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ICAL REVIEW OF THE SUBJECT.

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PRESBYTERIAN EYE AND EAR HOSPITAL, BALTIMORE; OPHTHALMOLOGIST TO THE  
BALTIMORE AND OHIO RAILROAD.



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IT is seldom that we meet a case where all the conditions are favorable for thoroughly testing the truth of the infectious origin of sympathetic ophthalmia, and I am satisfied that the case here reported, together with the laboratory experiment, form a valuable supplement to my earlier work on this subject.

The following typical case of sympathetic ophthalmia came to the Presbyterian Eye and Ear Hospital early last summer.

J. M., forty-one years old, farmer; while endeavoring to dig out a large stone deeply imbedded in the earth, a piece of the pick broke off and flew into his right eye. This was on June 1, 1891. He kept on, however, with his work though seeing very indistinctly with the wounded eye. He was not conscious of any pain at the time. He continued regularly at his farming for three days longer, when pain and dimness of sight compelled him to rest. He came to the hospital on the fifth day. At this time he had only light-perception left in the wounded eye. The eye was exceedingly sensitive to the touch. He remained in the hospital three days, and left with directions what treatment to follow, and with the understanding that he should return in case the pain persisted. After he had been at home six weeks, and suffering all the time, his good eye began to show signs of sympathy,

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photophobia, lachrymation, and dimness of vision, and according to his account he could not see a horse a hundred yards away. Before this he possessed unusually acute vision. His family physician treated him with blisters and cold applications to eye, and sight improved. Thursday, August 13th, he came to the hospital again, and the condition of his eyes was as follows :

In the injured eye light-perception was gone. Eyeball very sensitive to touch. At the point of the wound, the sclera was injected, cornea clear, pupillary margin entirely bound down by adhesions to anterior capsule. His good eye had a vision of  $\frac{1}{200}$ . The anterior capsule showed abundant inflammatory deposits upon its surface, together with numerous evidences of old iritis all around the pupillary margin. Indeed, it was difficult to make out the fundus with any distinctness on account of the general dirty appearance of the lens. He complained of great pain in forehead and in the region behind the nose. He was persuaded to have the eye enucleated, and I prepared to have everything ready to make cultures from the vitreous and anterior chamber.

The eye was removed, and after sterilizing with a hot knife a point at the corneo-scleral junction not far from the wound, I entered the anterior chamber with a spade-knife, which had been sterilized by passing it several times through an alcohol flame. I withdrew the knife and followed it with a platinum wire loop, which was stirred up in the anterior and posterior chambers of the eye, and *smear* cultures on agar were made, also three Esmarch tubes.

These tubes were subjected to the proper temperature in an oven for as long as ten days, and not a sign of growth showed itself. Prof. Welch, Dr. Flexner, and myself each examined cover-slips made from the vitreous and anterior chamber, but discovered no organisms.

I then obtained a rabbit, and made a small opening into the anterior chamber with an iridectomy knife. I may add that all the instruments were thoroughly sterilized. An iris-forceps was introduced into the anterior chamber of the enucleated eye, and a regular iridectomy was performed. I found the iris very hard to pull away from its adhesions to the lens capsule, but managed to draw out and cut off a good-sized piece of the iris. This latter was then forced into the anterior chamber of the rabbit's eye, and moved about several times in the chamber, and partly drawn out and left.

In one week's time, with the exception of a slight blush about

the wound, the rabbit's eye showed no evidence of disease, and in two weeks this injection had faded entirely away, and only a slight prolapse of the iris at this point gave any evidence of the operation. The cornea remained clear throughout, and the prolapsed iris was simply the result of the manipulation, and in no way interfered with the functions of the eye,—just what we sometimes see in cataract-operation without iridectomy. During the operation I took pains to bruise the tissues about the incision, thus imitating, as far as possible, the conditions peculiar to a penetrating wound of the eye.

