

The bacteriology of conjunctivitis / by S. Hanford McKee.

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McKee, Samuel Hanford, 1875-1943.
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Publication/Creation

[Philadelphia] : [Lea Bros.], 1906.

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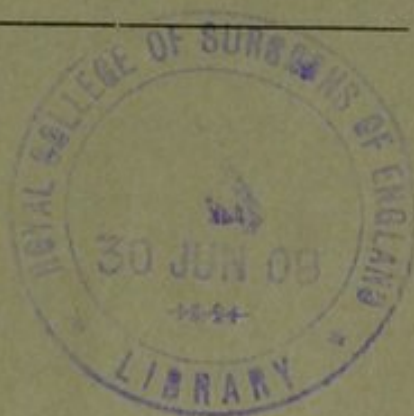
The Bacteriology of Conjunctivitis.

BY

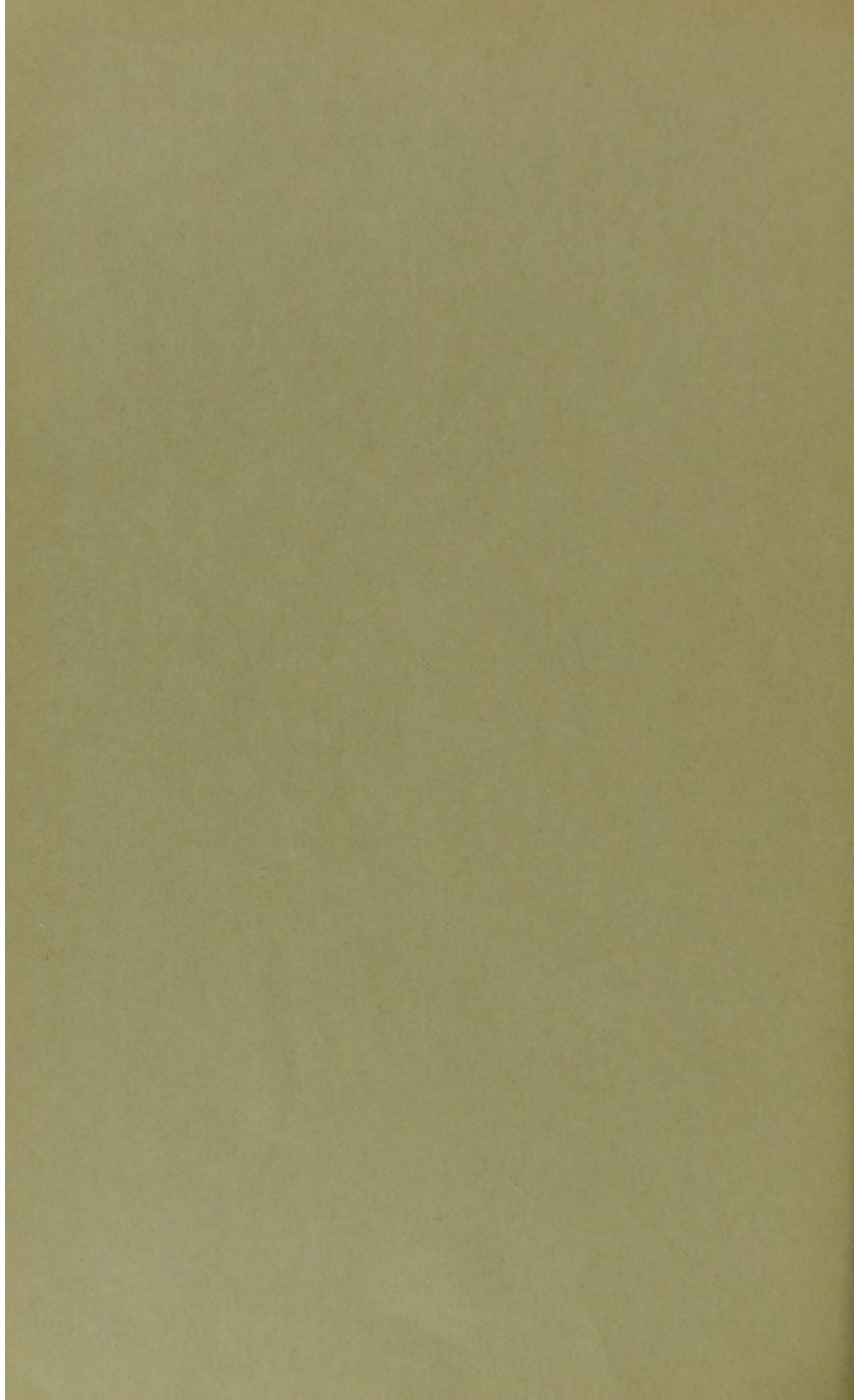
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FROM THE
AMERICAN JOURNAL OF THE MEDICAL SCIENCES,
JUNE, 1906.





