A CASE OF ACUTE STREPTOCOCCAL ENTERITIS.

BY

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THE case we are about to describe is of interest, on account of its resemblance to cases of so-called ptomaine poisoning. We are indebted to Dr. J. W. F. Jewell, of Balham, who had charge of the patient, for the following history of the case:—

Clinical History.—A gentleman travelled by train from Scotland to London. On the journey he partook of tinned fruit, and was seized, some six hours later, with vague pains in the abdomen. The pains gradually increased, and in fifteen hours after the first symptoms intense diarrhoea and vomiting supervened. When first seen by Dr. Jewell, twenty-five hours after the onset, he was completely collapsed, but conscious, and complained of agonising pain in the abdomen and over the region of the heart. The pulse was scarcely perceptible and the heart sounds were almost inaudible, the respirations 60 a minute, the lips blue, the face congested, the temperature in the groin was 105°. Brandy and milk were administered by the mouth, and $\frac{1}{2}$ gr. of morphine was given hypodermically. In about half an hour the sickness and diarrhoea stopped and the pain in the abdomen was relieved. Injections of strychnine and digitalis revived the pulse, and the cyanosis was relieved by inhalations of oxygen. About an hour and a half before death he suddenly got worse, and although transfusion with saline solution revived him for a time, he gradually became unconscious, and died thirty hours after the first onset of the symptoms.

Necropsy.—A *post-mortem* examination, at which one of us was present, was made by Dr. Jewell ten hours after death. About 2 pints of turbid fluid were found in the peritoneal cavity. The mucous membrane of the stomach was slightly congested, but not more than could be accounted for by the constant vomiting. The mucous membrane of the first 4 feet of the small intestine was deeply congested and cedematous, and was blackened in patches. The intestines contained a moderate amount of liquid material. There was hypostatic congestion of the lungs, and the endocardium was blood-stained. The rest of the organs appeared quite normal. There was no wound or abrasion in the skin, with the exception of minute punctures produced by subcutaneous injections. Specimens of the heart blood, the peritoneal fluid, the liver, and the wall and contents of the first part of the small intestine, were collected in sterile tubes under the usual aseptic precautions.

Microscopical Examination.—The intestinal contents were examined microscopically, and showed a large number of streptococci in addition to other bacteria. The juice from the wall of the affected portion of the small intestine was examined microscopically, and showed a moderate number of streptococci, but no other bacteria. The heart blood showed, on microscopical examination, a large number of cocci in chains and pairs, and a few large bacilli. Inoculations were made in broth, on the surface of agar, and in the depth of glucose-gelatine. In all the tubes pure cultivations of streptococci were obtained. The juice from the liver showed, on microscopical examination, many cocci in chains and in pairs, and a few large bacilli. Inoculations were made in broth, on the surface of agar, and in the depth of glucose-gelatine. In all the tubes pure cultivations of streptococci were obtained. The peritoneal fluid showed, on microscopical examination, a few bacilli, but no cocci. Inoculations were made in broth, on the surface of agar, and in the depth of glucose-gelatine. In all the tubes cultivations of the bacillus coli were obtained. Sections of the small intestine showed the presence of diplococci and streptococci.

Inoculation Experiments.—The streptococcus isolated from the liver and heart blood was cultivated upon various media, and gave all the characters of the streptococcus pyogenes. A mouse inoculated subcutaneously with $\frac{1}{2}$ c.cm. of a broth cultivation died in three days with streptococci in the blood and organs. Another mouse fed upon bread soaked in a

broth cultivation was not affected. A rabbit and a guinea-pig inoculated with 1 c.cm. of a broth cultivation suffered from transient cedema at the seat of inoculation, from which they recovered.

REMARKS.

In this case the symptoms were those that are usually attributed to ptomaine poisoning, that is to say, to the ingestion of toxic products of bacteria. The bacteriological examination pointed to an actual infection with streptococci starting in the wall of the jejunum. They were found in large numbers in the intestinal contents, in the tissues of the inflamed portion of intestine, in the blood of the heart, and in the liver. The streptococcus, as far as morphological and cultural characters were concerned, was similar to the streptococcus pyogenes; it was pathogenic to mice on subcutaneous inoculation, and produced transient local lesions in a rabbit and guinea-pig. The bacillus, which in addition to the streptococcus was found in small numbers in the blood and liver, was probably an anaerobic putrefactive bacillus growing only at the temperature of the body. It did not grow in broth or on agar at 37° C., nor in the depth of glucose gelatine at 20° C.

