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ETIOLOGY AND PATHOLOGY OF SYMPATHETIC OPHTHALMIA.*

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In recent years the pathology of sympathetic ophthalmia has been the subject of numerous careful investigations by prominent ophthalmologists which, however, resulted in quite contradictory opinions. Deutchmann gave the experimental proof of what Mackenzie (A Practical Treatise on the Diseases of the Eye, 4th ed. p. 597) tought fifty years ago, that "the chief medium through which sympathetic opthalmitis is excited, is the union of the optic nerves," with the conclusion that the microörganisms from the infected eye apparently enter the optic track in four different ways: 1st, from the perichoroidal space; 2nd, directly from the choroid into the pial sheath of the optic nervee 3rd, from the sheathes of the central vessels along their branches which radiate into the optic nerve, into the pial sheaths and the intervaginal space; 4th, sometimes probably from Tenon's capsule. (Deutschmann: On Ophthalmia migratoria.) Others, who did not succeed in obtaining the same results, consider it still an open question; and yet others, with Schmidt-Rimpler (*v. Græfe's Arch.* 38. 1.) as representative, adhere to a modification of the old theory advanced by Heinrich Mueller, that the ciliary nerves convey the disease from the first to the second eye. Deutschmann with Leber (*von Græfe's Arch.* 27) also acknowledges this, but only for the *sympathetic irritation* which is a reflex neurosis and an entirely different disease, independent of *sympathetic* or, as he calls it, *migratory ophthalmia.* The former is permanently cured by removal of the diseased eye, whereas sympathetic ophthalmia is not influenced by it at all. Both diseases, however, may coexist in the same eye but perfectly independent of each other, or one may precede the other. The sympathetic irritation is not a milder form of sympathetic inflammation, as has been supposed, although eyes which cause sympathetic ophthalmia may also produce sympathetic irritation.

As pointed out by Schweigger, there is no typical form of sympathetic ophthalmia; it is only a diagnosis of probability. This may reach almost certainty, if a normal eye becomes diseased after an affection of the first eye, under conditions which, according to experience, deserve some value: the form of disease of the first eye; that of the second eye; and the interval between both, generally of from two weeks to four months. Schirmer (*von Græfe's Arch.*, 38. 4), gave a critical review on sympathetic ophthalmia of the publications of the last years and came to

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the conclusion which Albrecht von Græfe, 1866, pointed out, that an inflammation of the uveal tract is necessary to produce a sympathetic affection. And it is only by the development of *irid-ocyclitis* that sympathetic ophthalmia may be aroused by intraocular tumors, formation of bone in the choroid, incarceration and laceration of the ciliary body or iris, and that this inflammation is due to infection. In subconjunctival ruptures of the globe the irido-cyclitis is to be attributed to an invasion of microbes by minimal lesions of the conjunctiva, or if it sets in later by small defects of the scar, perhaps only abrasions of the epithelium (Wagenmann, *von Græfe's Arch.*, 34. 4). That infection must occur was clearly demonstrated in a case of intraocular cysticercus of Pincus (*von Græfe's Arch.*, 40. 4), which in fourteen years had brought about extensive degeneration of the globe with dislocation of the lens, without disturbing the second eye. After extraction of the lens the wound did not heal well and became infected, producing severe iridocyclitis and, after eight weeks, serious plastic uveitis of the other eye.

Aseptic perforating wounds, as for instance in operations, heal without reaction, whereas minimal quantities of microbes, brought in contact with them, cause severe inflammations, and this inflammation of the uveal tract represents the relation between injury and sympathetic ophthalmia.

The rare occurrence of sympathetic ophthalmia in *panophthalmitis*, the severest form of infectious inflammation, seems to be in apparent contradiction to these observations, especially since Schmidt-Rimpler proved by cultures the presence of staphylococcus pyogenes aureus in an eye affected with panophthalmitis for four weeks, and Schirmer in a case of metastatic panophthalmitis of three weeks duration. This has been utilized as an important argument against Deutschmann's theory. There are, however, some cases of sympathetic ophthalmia after panophthalmitis observed lately by Schirmer, Scheffels and Deutschmann. The latter (*Beitrage z. Aug.* 10 p. 50) assumes with Leber, that in panophthalmitis the microorganisms are removed with the flow of pus out of the perforated globe, or are destroyed by the profuse suppuration, and with Gifford, that the lymph-channels become obstructed by the accumulation of puss and fibrinous products, thus impeding the migration of micro-organisms. In those cases in which panophthalmitis creates sympathetic ophthalmia, Schirmer surmises a mixed infection with the hypothetical coccus of Sattler, which ordinarily is destroyed by the more virulent staphylococcus. Deutschmann suggests instead of the coccus any bacterium which is more apt to follow the tract of the optic nerve, than the staphylococcus pyogenes is in man.