One cannot read the literature of this subject for a single year without being struck by the want of certainty that exists as to its exact nature, and I mean that this has been the case every year even since Deutschmann's experiments. The solution proposed by Deutschmann and the history of his experiments are praiseworthy, and few scientific articles may be read with more interest by all medical men than his contribution to the pathogenesis of sympathetic ophthalmia. Let me review briefly his experiments.

The earlier experiments of Deutschmann were made with the spores of the *aspergillus fumigatus*, and consisted in making repeated injections of a suspension of this organism into the corpus vitreum of a rabbit. Choroido-iritis followed the first injection, and at the end of four weeks, or a few days after the fourth injection, he discovers choroido-iritis and opacities in the vitreous of the fellow-eye. The animal is killed, and the microscopic examination confirms the diagnosis. Evidences of inflammation are seen throughout the inoculated eye. Interstitial inflammation of the optic nerve extending up to the chiasm, with an involvement of the latter, is seen, the process passing on down to the other eye by way of its optic nerve. The iris and ciliary region of the sympathetically affected eye were not examined. The posterior half of the eyeball shows abundant signs of inflammation in round-cell infiltration. He concluded therefore that a sympathetic inflammation may be produced in one eye by the introduction of infectious matter into the other eye, and that the track of this inflammation is along the optic nerve and its sheaths. Inasmuch, however, as he

regarded the inflammation resulting from the inoculation with the *aspergillus fumigatus* as the result of chemical irritation, and knowing that such irritation is rarely, if ever, concerned in the production of sympathetic ophthalmia, he resorted to the pus organism for the inoculating material. He injects two or three drops of a suspension of *staphylococcus aureus* into the vitreous of one eye. The animal dies of meningitis on the third day. To avoid this complication, he uses a very dilute suspension of the same organism and experiments on five rabbits. Only one of the animals gives a negative result, negative in so far that after remaining alive for several weeks no change was observed in the fellow eye.

Meningitis does not occur in any of these cases, but all the rabbits die of general infection at periods ranging from five or six days to three weeks. As regards the microscopic examination, round-cell infiltration with micrococci were to be found in both optic nerves and chiasm and in the posterior half of second eye; a typical case of sympathetic ophthalmia, he concludes, in all but one feature, namely, in the non-participation of the iris and ciliary region of the second eye. And the reason the iritis is absent is because the animal dies before the organisms have time to reach the anterior portion of the eye.

In reading the account of these experiments one is forcibly struck with their simplicity; and in these five experiments the result of each one never fails to confirm the result of the foregoing, so that after coming to the end of Deutschmann's work one feels that there is strong reason to believe that the theory is proven. I doubt whether any scientific problem in pathology has ever been proven so smoothly.

The nature of sympathetic ophthalmia has always been an interesting topic of discussion among ophthalmologists, and when Deutschmann's work appeared in 1882 it can be imagined with what satisfaction the account of his experiments was read and how generally they were accepted.

As is always the case in experimental pathology, any special solution of a problem is subjected to verifying tests at the hands of different observers. Such has been the fate of this class of work for years, and it is no uncommon thing to

find what seemed a valuable discovery fall into disrepute simply because it could not stand the test in the hands of others. And such a course is right, as any one can readily see. The explanation of any phenomenon in medicine only becomes valuable when that explanation can be verified by others than the originator. The things in the science of medicine which remain are those things which have been proven by many, both in the laboratory and in the hospital, and the things which have been discarded and are forgotten are those things which have been found worthless except possibly in the hands of one man.

Such striking and uniform results as those which attended the experiments of Deutschmann would seem to promise an easy confirmation, and it was almost with this conviction that I entered upon the experiments published in these ARCHIVES three years ago (vol. xvii., 187-213). The first parallel experiments of Deutschmann's work were made by Dr. H. Gifford,<sup>1</sup> of Omaha, who at the time he was engaged in this work was serving as one of Horner's assistants in Zürich. I shall not go into an account of his experiments in detail, but will simply state that after repeating Deutschmann's experiments on seventeen rabbits, he failed on any point to confirm the work of the latter. Eighteen months later I commenced my own work on this subject, and after spending many months in a series of thirty experiments I obtained nothing but negative evidence from Deutschmann's point of view.