THE BACTERIOLOGY OF CONJUNCTIVITIS.¹

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BACTERIOLOGY had no sooner made its appearance in medical science than ophthalmologists looked in this direction for knowledge to help clear up misunderstood conditions of the diseased conjunctiva.

In 1883 Koch, while working on the cholera epidemic in Alexandria, examined the conjunctival discharge in some cases of Egyptian ophthalmia. He found there two micro-organisms, a diplococcus, very similar to the gonococcus, and a very fine bacillus, which resembled the bacillus of mouse septicæmia. Two years later Weeks, of New York, had an opportunity of seeing numerous cases of acute conjunctivitis. In the conjunctival discharge he constantly found this short, fine bacillus which Koch had seen in Egypt. Weeks proved this bacillus to be the etiological factor in this form of conjunctivitis.

In 1886 Morax and Axenfeld separately described a diplobacillus, which they believed was the cause of a chronic form of blepharoconjunctivitis. This opinion was shortly afterward concurred in by Peters and Gifford.

In 1894 appeared the work of Parinaud and Morax on pneumococcus conjunctivitis, followed two years later by reports from Axenfeld, Gasparrini, and Gifford. From this beginning, some twenty years ago, the study of the bacteriology of the conjunctiva, both in health and disease, has gone steadily on, until to-day in many of the continental clinics, especially in those of Germany, a thorough bacteriological examination of the conjunctival secretions forms part of the routine work.

At the Montreal General Hospital we have been following this work in bacteriology for some time past. All cases of conjunctivitis, hyperæmia of the conjunctiva, and cases for operation are examined by means of smears and the inoculation of media.

¹ Read before the Montreal Medico-Chirurgical Society, November 3, 1905.

The work begun by Axenfeld, Uhthoff, Morax, Weeks and Gifford has borne such fruit that the old classification of conjunctivitis, according to clinical features, into catarrhal, purulent, membranous, granular, phlyctenular, with their sub-divisions, is passing, and to-day the different forms are receiving their names according to pathological and bacteriological findings.

While we are still unable to bring all cases of conjunctivitis under this classification it enables us to divide conjunctivitis into two groups.

1. Conjunctivitis with no known bacteriological cause: as conjunctivitis from foreign bodies, errors of refraction, trachoma, follicular conjunctivitis, spring catarrh.

2. Conjunctivitis with a definitely known bacteriological cause: as blennorrhœa from the gonococcus, streptococcus, pneumococcus, bacillus coli communis, conjunctivitis from Morax-Axenfeld's diplobacillus, Koch-Weeks bacillus, pneumococcus, bacillus of diphtheria, streptococcus, bacillus of influenza, and pseudo-gonococcus.

To discuss this second group separately and in detail would, in a paper of this kind, be out of place. Such forms as conjunctivitis from streptococcus, the bacillus coli communis, the bacillus of ozæna, the diplococcus of meningitis, Friedländer's bacillus, and the bacillus mucosus capsulatus are all exceedingly rare. These forms are of more interest as possibilities than important as factors in conjunctivitis, and for this reason I feel that they may be justly passed over.

The bacteriology of the different forms of blennorrhœa is well known, hence I shall take up here the three most common and important forms of conjunctivitis, describe the bacteriological causes and clinical pictures, and discuss the therapy to which each best reacts.

1. *Conjunctivitis caused by the diplococcus lanceolatus or pneumococcus.* This form was first described by Parinaud and Morax in 1894. Two years later appeared the reports of Axenfeld, Gasparini, Pichler and Gifford. This affection favors northern climates, appears at the coldest seasons of the year, and is often associated with coryza. It has been seen following measles (Haertel 3 cases).