Such a mixed infection is also to be supposed in sympathetic ophthalmia after *gonorrhœic* and *tuberculous* iritis, as in all the cases so far published a corneal perforation occurred which allowed the invasion of other microbes.

The sympathetic inflammation of the second eye appears in two forms: Sympathetic uveitis in its various fashions and localizations, and papillo-retinitis. Both may be combined; often the latter may not be visible on account of opacities of the media, especially when associated with choroiditis. Schirmer mentions only five cases in which papillo-retinitis preceded the uveitis, and thinks that papillo-retinitis alone is very rare and gives a much better prognosis than uveitis. Its dependence on the sympathizing eye was shown by the fact, that after enucleation it healed rapidly, though not at once as in sympathetic irritation. From this Schirmer infers that it is produced by toxines, and if caused by micro organisms the inflammation will spread to the uveal tract.

Deutschmann found that *neuritis and neuroretinitis* of the second eye are more frequent than formerly supposed. The examination of human eyes which have been removed after they had given rise to sympathetic ophthalmia, revealed that neuritis and perineuritis were the rule. The discs of Deutschmann's rabbits were reddened and under the inner medullary stripe four to five yellow prominent choroidal spots of the size of a pin's head owing to circumscribed round cellinfiltrations of the choroid.

As a typical *ophthalmoscopic* picture of sympathetic ophthalmia, Hirchberg (*C. Bl. F. A.* 1895, p. 80) describes light foci in the periphery, slightly resembling the specific patches, which may also be observed in the eye first affected. Casper (*Klin. Mon. f. Aug.* 1895, p. 179) saw an

analogous condition in a case of sympathetic disseminated choroiditis.

Sympathetic inflammation of the uveal tract appears as iritis serosa, iritis plastica, irido-cyclitis, plastica or maligna, irido-choroiditis, or they may pass from one into the other. All three parts of the uvea are generally affected, as autopsies have shown, but often during life the condition of the choroid cannot be ascertained. The disease mostly starts in the iris, but it may also advance from behind forward. If uveitis posterior or anterior are primary, the explanation by the migration theory is: Through the perichoroideal space, perhaps from the posterior pole of the globe along the sheathes of the long ciliary vessels the microbes or their toxines may rapidly advance to the anterior portion of the uveal tract and display earlier the clinical symptoms, before the process at the optic disc becomes noticeable. The serous iritis is not as malign as the plastic uveitis which shows a tendency to relapses, always leaving the eye in a worse condition than before, and mostly ends in atrophy of the globe.

Sympathetic ophthalmia does not set in before fourteen to eighteen days after the affection of the first eye, generally in four to six weeks. A maximum interval cannot be set down as a rule, but the longer the intermediate time the more the probability, that the disease of the second eye is of an idiopathic nature. A phthisical eye without any signs of irritation does not cause sympathetic ophthalmia. If after several years an affection of the second eye occurs, the first eye has never been quiet, or it shows some recent inflammation, either by a new infection or a revival of micro-organisms, which have been latent like spores, or from time to time increase to such an extent that they cause a new inflammation.