Booker,¹ in an investigation into the causation of infantile diarrhoea, attributes some of the cases to infection with a streptococcus. Tonarelli² describes a form of enteritis with typhoid-like symptoms caused by a streptococcus. The introduction of cultivations of this streptococcus into the stomach of rabbits after previous alkalisation of the contents, caused diarrhoea followed by death. At the *post-mortem* examination a blood-stained serous exudation was found in the peritoneal cavity, and there was hyperæmia of the mucous membrane of the intestine without ulceration. Streptococci were present in the exudation and in all the organs. Hirsch³ describes a fatal case of diarrhoea in a child in which streptococci were present in large numbers in the faeces during life, and were found in the heart blood and in the organs after death. The streptococcus isolated was difficult to cultivate, and would not grow on ordinary broth or gelatine. It was pathogenic to white mice. Tavel and Equet and de Cérenville have also ascribed cases of enteritis to the presence of a streptococcus.

REFERENCES.

¹ Johns Hopkins Hospital Reports, Vol. vi. ² La Riforma Medica, 1896, Nos. 97 and 98. ³ Centrabl. für Bact. xxii, 14 and 15.

THE DIAGNOSIS OF DIPHTHERIA OF THE CONJUNCTIVA.

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DIPHTHERIA of the conjunctiva is supposed to be a rare affection in Great Britain, although known to be common in some other countries—as Northern Germany and Southern France—where it is especially frequent during epidemics of throat diphtheria. No age is exempt, but it attacks for the most part young children, probably because they are more exposed to infection than older people. According to statistics, females appear to be slightly more liable than males. The ailment, as a rule, is bilateral, but an interval, amounting to some days, generally elapses before the second eye suffers. It is frequently associated with diphtheria of the fauces, nose, or other parts. It is prone to affect those whose powers of resistance have been lowered by some recent illness—as measles, scarlet fever, or whooping cough. It has been often observed to follow impetigo of the face or lids, but this may be a mere coincidence, seeing how common the latter are among unhealthy children. A foregoing affection of the conjunctiva, as trachoma or phlyctenular disease, predisposes, it is thought, to its development. The connection, however, can scarcely be a very close one.

The two following instances of conjunctival diphtheria, which have been carefully followed throughout their course, have recently fallen under my notice.

F. A., aged 4 years, was brought to the ophthalmic department of the North-Eastern Hospital, on February 9th, 1898, on account of her left eye, which had been inflamed for seven days. The child was delicate. She had suffered from empyema about two years before she came under my

notice, but had had no recent illness. Nobody else in the house was affected. When examined her state was found to be as under: The lids of the left eye were red, swollen, and half-shut, but they could be everted without any particular difficulty; a certain amount of thin yellowish-white discharge was present about them. The conjunctiva of the lower lid was covered with thick, semi-opaque membrane, detached and lying loose along the palpebral margin; a similar membrane was observed to cover the superior *cul-de-sac*. Cornea clear; no chemosis. The angular glands were slightly but equally enlarged upon the two sides. No changes detected in throat or nose; no discharge from vulva. The general state of the child appeared to be good. Cover-glass preparations made from the membrane, and stained with carbol methylene blue and with weak fuchsin, showed a few cocci and diplococci, together with a larger number of bacilli, in some instances segmented. The latter retained their colour when Gram's method was employed. Tubes of agar-agar and of blood-agar were smeared with morsels of membrane, and placed in the incubator. Meanwhile, pending a precise bacteriological diagnosis, the inflamed eye was washed six times a day with sublimate lotion (1 in 5,000), while the everted lids, previously freed from membrane and discharge, were painted once a day with a 2 per cent. solution of silver nitrate.