The clinical picture, as pointed out by Axenfeld, varies greatly in severity. The inflammatory signs may be very slight, and the disease may run its course in a few days. Such a case was the only one I have seen here:

A woman of middle age who came to the Out-patient Department at the Montreal General Hospital, and gave a history of having had an unpleasant feeling in the eyes for some two days. The clinical picture was hardly that of a conjunctivitis, yet from a smear hundreds of encapsuled, lanceolate diplococci, positive to Gram's stain, were seen.

In this mild form the disease may run its course in a few days, or it may increase in intensity simulating a severe blennorrhœa. As a rule, though, the clinical picture is as follows: Both eyes involved. Slight red-rose œdema, with increased watery secretion, followed by a severe, purulent discharge and intense swelling of the lids. A pseudomembrane may develop, and often there are small phlyctenular formations about the corneosclerotic margin. Small hemorrhages are common, especially about the upper lid.

The diagnosis can be easily made by making a smear on a glass slide in the following way: with a platinum needle one takes a loop-full of pus from the conjunctival sac proper, not from the edges of the lids, but preferably from the inner canthus. The pus is smeared well over a glass slide and "teased" out so that perhaps the whole slide is covered. It is then dried, fixed by passing three times through a flame, and stained by Gram's method as follows: aniline gentian violet 25 secs., washed with water; Gram's iodine 15 secs., washed with alcohol until no blue comes away, washed with water, counter-stained with safranin, 5 per cent. solution, 5 secs.

The slide is then dried and examined with an oil-immersion lens. Pairs of small, oval, or lanceolate organisms will be seen lying free or in the pus cells. They will be found positive to Gram's stain. The broad ends of the cocci will be seen in apposition, and one coccus may be larger than the other. The capsule in the smear preparations is generally well marked.

The appearance of the smear may be very characteristic, but I believe it is necessary here, more than in any other form of conjunctivitis, to inoculate media. On more than a few occasions I have seen pus that gave negative results on film preparations give pure cultures of the pneumococcus. The diplococcus of pneumonia is widespread pathologically and geographically; it is not necessary to enter into its cultural characteristics further than to say that it grows best on alkaline media, forming transparent, round colonies.

In the severe cases the disease seems to reach its height in five to six days, and after this there is an important lessening in the symptoms and in the appearance of the eyes. Corresponding to this change Axenfeld has shown that there is a lessening in the number or a complete absence of pneumococci. Here is where error as to the etiological factor is liable to occur. Examining the discharge at this time we shall find the ordinary pyogenic organisms and the bacillus xerosis, with the result that they will probably be put down as the cause of the conjunctivitis. The ordinary course of a pneumococcus conjunctivitis may be complicated by (1) ulceration of the cornea. This is a very serious complication, and one requiring the very closest attention and care. Happily, however, the infiltration of the cornea so often seen here but rarely goes on to ulceration. (2) Toxin iritis, set up without any abrasion of the cornea. Gasparrini saw a number of such cases in which the onset of the

iritis was marked by severe pain and swelling of the preauricular glands.

Axenfeld and Rymovitch report that the iritis may last some time after all conjunctival symptoms have disappeared. The possibility of either of these complications deserves more than a passing note, especially ulceration of the cornea, for it is now well recognized that eyes which have undergone a severe ulceration of the cornea are dangerous eyes, inasmuch as there is a possibility of their setting up sympathetic ophthalmia.

The treatment in pneumococcic conjunctivitis consists in the ordinary measures adopted in conjunctivitis cases.

In addition to this the application of a solution of protargol, gr. x-5j, to the conjunctival surface, and the instillation of drops of chloride of zinc, gr. $\frac{1}{2}$ -5j, are advised, while in severe cases anti-pneumococcus serum in doses of 10 c.c. forms a routine treatment in many clinics.

2. *Koch-Weeks Conjunctivitis.* In 1885 when in Egypt, working at Egyptian ophthalmia, Koch found in the purulent conjunctival discharge two different organisms. One, a diplococcus, was very similar to the gonococcus, while the other, a small bacillus, simulated the bacillus of mouse septicæmia.

