprechung der pathophysiologischen Grundprinzipien des Nervismus (Neuropathologie) werden die therapeutischen Ergebnisse mittels der Novokainblockade des Ciliarganglions bei verschiedenen Augenerkrankungen (Keratitis, plastische Iritis, chronische Uveitis) besprochen. Befriedigende Ergebnisse wurden erzielt in der Behandlung von Keratitis rosacea, Marginalgeschwür, Cornealinfiltrat durch biganglionäre Blockade. (Blockade der Ggl. ciliare und sphenopalatinum). Bei lymphatischen Augenentzündungen und purulenten Iritiden war die Kombination der Blockade mit perilimbarer subconjunctivaler Novokaininjektion erfolgreich. Pharmakodynamische und praktische Erfahrungen bezüglich der Pupillenverengung als Wirkung verschiedener Miotica nach Blokkade des Ganglion ciliare werden besprochen (Pilokarpin wirksam, Eserin unwirksam nach der Blockade). Es wird die Einwirkung der Blockade auf den Augendruck, die Permeabilität der Blut-Kammerwasser-Schranke geschildert, weiterhin Versuche mit TEAB, deren Einzelheiten später behandelt werden sollen.

Résumé.

L'auteur expose les principes physiopathologiques fondamentaux du « nervisme » (Neuropathologie), et examine les résultats obtenus dans le blocage à la novocaîne du ganglion ciliaire dans différentes maladies oculaires (kératites, iritis plastique, uvéite chronique). Le blocage biganglionnaire a donné de bons résultats dans le traitement de la kératite rosacée, des ulcères marginaux et infiltrats cornéens (bloc des ganglions ciliaire et sphénopalatin). La combinaison du blocage avec l'injection sous-conjonctivale périlimbique de novocaîne a vaincu les inflammations lymphatiques et les iritis purulentes. Discussions des expériences pharmacodynamiques et pratiques sur l'effet de différents miotiques sur le rétrécissement pupillaire après blocage du ganglion ciliaire (pilocarpine efficace, ésérine inefficace). Description de l'effet du blocage sur la tension intra-oculaire, la perméabilité de la barrière hémato-oculaire, puis des essais avec le TEAB dont les particularités seront discutées plus tard.

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Die akkommodative Linsenverschiebung als Ausdruck antagonistisch wirkender Kräfte*.

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1. Mitteilung.

Von Scheiner wurde erstmalig und später auch von Descartes die akkommodative Refraktionszunahme mit einer vermehrten Linsenwölbung in Zusammenhang gebracht. Pemberton und Young sowie in neuerer Zeit noch Krauss und Gillessen nahmen in der Linse selbst kontraktile Muskelfasern an, wodurch die Änderung der Linsenform hervorgerufen werde. Von Langenbeck und Cramer sowie von v. Helmholtz konnte die akkommodative Gestaltsänderung der Linse nachgewiesen werden.

Der extrakapsuläre Akkommodationsmechanismus.

Nach der v. Helmholtzschen Akkommodationslehre kommt es bei der Kontraktion des Ziliarmuskels zu einer Entspannung der Zonulafasern, die wieder infolge der Elastizität der Kapsel von einer Zunahme der Linsendicke und der Flächenkrümmung begleitet ist.

Es sei mir nun gestattet, zunächst noch einmal die innerhalb und außerhalb der Linse liegenden, an den akkommodativen Vorgängen beteiligten Faktoren und physikalischen Gegebenheiten kurz aufzuzeigen, um dann eine Darstellung meiner Auffassung von dem Akkommodationsverlauf zu geben.

^{*} Auszugsweise vorgetragen auf dem «augenärztlichen Fortbildungskurs» am 3, 8, 1951 in Berlin.