For the first few months I used dogs as subjects, as I supposed they would be less likely to succumb to the effects of a general infection, and in consequence would enable me to follow out more accurately the theory, and my results proved that I was right, as none of the animals, with the exception of one case, showed any evidence of constitutional disturbance. Until this time the character of my work had differed in only one point from that of Deutschmann, namely, in the fact that mine were made on dogs. Thinking that this difference might impair the value of my work as a control of that of Deutschmann, I concluded to repeat his

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<sup>1</sup> *Ibid.*, vol. xv., 281-295.

experiments on rabbits. This line of experiments consisted of fifteen in number, and they resulted just as did the first series; in other words, at no time during the life of the animal could any sympathetic disturbance be detected in the second eye, and though an ophthalmoscopic examination was made every day the fundus of the second eye never indicated the slightest departure from the normal, and I may add that the microscopic examination only served to strengthen this state of the case.

My work then, so far as verifying the results of Deutschmann's experiments, resulted negatively. As I remarked in my previous work on this subject, the microscope always showed infiltration of the intraocular end of the infected eye. A moment's glance was sufficient to tell me that. The excess of the nuclei present over what is seen in the normal condition was too apparent to be mistaken, but any noticeable progress of this increased nucleation for more than a short distance from the eye was never observed.

Mazza<sup>1</sup> experimented also upon rabbits and guinea-pigs, but reports only failures from Deutschmann's point of view. Nor did this observer notice any change in the second eye with the ophthalmoscope. In those animals that had died of meningitis cocci were to be found in the optic nerve and its sheaths.

And finally I would call attention to the work of Limbourg and Levy<sup>2</sup> of Strassburg. These experimenters inoculated twenty-five rabbits and seventeen guinea-pigs after the method of Deutschmann. As the changes in the inoculated eye resembled precisely those observed in my own experiments, I shall only allude to the condition of the second eye. To use their words "as regards any changes in the second eye which could be looked upon as sympathetic, none were observed with the exception of a very doubtful hyperæmia of the fundus. The examination for organisms was in every case negative." Their work simply confirms my own. It is surprising that the authors after finishing such a valuable piece of work did not feel themselves justified in

<sup>1</sup> *Bericht über den VII. Internat. Ophthal. Congr.*, zu Heidelberg, 1888.

<sup>2</sup> *Archiv. f. experiment. Path. u. Pharmak.*, Bd. xxxviii., S. 153-166.



drawing any further conclusion than as follows: "It follows from these experiments how difficult a thing is the experimental investigation of this question."

It would seem that Limbourg and Levy were so influenced by Deutschmann's views as to distrust their own work, and yet their experiments were far more exhaustive than those of the latter. Even if they did not feel warranted in expressing in so many words their doubts as to the value of Deutschmann's work, they certainly had a right to conclude that it is impossible by the method employed to produce a sympathetic ophthalmia in a rabbit.

As regards the discovery of organisms in an eye which has been enucleated for fear of sympathetic disease in the other eye, experience differs widely, and even this point is too often decided in the negative to admit it as an additional support of the germ theory of the disease. Deutschmann rarely failed to find organisms in an eye enucleated to avoid sympathetic trouble, and though I have examined at least a score of such eyes I have succeeded in detecting organisms in but one case, and that was when the injury dated only two weeks back, a fact which has led me to conclude that the very questionable agency of micro-organisms in the production of sympathetic ophthalmia is rendered more unlikely when the sympathetic disturbance makes its appearance from two to six months after the injury.

Ohlmann<sup>1</sup> records recently having examined thirty eyes enucleated to avoid sympathetic disturbance, and in not a single one did he find organisms.