In 1887 Weeks, of New York, reported having seen this bacillus in many cases of acute epidemic conjunctivitis, which seemed especially prone to occur in the spring and fall of the year. In the secretion from these cases he constantly found many fine bacilli, which he proved to be the cause of the conjunctivitis, but he was unable to cultivate it in pure culture. With a mixed growth of the bacillus xerosis he was able to set up a typical conjunctivitis. In 1890 he reported at Berlin that he had been able to grow the small bacilli in pure culture, and that he had seen it in over 1000 cases.

In 1894 Morax published his work on the cultural characteristics of the Koch-Weeks bacillus. He had inoculated his own conjunctival sac, and described the course of the disease.

Epidemics have been reported from many quarters. Hamburg supplied a large epidemic, which was studied by Wilbrand, Saenger, and Stachlin.

In 1897 Greeff had an opportunity of studying this form of conjunctivitis at the Charité Clinic in Berlin. Again, in 1899, a big epidemic in Czernowitz was reported by Kamen. He reported, also, that he had been able to grow the bacillus to many generations on human-blood serum.

The Koch-Weeks bacillus has been almost universally reported, until it is now recognized as the commonest cause of acute contagious conjunctivitis.

After an incubation period of two to three days Koch-Weeks conjunctivitis presents the following clinical picture: congestion of both palpebral and bulbar conjunctivæ; profuse mucopurulent

discharge, with chemosis and infiltration about the corneosclerotic margin. The discharge is profuse enough to simulate a blennorrhœa, without the œdema. Examination of the pus will reveal the etiological factor. Having smeared some pus on a slide, fixed it and stained as before described, we shall find in the pus cells, or lying between them, very fine Gram-negative bacilli, single or in groups. Their length varies between 0.5 and 2 μ , while their breadth is constant. Their corners are somewhat rounded. They resemble the bacillus of mouse septicæmia and the bacillus of influenza, but are thinner and longer than the latter. They stain well by a weak solution of carbol-fuchsin, ten minutes. (Axenfeld.)

These bacilli are not easy to find on the glass slide, and are very hard to cultivate. The colonies die out very quickly, never lasting more than three to four days. They grow only upon specially prepared media, and even then the growth is generally a mixed one. Agar with ascitic or hydrocele fluid and human-blood serum form the best media to cultivate them upon. On ascitic agar one sees, after twenty-four to thirty-six hours in the incubator, shiny, transparent points along the surface of the agar, very tiny and very hard to see.

Slides prepared from the growth show the bacillus of same size and shape, and with same staining qualities as the bacillus obtained from the conjunctival pus. Koch-Weeks conjunctivitis generally runs a course of three to four weeks, but may, of course, last longer and become fairly chronic. It is often much harder to cure in children than in adults. I can recall two cases occurring in children, in which, notwithstanding daily treatment, the disease ran a course of over six weeks.

The complications liable to occur here are ulceration of the cornea and iritis; fortunately these are seldom seen. Koch-Weeks conjunctivitis is one of the most contagious diseases we have to deal with in ophthalmology. The treatment here is the application of cold compresses, and the smearing of the conjunctiva with a solution of nitrate of silver. The application of the nitrate of silver was shown by Morax to greatly diminish the numbers of the bacillus.

3. *Conjunctivitis of Morax-Axenfeld.* This affection of the conjunctiva was first reported by Morax in 1896. He described the clinical picture, the etiological factor—a diplobacillus—and stated that with a pure culture of the diplobacillus he had been able to set up a typical conjunctivitis. During the Ophthalmological Congress in Heidelberg, in the same year, Axenfeld reported having studied this condition in fifty-seven cases which he had seen in Marburg. He also showed preparations of the diplobacillus which he had grown in blood serum. Morax called it “conjunctive-subaigue;” Axenfeld from its chronic qualities “chronischen diplobacillen conjunctivitis.” It is known as diplobacillary conjunctivitis of Morax-Axenfeld.

Since 1896 the presence of this form of conjunctivitis has been reported from many clinics, in different countries, until, at the present time, it is one of the best known and most frequently seen diseases of the conjunctiva in Europe. In America, too, its presence has been reported—in Philadelphia by de Schweinitz and Veasey, in St. Louis by Alt, and in Omaha by Gifford. Up to last summer its presence had not been noted in Canada, but since July, of one hundred and thirty-eight cases of conjunctivitis and hyperaemia of the conjunctiva examined, I have found forty-nine cases of Morax-Axenfeld conjunctivitis, showing it is a very common form in Montreal.