The culture tubes were examined twenty-four hours after inoculation, when the agar-agar was found to show colonies of two kinds: (1) largish yellow, and (2) smaller grey. The former were made up of cocci, and the latter of bacilli, both staining by Gram. One of the blood-agar tubes contained four discrete greyish-white colonies, the diameter of which measured from 1.5 to 2 mm. These, when examined with the microscope, were found to consist of bacilli indistinguishable from those of diphtheria. A second tube of blood-agar included numerous colonies, of which some were yellow (staphylococcus pyogenes aureus), some white (staphylococcus pyogenes albus), and others greyish-white (Klebs-Loeffler bacilli, long variety). Subcultures upon various media were made from these different colonies, but no other organisms were found. The last step was to inoculate a couple of tubes of neutral broth with an agar subculture of the Klebs-Loeffler bacilli. After two days at 37.5° C., an abundant growth was obtained, while the fluid manifested a markedly acid reaction.

There being now no doubt as to diagnosis, the child was admitted to hospital on February 12th, and placed in the diphtheria ward. According to the notes made by Mr. C. G. Burton, house-surgeon, the temperature was 99° F., pulse 100 and respirations 28. General condition good. Patient walked to hospital. Mouth, nose, tonsils, and pharynx normal; no laryngeal symptoms. Submaxillary glands enlarged upon left side, but scarcely to be felt on the right side of the neck. No cough; no physical signs in chest. Skin showed no rash. Urine, 1015, acid, urates, but no albumen. 10 c.cm. antitoxin injected. The affected eye to be washed every four hours with a lotion containing to each ounce of water 4 gr. of quinine and 2 drops of sulphuric acid. Treatment of no other kind adopted.

February 13th. There is still membrane upon the conjunctiva, but it is easily washed off; swelling of the lids and redness of eye less marked. Urine contains no albumen. Child talks and plays with her toys.

February 14th. Knee-jerks present.

February 15th. The eye is better, although a piece of membrane was again found to have formed this morning. Mr. Burton carefully banded the affected eye, with a view of preventing infection of its fellow.

February 16th. Lids still a little puffy, but child opens eye widely. Palpebral conjunctiva thick, red, and smooth; no membrane present. Urine contained no albumen. Ung. hydr. oxid. flav. cum atrop., bis die.

February 20th. Slight amount of mucous discharge from left eye, the conjunctiva of which is still rather red and thick. Temperature, bowels, and urine normal. Appetite good. Conjunctiva of left eye to be painted once a day with a 2 per cent. solution of silver nitrate.

February 25th. The cornea is clear, and the eye now seems to have little the matter with it. Knee-jerks present. General health good. Discharged from hospital, and mother requested to bring the child to the out-patient department from time to time.

March 23rd. Child attended at hospital. Left eye free from any redness or discharge. Knee-jerks present. Urine, acid. No albumen. The mother stated that for a few days after the child had left hospital she noticed a little blood-stained secretion run from the left nostril, but that this soon ceased.

M. R., 10 months old, was brought to the Ophthalmic Department of the Evelina Hospital on February 25th, 1898. Her right eye, so it was stated, had been red and swollen for five days, although there had been but little discharge. The child, who was fretful and looked ill, had not suffered from measles, whooping-cough, or scarlet fever. For the past four months, however, she had been under treatment for bronchitis and "running ears." Upon inquiry it was ascertained that a brother, aged 6 years, had developed a diphtheritic throat in September, 1897, and on that account had been sent to an isolation hospital. He was returned at about Christmas, and had been living in the same house as the patient since. Upon examination of M. R., the lids of her right eye were noticed to be swollen and half closed, and to have traces of dried secretion about them. When they were drawn apart, threads of glutinous discharge were seen to stretch from one lid to the other. The palpebral conjunctiva was red and thick, and on everting the somewhat indurated upper lid (which could be done with more or less difficulty) a thin greyish pellicle could be observed to cover the upper *cul-de-sac*. The membrane could be readily wiped away, but was speedily reproduced. The cornea was intact, and there was no chemosis. The right preauricular gland was not involved, but the corresponding angular glands were rather enlarged. No membrane was found either on the tonsils or the uvula. There was some colourless discharge from the nostrils and ears, but this was not offensive to the sense of smell. Cough was severe and frequent; no physical signs in chest save a few rhonchi; respirations 44; pulse 116; nothing abnormal detected in heart: urine, acid, no albumen. Knee-jerks well-marked. Temperature 98.6° F. Cover-glasses smeared with a morsel of the detached membrane and stained in the usual way showed a few cocci and bacilli, but none of the latter were beaded. As I suspected that the inflammation might be of diphtheritic nature, the child was admitted to Charlotte Ward. She was placed upon milk diet; no application except distilled water was used to the eye; and 4,000 units of antitoxin were at once injected. Meanwhile two tubes of blood serum were inoculated with membrane and placed in the incubator. After