It should be remembered that sympathetic ophthalmia is a very rare disease. I can safely say that, in by far the majority of cases where I have performed enucleation, it has been on an eye which had been sightless for many months, certainly for many weeks and frequently for years, and this I feel sure has been the experience of most ophthalmic surgeons. In other words, enucleation is practised almost invariably as a precaution against the disease, and when we consider how all-pervading organisms are, is it not strange that, if they are really factors in this disease, they do

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<sup>1</sup> *Archiv. f. Augen.*, Bd. xxii., 1.

not begin their work sooner, or is it not stranger still that in the majority of cases they accomplish nothing? When we consider the fact that organisms have almost certainly been introduced into all eyes which have been destroyed by penetrating wounds, and furthermore that a large number of such patients have carried these sightless eyes for a long time,—when we consider this, there remains a striking lack of anything like cause and effect between the opportunity offered the organisms to do their work and the actual occurrence of the disease. These remarks though are simply by the way, for I do not desire to pronounce myself positively against the infectious origin of the disease.

As to the experiments on rabbits, guinea-pigs, and dogs, the weight of evidence goes to show that not only is there no analogy between the disease, as seen in man and these animals, but that sympathetic ophthalmia cannot be produced in these animals through the agency of the staphylococcus, and that consequently such a character of experiments can throw no positive light on the subject.

It is unaccountable how Deutschmann discovered in every case such uniform conditions of neuritis extending along both optic nerves including the chiasm. Professor Deutschmann, no doubt, rejects the possibility of having mistaken the normal for the pathological condition, but I would again, as in my former work, emphasize the fact, that there is no question about the difficulty of differentiating unless one has at hand sections of a nerve which are known to be *normal*, and with which we can compare the supposed pathological section.

The rabbits, it will be remembered, all die at the end of two or three weeks, and in consequence the chief distinguishing feature of a neuritis at this stage is the increase in nuclear elements, and upon this point we must mainly rely in making our diagnosis. Changes in the *nervous* bundles are not readily demonstrable features of a neuritis of three weeks' duration. And though one will invariably detect an increased number of nuclei at the intraocular end of the infected eye, one will be astonished to find on comparing such a section with a normal eye what an enormous number of nuclei are present in the latter (physiological condition).

But, apart from this, in the light of all the control work that has been put upon this subject, and with nothing but negative results, it seems unreasonable to look upon the infection theory as demonstrated by the experiments of Deutschmann as anything yet awhile but an idea.

And finally, to return to my experiment in the laboratory. It seems to me that this is a most valuable test of the question as to what rôle bacteria play in the production of the disease. We have here an undoubted case of sympathetic ophthalmia, and if bacteria in the injured eye gave rise to the sympathetic trouble, it is reasonable to suppose that the means employed to discover them would have been successful, and that the experiment on the rabbit would at least have suggested something which might be regarded as positive evidence.