Quite a number of cases are published in which sympathetic ophthalmia broke out within three to four weeks after preventive enucleation, optico-ciliary neurotomy or neurectomy. In two of Nettleship's cases enucleation was performed one to two days after the injury, but the latter had extended also to the orbit and caused inflammation of the orbital tissues, and this gave rise to the sympathetic affection seven and five weeks afterwards. When the sympathetic ophthalmia exists before enucleation even in a slight degree, the latter does not prevent its malignity. It has been anatomically proven, that both ends of the optic nerve after neurotomy become again united and that a regeneration of the ciliary nerves takes place in that way, that from the central stumps numerous twigs grow into the sclera and the sensibility returns. Therefore if the ciliary nerve theory is wrong and the optic nerve exclusively conveys the virus or sympathetic ophthalmia, then, according to Scheffels, (*Klin. Mon. f. Aug.* 1890) an early and thorough resection of the optic nerve must prevent sympathetic ophthalmia in all cases. Should the latter occur only in one case of resection rightly performed, the whole theory of migration through the optic nerve falls to the ground. Trousseau observed such a case of sympathetic ophthalmia with ensuing blindness two months after resection of the optic nerve of 4 to 5mm. length.

Deutschmann, presupposing a reunion of the stumps, considered this question of such principal importance, that he undertook new experiments for its explanation. (*Beitraege*, hft 10). A piece of three to four mm. of the left optic nerve of rabbits, which was 14 mm. long from the chiasma to the globe, was resected, i.e. the 4-5 to 3-5 part of the whole length, corresponding to Schweigger's claim for effectual neurectomy of ten mm. of the human optic nerve, which measures 38 mm. Two months later one animal died accidentally. Immediately after death he injected ¼ of a Pravaz's syringe of India ink into the subdural space of the skull, and 15 minutes afterward India ink was found in the intervaginal space of the whole right optic nerve. The ends of the left optic nerve were connected by a tract of connecting tissue 2 mm. long, in which as well as in both ends India ink was seen down to the globe. His deductions were: Resection of the optic nerve permanently destroys the nervous conduction, but the nerve ends become reunited by connective tissue. It communicates with the central and peripheral vaginal spaces and leads the lymph current from the brain to the bulbar end more slowly and not as readily as in the normal vaginal space, but without essential difficulty" (p. 27). He further assumes, that microbes or their toxines may proceed against the lymph current from the globe to the chiasma as

well as the India ink did with the lymph current to the globe. At the instance of these experiments Wagenmann (*v. Græfe's Arch.* 41, i, p. 182) modified the regular resection by thorough cauterization of the peripheral end of the resected optic nerve in order to increase the protection undoubtedly furnished by neurectomy, but leaves the proof to later experiments. Velhagen (*Arch. f. A.* 29, No. 14) imitated Deutschmann's experiment, but with opposite results. Staining fluid injected 5 weeks after neurectomy into the arachnoidal space under high pressure did not ooze from the central optical stump, which was tightly sealed by cicatrical tissue. He infers from this, that, if the mode of cicatrization in man is similiar to that in rabbits after neurectomy, no micro-organisms from the interior of the globe can enter the central optical sheath after a lapse of time sufficient for cicatrization.

The migratory theory has met with opposition mostly by Schmidt-Rimpler (*l.c.*), who observed two cases of sympathetic ophthalmia, one and a half years after optico-ciliary neurectomy, and mentioned as the chief point, that no micro-organisms were found in the resected piece nor in the globe which was afterwards enucleated, so that no micro organisms could have migrated to the other eye. Nordensen, Berry, Ayers, Alt, Randolph, Kuhnt, Ohlemann, Greef, Uhthoff, Schirmer did not find micro-organisms in the eyes which had been removed after sympathetic ophthalmia had taken place. Positive in regard to bacteria in enucleated eyes were the investigations of Limbourg, Levy, Sattler, Snellin, Leber, Abraham, Story, Angelucci, Basevi, Secondi, Waldispuehl, Berry, and Finlay, who used Knapp's material. Deutschmann found micro-organisms in all cases observed in three years after publication of his monograph. (Staph. alb., slender bacteria, clumsy bacilli). Cultures made of two cases showed staphylococcus pyog. aur. He does not infer from this the staph. to be the producer, but thinks that the frequency of obtaining the staph. in cultures is due to a mixed infection with this coccus. In regard to the fact, that not all succeeded in finding micro-organisms in the eye which had been enucleated on account of causing sympathetic ophthalmia, Deutschmann 1, questions whether those eyes really caused sympathetic ophthalmia, the diagnosis being one of probability only. 2d, Micro-organisms often cannot be found any more in eyes, in which they effected great changes, creating their own destruction. 3d. In cases of undoubted sympathetic ophthalmia the interior of the injured eye may be free from micro-organisms, although it is infected, but they are found in the optic nerve, in the intervaginal space and on the surface of the globe. From here, *i.e.*, from Tenon's capsule the microbes may enter the intervaginal space of the optic nerve and migrate to the second optic nerve and globe, as demonstrated by recent experiments of Deutschmann, in accordance with Quincke and Zellweger. Deutschmann had used in his experiments spores of aspergillus fumigatus, croton oil, pus, then cultures of staph. pyogen. aureus and albus, and of streptococcus. Alt produced sympathetic ophthalmia, with abrus prægatorius — injections into one eye; Gayet with pus of the tear sac; Basevi with bacilli from enucleated human eyes, which had given rise to sympathetic ophthalmia; Parisotti with staphylococci. The only track (also found by Gifford) between both eyes, which contained continuously the inoculated bacilli is the intervaginal space of the optic nerves and their sheathes. Deutschmann had in his first series of thirty-five experiments twelve positive results, *i.e.*, thirty per cent.; of the last thirty-five only two; and considers it as experimental luck to obtain positive results, emphasizing the rare occurrence of sympathetic ophthalmia even after severe infections of human eyes. Ohlemann found of 556 severely injured eyes of Schweigger's clinic only two which had given origin to sympathetic ophthalmia.