twenty hours each contained a limited number of colonies, of circular outline, discrete grouping, and of white colour. After the lapse of three days a few of these were found to be sulphur-coloured, and the others porcelainous white. The first-named, when examined with the microscope, were found to be made up of cocci, and the second of bacilli, both staining by Gram. Subcultures upon various media (agar-agar, blood-agar, gelatine, and broth) were made, and the sulphur-hued colonies were eventually found to consist of staphylococcus pyogenes citreus, while the white ones were composed of short Klebs-Loeffler bacilli.

February 26th. A piece of membrane was removed from the right upper lid to-day.

February 27th. Eye much better; no membrane on lids. Child fretful, and cough troublesome. Knee-jerks present. Temperature 97.6° F.

February 28th. Pulse 120, respirations 22. Urine acid; no albumen, no deposit.

March 1. Child is very fretful, crying incessantly, except when asleep. Voice rather hoarse. There is still some little discharge from the right eye. Knee-jerks present. Temperature 97.2° and 101.4° F.

March 2nd. The conjunctiva of right eye, although rather red, looks almost well, and there is no discharge. Child opens eye easily. Nothing amiss with throat. Knee-jerks present. Temperature 99° and 97° F., pulse 138 and 124, respirations 30 and 36. Patient allowed to leave hospital.

March 11th. Child brought out to out-patient department to-day, and found to be in good health. The right eye appeared to be normal in all respects.

DIAGNOSIS.

In considering the question of diagnosis, we must at the outset recognise the clinical fact that the severity of conjunctival diphtheria varies much. Thus, its signs are sometimes of so trifling a nature that they may be easily put down to a wrong cause, unless associated with diphtheria elsewhere, or followed by nervous sequelae. On the other hand, they may be so decided that the cornea may be destroyed within twenty-four hours; even life itself may be lost, although a fatal result does not seem to have been recorded unless diphtheria of other parts was also present. These latter cases are the only ones that have been looked upon as diphtheria of the conjunctiva—at all events until recently, when bacteriological researches have become more or less general.

Similar differences in regard to severity, it is well known, occur in many other inflammations of the conjunctiva. It would be a truism to say that in diphtheria of the conjunctiva (as in all ailments due to microbes) the clinical appearances must depend upon the relationship that exists between two factors: (1) the virulence of Klebs-Loeffler and of any associated germs; (2) the resisting powers, local and general, possessed by the patient. There is experimental proof that the virulence of certain bacteria may be heightened or lowered according to environment, as in Marmorek's well-known and widely quoted experiences. That observer found that the pathogenic powers of the streptococcus pyogenes might be exalted to a high pitch by alternately growing it in guinea-pigs and in a medium made of human blood-serum and bouillon, while even a highly virulent culture soon lost its malignant properties when grown *in vitro*. As to the second point, every practical surgeon knows that the clinical appearances of a particular affection will vary according to the patient's age, family tendencies, state of health, and so forth.

We must, I think, now recognise, with certain Continental writers, that diphtheria of the conjunctiva may clinically be met with under three forms—namely, the interstitial, the superficial membranous, and the merely catarrhal.

Indeed, the diagnosis of conjunctival diphtheria is by no means so simple an affair as one might at first sight be inclined to think. The history of the case may sometimes lead one to a correct conclusion. There may, of course, be a clear history of infection, as when a physician engaged in examining a diphtheritic throat, is so unlucky as to have a morsel of the specific membrane coughed into his eye. In such an event, the presumption will be that any resulting inflammation in the physician's eye will be of diphtheritic nature.

As an instance of the same sort take, again, a case related by Fuchs: A child, labouring under throat diphtheria, was placed in the children's ward of a general hospital. The consequence was that, whereas the patient's right-hand neighbour developed faucial diphtheria, his left-hand neighbour soon showed symptoms of conjunctival diphtheria. Therefore a clear history of infection, when it can be got, is of great value in helping towards a correct diagnosis. In the same sort of way, importance must be attached to the prevalence of diphtheria in the neighbourhood whence the patient comes or the house where he lives, as in the case of M. R.