The first case I saw was typical enough to describe. A middle-aged woman, Canadian, housewife, came to the Out-patient Department of the Montreal General Hospital and complained that her eyes had been "sore" for the past five days. This was the first time she had ever had trouble with her eyes. The condition was as follows: both eyes involved; the edges of the lids showed marked blepharitis (blepharoconjunctivitis); the inner and outer canthi had a reddened appearance (angular conjunctivitis); the conjunctival sacs contained a small quantity of grayish-yellow discharge; palpebral conjunctivæ very injected; the superficial vessels prominent; while the slight involvement of the bulbar conjunctiva made the contrast marked. The picture was that of diplobacillary conjunctivitis, and I remarked to the chief of the clinic at the time that if a smear were made it would probably show the diplobacilli.

This was done, and the film was found to contain hundreds of square-cornered, Gram-negative diplobacilli, about 2μ long and 1μ wide. Culture tubes were inoculated and pure growths of the diplobacillus obtained.

This case serves to show well the clinical picture, which varies from little more than hyperaemia of the palpebral conjunctiva to marked blepharoconjunctivitis. The two eyes are generally successively involved. Beginning as a slight catarrhal condition of the lids diplobacillary conjunctivitis increases in severity, and in twenty-four to forty-eight hours there will be seen marked reddening of the lids, especially at the inner and outer canthi, some maceration of the skin, and, in the conjunctival sac, a varied amount of watery discharge, which gives the reddened lids a moist appearance. There is in this form of conjunctivitis an absence of conjunctival chemosis. Only to-day at the Out-patient Department of the Montreal General Hospital I saw three new cases which, taken together, were exceedingly interesting. Each case showed a somewhat different clinical picture, and still was characteristic. The first was hardly more than a hyperaemia of the conjunctiva, with marked lacrymation; the second was characterized by marked reddening at the outer and inner canthi; while the third case was one of marked blepharitis. Each of these cases gave a growth of the diplobacillus

on serum, and they are reported here to show how varied the clinical picture in diplobacillary conjunctivitis may be.

The diplobacillus of Morax-Axenfeld, while not hard to cultivate, grows best on blood serum. After twenty-four to thirty-six hours in the incubator one sees over the surface of the serum tiny depressions. The surfaces of these indentations are moist. They gradually spread, increasing in depth and width, gradually liquefying the blood serum. Besides blood serum the diplobacillus of Morax-Axenfeld will grow on agar mixed with ascitic or hydrocele fluid, serum agar, or serum bouillon, while Axenfeld and Erdmann now report having grown it on ordinary glycerin agar. Erdmann grew it on this medium to seventeen generations. The best and by far the most satisfactory medium, however, is blood serum.

The diplobacillus is not pathogenic for ordinary laboratory animals. I have tried in the laboratory at the Montreal General Hospital to set up a conjunctivitis. With a loop-full of a twenty-four-hour growth I inoculated the conjunctival sacs in a rabbit and in a guinea-pig, but not the slightest reaction followed. Later, with a needle, I abraded the corneal epithelium in the guinea-pig and inoculated the sac and cornea, with negative results.

For man, however, it is pathogenic. Morax set up a typical conjunctivitis in a colleague's eye.

Some two weeks ago I inoculated a conjunctiva, which I had proved to be free from bacteria, with a loop-full of a twenty-four-hour growth of the diplobacillus. I lost sight of the patient for some days, but when I saw him one week later he had a well-marked, typical, diplobacillary conjunctivitis. Smears were made and showed the diplobacillus, while cultures gave a pure growth.

This form of conjunctivitis is exceedingly chronic in its course. It will last for years. One patient, a French-Canadian, told me he had had sore eyes, with reddened lids, all his life. Even with treatment it is a matter of some four to six weeks' constant attention before the patient can be pronounced cured.