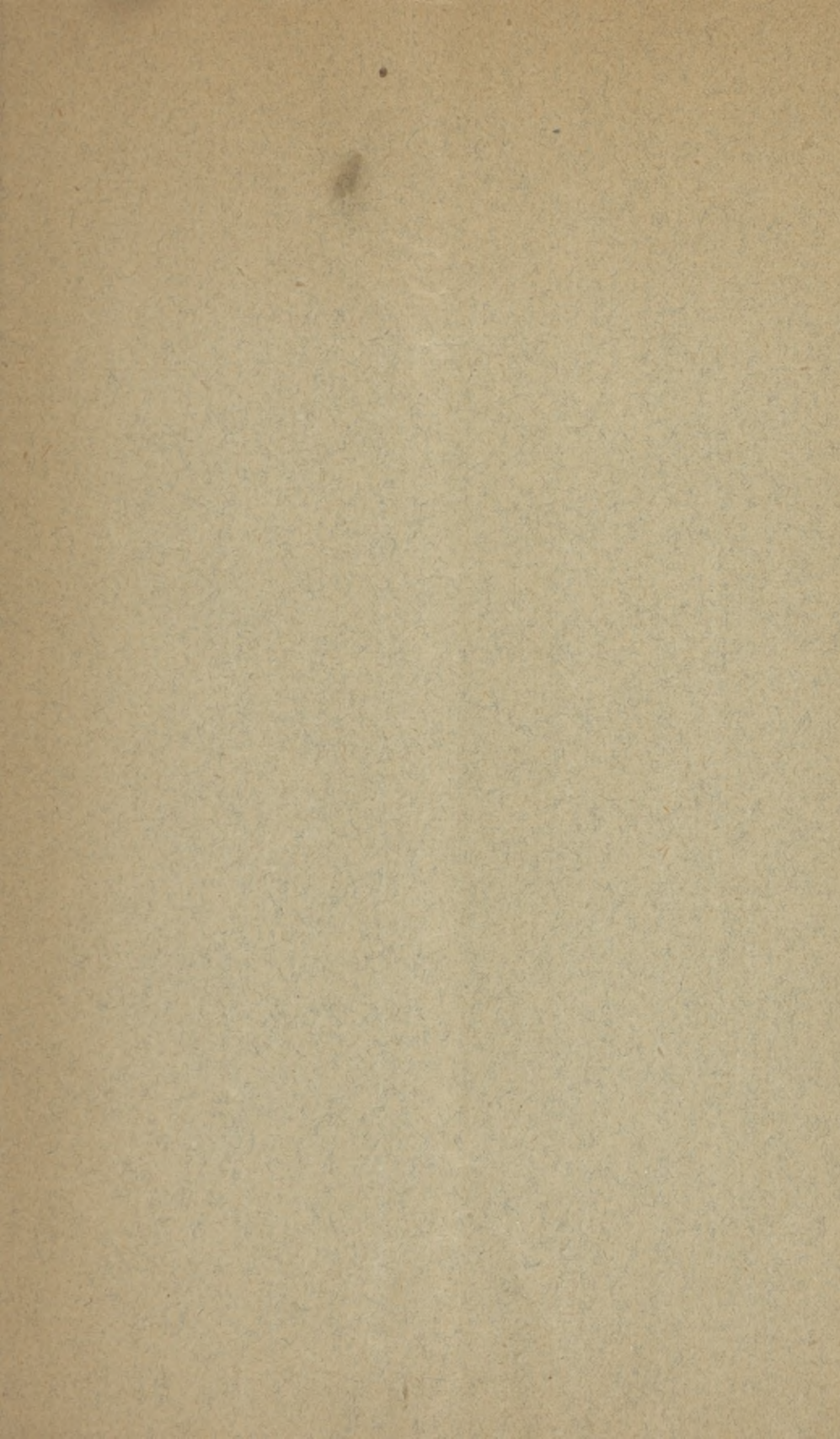
The reasonableness of the infectious origin of sympathetic ophthalmia no doubt accounts for the general acceptance of the theory, but we ought to recollect that this theory owes almost its entire support to a few experiments with the pus organism. And if there is an organism which we might almost predict would not produce the disease it is the pus organism. Purulent inflammation of the eyeball, in a word "panophthalmitis," where the pus organisms are most abundant, as a rule do not give rise to sympathetic ophthalmia.

As I have said before, I do not wish to be regarded as absolutely arrayed against the infection theory, but against the theory only so far as the pus organism is concerned. There are many organisms about which we know nothing, with which it might be possible to produce the disease in animals; and, again, sympathetic ophthalmia may have its own specific organism.

It is possible too that the disease is not of bacteric origin, but that an organism of some other class may be present. And again, we have strong reason for believing that the lower animals do not have sympathetic ophthalmia, just as they do not have many other diseases peculiar to the human race.

The experiment here recorded I regard as strong proof against the views set forth in the work of Deutschmann.





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