The coexistence of diphtheria of the fauces, nasal or buccal mucous membrane, skin, vulva, or elsewhere, would suggest the nature of the eye mischief; but, even then, proof as to the identity of the two affections would be lacking in the absence of a bacteriological examination. The occurrence, within two to five weeks after inflammation had subsided, of loss of knee-jerks or of pareses in various parts of the body would be almost conclusive² with regard to the nature of the antecedent eye ailment. Such cases have been recently recorded in England by Mr. Silcock,³ Dr. Collins,⁴ and others. But these signs, valuable though they be, come too late to be of any service from the therapeutic point of view, which is all-important now that we possess antitoxin. In diphtheria of the fauces or larynx, as everybody knows, the urine is often found to contain albumen from an early period of the disease, and this sign would be helpful if it chanced to coincide with a membranous conjunctivitis, as in cases lately reported by Dr. W. J. Collins⁴ and by Mr. Percy Flemming.⁵ Albumen, however, has not been present in any of my patients. Indeed, in this particular form of disease, as in wound diphtheria, the existence of albumen is possibly the exception rather than the rule. Still, it is always advisable to test the urine of any patient who presents membrane upon an inflamed conjunctiva.

One must recollect that the mere presence upon the palpebral conjunctiva of a false membrane is not conclusive as to the nature of the inflammation. As a matter of fact, a fibrinous exudation may take its appearance in almost any form of conjunctivitis, supposing the inflammation to be severe enough to give rise to a coagulation necrosis. For example, it is not unknown in the purulent ophthalmia of the newly-born, as pointed out by Chaisaignac⁶ many years ago. It forms an almost constant sign of the inflammation set up by pneumococci; it is sometimes seen in that form of conjunctivitis which is associated with Weeks's bacilli; while I have observed it along with pus cocci, as in a case recorded by me in the *Lancet* of November 13th, 1897. Apart from these acute conditions, there is a curious chronic affection, where a thick greyish, fibrinous exudation is seen upon the palpebral conjunctiva for weeks or months together. The malady does not seem to be contagious, generally occurs in delicate children, and sometimes implicates the cornea. Instances have been reported in this country by Hulme,⁷ Mason,⁸ Hogg,⁹ Nettleship,¹⁰ Critchett,¹¹ Juler,¹² Bronner,¹³ and Stanford Morton.¹⁴ Then, there is the fact that false membrane may follow injuries to the conjunctiva, whether mechanical or chemical. Lastly, cases have been published by Sourdille,¹⁵ Aubineau,¹⁶ and by H. Coppez,¹⁷ where Klebs-Loeffler bacilli were present, but membrane was absent. Hence there is nothing in the least pathognomonic about the presence (or absence) of these fibrinous conjunctival deposits. Neither can any conclusion be safely drawn from the naked-eye characters of the film, which in diphtheria is sometimes but lightly adherent to the mucous membrane, whereas at other times it can be peeled away with difficulty or not at all. Any attempt to base a diagnosis upon the state of the underlying conjunctiva when the membrane has been stripped off appears to me fallacious. At all events it could only be in the most pronounced cases, where the subconjunctival tissues were densely infiltrated ("brawny"), that a conclusion might, with tolerable certainty, be reached as to the nature of the diseased process. The existence of small, dusky-red hæmorrhages, scattered over the surface of the diphtheritic plaques, has been a notable feature in some of my cases, although not observed in the present ones. For my part, however, I should hesitate to lay any great stress upon the point.

It is now well known that the preauricular glands (between which and the conjunctiva there is a direct connection) are liable to become involved in various forms of conjunctivitis. Some few years ago I¹⁸ described a case of unilateral conjunctival diphtheria, in which the corresponding preauricular gland was swollen and markedly tender. But further experience has convinced me that no dependence is to be placed upon this sign, since the glands in question sympathise more or less with many of the severer conjunctival inflammations, especially when due to such organisms as tubercle bacilli and gonococci. For that matter, it was not observed in the two cases that form the text of the present communication. A similar remark applies to implication of other glands, as those

about the angle of the jaw, which may or may not be enlarged.