It was formerly thought that the course of diplobacillary conjunctivitis was never complicated by ulceration of the cornea, but within the last year a number of such cases have been reported. We had one case at the Montreal General Hospital. An elderly man, a farmer, came to the hospital and complained that six days previously he had struck his eye with a twig of a tree. He paid no attention to this at the time, and on the day following his eye was inflamed and painful. He consulted a physician, who treated him for five days and then sent him to Montreal. His condition upon admission was as follows: Right eye, central third of the cornea deeply ulcerated; edges infiltrated. The only parts of the cornea clear was a small area above; anterior chamber about half-full of pus; iris dull; pupil dilated; conjunctival sac full of grayish discharge. Upon entry the patient received the treatment for serpiginous ulcer

of the cornea. The following day I made a bacteriological examination of the pus, both from the ulcer of the cornea and from the conjunctival sac. Diplobacilli in hundreds were found upon each slide, and from the surface of the ulcer were the only bacteria seen. The slides from the conjunctival sac showed cocci as well, which, on culture, were found to be *staphylococcus aureus*. The diplobacilli were grown on serum, but did not grow on agar, which characteristic helped to exclude the possibility of the diplobacillus being that of Petit. The patient was put on instillations of sulphate of zinc, one-half per cent. The eye quieted down; the ulceration healed rapidly. This case is of more than ordinary interest because of the fact that here was deep ulceration of the cornea caused by the Morax-Axenfeld diplobacillus.

It was formerly held that when diplobacilli were the cause of ulceration of the cornea the ulceration would be very superficial, and the diplobacillus would be that of Petit. It has now been shown, however, that the Morax-Axenfeld diplobacillus will set up deep ulceration of the cornea. Paul and Erdmann recently reported the cases from the Breslau and Marburg clinics, respectively.

The treatment in diplobacillary conjunctivitis is, par excellence, irrigations and instillations with the sulphate of zinc, gr. $\frac{1}{4}$ to 1 gr. to the ounce. This is a specific for this form of disease, and in four to six weeks the patient will be absolutely cured. If the treatment be desisted in too soon, recurrence is bound to occur. It is chronic in every sense, but reacts quickly and well to zinc therapy.

But it may be here questioned what is the value of all this minute examination? Will not certain stock remedies cure all cases of conjunctivitis? Certainly not. I, for one, do not think that a glass slide and a microscope will clear up all the difficulties of the clinician, far from it; but I do feel that thorough bacteriological examination of all cases of conjunctivitis will give assistance enough to the clinician to well repay him for his time and work. To-day it is not enough to say because a patient is brought to you with a purulent ophthalmia that it is caused by the gonococcus of Neisser. We must here make smear preparations and inoculate media. Can anyone doubt the value of the knowledge as to whether in this secretion one finds the gonococcus, pseudogonococcus, pneumococcus, streptococcus, Koch-Weeks bacillus, Morax-Axenfeld diplobacillus, diplococcus of meningitis?

One knows immediately what measures are to be undertaken and obtains valuable knowledge in regard to the prognosis. We know to-day, in streptococcus and pneumococcus infections of the conjunctiva, that we must not overlook serum therapy, that streptococcus infection of the conjunctiva is liable to be a very virulent disease, and I believe the streptococcus like the gonococcus is liable to enter normal corneal epithelium. We know that pneumococcus conjunctivitis is not so contagious as some other forms; that Koch-Weeks

conjunctivitis will go like wildfire through a family, a very important matter in such institutions as schools, and asylums, or any place where large numbers of persons are brought together. We know, too, that the gonococcus, streptococcus, and pneumococcus are liable to set up ulceration of the cornea, with all its possible destructive action; that the Koch-Weeks bacillus and the streptococcus are liable to set up toxin iritis; that even diplobacillary infection may set up ulceration of the cornea. Coming to milder conditions, ophthalmologists know too well of the troublesome condition they see in patients who have, to all appearances, hyperæmia of the conjunctiva set up by some uncorrected error of refraction. This is corrected; astringent drops prescribed; you do everything you can—with only moderate relief. Finally, you make a bacteriological examination, and you find the diplobacillus of Morax-Axenfeld, so often seen in this condition. You now know exactly what you have to deal with, and how to deal exactly with it. In spite of my enthusiasm over this subject, I am not one who thinks that with the bacteriological examination of the conjunctival secretions we have the “be-all and the end-all here”—far from it, but I do feel that associating bacteriological methods with clinical knowledge is placing the diseases of the conjunctiva on a basis as practical as it is scientific.

I would here express my thanks to Dr. J. W. Stirling, from whose clinic I obtained this material, also to Dr. H. S. Birkett, who enabled me to obtain the bacteriological drawings.

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