The objection has been made that the presence of cocci found in the optic nerves, the sheathes and in the intervaginal spaces was due to a general infection. But no observer ever found micro-organisms in the optic sheathes of patients or of animals, who had died from a general infection, and Deutschmann is of opinion, that if it ever should happen, which, however, is not probable, as then the staph. pyog. would be propagated by the blood vessels, not the lymphatics, they would be found perhaps in single foci, but not in continuous accumulations pervading the whole optic sheath, as in his animals.

Schmidt-Rimpler's theory of sympathetic ophthalmia is, that the irritation of the ciliary nerves of the injured eye gives only the disposition to sympathetic inflammation of the second eye by reflex disturbances of circulation and nutrition. The longer and the more marked these changes exist, the more and better prepared is the eye for the action of inflammatory (bacterial or chemical) agents. But there is no proof that mechanical irritation of the ciliary nerves causes inflammation of the second eye, (if there is no infection combined with it,) as incarceration of the iris in corneal or scleral wounds, or chronic glaucoma in which patients suffer from the most violent irritations of the ciliary nerves, or as the case of Pincus, (*l. c.*) in which an intraocular cysticercus kept up constant irritation of an eye for fourteen years, without creating sympathetic ophthalmia before the infection by the operation happened.

The *migration theory* explains best the long interval between the injury and the outbreak of sympathetic ophthalmia, as the microbes require some time to travel from one eye to the other. If sympathetic ophthalmia sets in three to four weeks after enucleation, the microbes had left the first eye at the time of enucleation, and are on their way on the optic nerve to the second eye. Deutschmann adds to his experiments a description of a case which furnishes the most valuable proof for his migration theory. After an iridectomy, which by infection terminated in phthisis bulbi, sympathetic ophthalmia of the other eye started with neuro-retinitis, afterwards opacities of vitreous, ciliary injection and irido-cyclitis, resulting in almost total blindness. The patient died of carcinoma of the stomach. Micro-organisms in both eyes, chiasma and both optic nerves showed that the optic nerves furnished the passage for their transmission. The micro organisms were bacteria, the species of which could not be ascertained.

Hirschberg (*l.c.*) supposes a creator of granulation tissue (bacillus), as the anatomical examination of recent diseases of the injured eye shows a similarity with tuberculosis (giant cells, granulation tissue) and not the cocci of suppuration. It requires further investigations to determine the producer of sympathetic ophthalmia.

All authors, even those who do not accept Deutschmann's experiments as convincing proof in regard to the way of propagation, consider the sympathetic ophthalmia as an infectious disease, so that it will express best the present state of the pathology and etiology of sympathetic ophthalmia, if we quote Deutchmann's conclusions of his latest work (p. 95:) "Sympathetic ophthalmia, as it was called, is a process of microphytic origin, propagated in the continuity of tissues from one eye to the other by the optic nerve; exceptionally a chemical action may be communicated from one eye to the other on the same track." He suggests instead of sympathetic inflammation, a name designating the disease better: ophthalmia migratoria.