In short, as it seems to me, the diagnosis of this ailment must be grounded upon one feature only—the presence of *diphtheria bacilli*. If these are found there can be no reasonable doubt as to the nature of the case, while their absence, after repeated and careful examination, tends to show that one is dealing with some other malady. In the latter event, a conclusion must be based on (a) the organisms demonstrated in membrane or discharges from the eye; (b) the general features of the inflammation; (c) the history of the case. In conjunctival diphtheria, then, as in diphtheria of the fauces and elsewhere, the discovery of Klebs-Loeffler bacilli must be regarded as the only certain, trustworthy, and scientific way of diagnosing the disorder, a fact that I have emphasised elsewhere.¹⁹

It is hardly necessary to make any remarks as to the method of identifying the bacillus in question, since that is so well understood at the present time. I will merely say that in conjunctival diphtheria the making of cultivations should not be employed to the exclusion of simpler means. Morax²⁰ has pointed out (and I am in a position to confirm his statement) that in a certain number of cases the discharge from the eye contains only that microbe which is the cause of the inflammation. Hence, in marked instances, examination of film preparations has brought to light such numerous and characteristic Klebs-Loeffler bacilli that he has been able at once to affirm the nature of the disease. There is one other point that should certainly be alluded to—namely, the confusion likely to arise between Klebs-Loeffler bacilli on the one hand and xerosis bacilli on the other. The latter are to be found in very many cases of conjunctivitis, and so marked is their resemblance to diphtheria bacilli that a mistake may be easily made if the investigation be not conducted with an eye to the fallacy.

Briefly, the main points of distinction are these:

1. Both stain by Gram's method, but in my experience the diphtheria organism loses its gentian violet, when in alcohol, much more quickly than the xerosis bacillus.
 2. Klebs-Loeffler bacilli, according to Dr. Eyre,²¹ give rise to an acid reaction when grown in neutral bouillon or milk, while xerosis bacilli never do.
 3. The xerosis organism when inoculated into guinea-pigs, causes nothing more than a swelling at the site of puncture.
- The last test (3) cannot, of course, be carried out except under licence from the Secretary of State.

NOTES AND REFERENCES.

- ¹ Fuchs, *Textbook of Ophthalmology*, 1894, p. 84. ² A similar form of paralysis may follow measles, typhus, and typhoid, so that it cannot be taken as wholly conclusive of a preceding diphtheria. At the same time, it may occur as a sequel to the mildest attacks of diphtheria, and is much commoner after that than after other zymotic disorders. ³ Silcock, *St. Mary's Hospital Gazette*, December, 1896. ⁴ Collins, *Lancet*, June 27th, 1896. ⁵ Flemming, *Lancet*, October 2nd, 1897. ⁶ Chaisaignac, *Ann. d'Oculist.*, 1847. ⁷ Hulme, *Med. Times and Gazette*, October 31st, 1863. ⁸ Mason, *Oph. Hospital Reports*, 1871. ⁹ Hogg, *Lancet*, March 1st, 1873. ¹⁰ Nettleship, *St. Thomas's Hospital Reports*, 1880. ¹¹ Critchett, *Trans. Ophth. Society*, vol. iii, p. 1. ¹² Juler, *ibid.* ¹³ Bronner, *Trans. Ophth. Society*, vol. xiii, p. 26. ¹⁴ Morton, *Trans. Ophth. Society*, p. 29. ¹⁵ Sourdille, *Rev. des Mal. de l'Enfance*, 1895, p. 68. ¹⁶ Aubineau, *Essai sur l'Applic. de la Sérothérapie dans le Trait de la Diphthérie Conjunctivale*, Paris, 1895. ¹⁷ Coppez, *Rev. Gén. d'Ophthalmologie*, 1896, p. 51. ¹⁸ Stephenson, *Medical Press and Circular*, March 23rd, 1892. ¹⁹ Stephenson, *Epidemic Ophthalmia*, 1895, p. 12 (Young J. Pentland, London and Edinburgh). ²⁰ Morax, *Ann. d'Oculist.*, April, 1895. ²¹ Eyre, *Journal of Pathology and Bacteriology*, July, 1896, p. 54.

SYMPATHETIC OPHTHALMIA.*

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SYMPATHETIC ophthalmia is to be sharply defined from sympathetic irritation, the latter being recognised by functional changes only in the second or sympathising eye, while sympathetic ophthalmia is always characterised by visible organic changes of the nature of irido-cyclitis. Sympathetic ophthalmia never comes on in less than a fortnight from the time

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