**Pemphigus of the conjunctiva : report of a case with microscopic findings / by Walter Baer Weidler.**

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# PEMPHIGUS OF THE CONJUNCTIVA*

## REPORT OF A CASE WITH MICROSCOPIC FINDINGS

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Pemphigus of the conjunctiva is one of the grave diseases of the eye, and was recognized and diagnosed as such as early as 1800. Before this time it was classified with the urticarias and scabies, involving the face and eyes; many others considered it a xerosis of the conjunctiva. When this condition affects the eyes it is usually bilateral, although often unequal in the degree of severity.

There does not seem to be any constant relation between the duration of the skin affection and the development of the eye lesions. Pemphigus may affect the conjunctiva primarily, but this is rather rare, and in some of the cases so reported the lesions of the skin or mucous membranes may have been overlooked.

The course of the disease is usually very slow, extending over a period of years. Samelsohn[1] mentions a case that lasted over seven years, with little or no atrophy of the conjunctiva following, while, on the contrary, in Silcock's[2] case the one eye was completely destroyed in six weeks and the other one seriously damaged. There is no definite course or duration in pemphigus of the conjunctiva.

Crocker,[3] in speaking of pemphigus of the skin, mentions this disease as rare, occurring once in 500 cases in the skin dispensaries of England and America. It is more often seen in England and continental Europe. There are very many different forms of pemphigus, but perhaps pemphigus chronicus is most frequently seen. Typical cases of this peculiar form show oval bullæ, with

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1. Samelsohn: Ber. d. ophth. Gesellsch., 1878.
2. Silcock: Tr. Ophth. Soc. U. Kingdom, 1897, p. 1
3. Crocker: Text-Book on Dermatology.

tense walls and translucent contents usually bilateral, being most abundant on the face and trunk, often appearing in crops from ¼ to 1 inch in diameter with a tendency to coalesce. The duration of each bulla is a few days, but the disease may last indefinitely. In rare instances the disease may be localized in the conjunctiva. Pemphigus of the mucous membranes may appear in all of its forms, affecting the pharynx, larynx, nose and stomach.

In regard to the etiology of the disease, sex and heredity seem to be of little importance. Crocker inclines to the nervous hypothesis as an explanation for the eruption. Just what this defect is due to we are not as yet certain, but the vasomotor centers may be the root of the trouble, or, as Schwimmers concludes, it may be a trophoneurosis. The latest theory that has been advanced is that the toxins affect the nerve-endings.

## REPORT OF CASE

*Patient.*—Mr. L. L., aged 70, Russian, said that he had never had any trouble with his eyes until six months ago, and at that time he was able to read the newspaper with glasses. He was first seen by me at the Manhattan Eye and Ear Hospital, Oct. 3. 1910.

*Examination.*—Right eye. Vision: Patient counted fingers at 3 feet. The iris was brown and reacted very sluggishly to light; tension was normal. The edges of the lids were covered with a dried secretion, yellowish in color, which matted the lids together. The lids were thick and shrunken. There was total symblepharon (the lids united to the eyeball, to their edges). The opening between the lids was about 8 mm. The bulbar conjunctiva was thick and thrown in folds over the cornea. A small portion of the cornea was visible. The eye presented somewhat the appearance of an old trachoma, with atrophy of the conjunctiva.

Left eye: Vision 20/200. The pupil was 3 mm. in diameter; the iris was brown and reacted to light, accommodation and convergence; tension was normal. There was the same matting of the edges of the lids. The symblepharon was very slight and deeply placed in the culdesac. At the limbus of the cornea there were several small whitish areas which, when gently rubbed with an applicator, bled freely. The conjunctiva was red and swollen, with the appearance of edema at places. The corneoscleral margin showed a number of small bleb-like formations of a pearly white color. The rest of the cornea was clear.

Oct. 20, 1910: The condition of the right eye was unchanged, except that the symblepharon had contracted more and the

opening between the lids was smaller. The culdesac of the left eye seemed to be more shallow, movement of the lids less free, and it was almost impossible to evert the upper lid. There was always free bleeding of the conjunctiva on the slightest attempt to open the eyelids wide.

The shrinking grew steadily worse in the right eye until it was impossible to separate the lids. The shape of the eyeball seemed to be preserved as far as could be determined by palpation. There was a curious swelling in the upper lid, directly under the skin, which may have been an enlargement of the lacrimal gland. There was also edema of the upper lid, which lasted for about two weeks.

The bulbar conjunctiva presented spots of necrosis in the left eye which were white and bled very easily on the slightest attempt to make any examination of the eye. After bleeding, there was immediate ulceration and formation of synechia between the conjunctiva of the eye and the lids. The bulbar conjunctiva was slowly extending over the cornea. The small areas of necrosis with the ulceration and free bleeding, followed by the formation of synechia, and later by cicatrization and contraction, and finally, by symblepharon, which gradually became more and more complete, indicated the steady progress of the disease. The secretion of tears had been absent for about a week. The cornea showed small ulcer formations in the upper half, and the patient had noticed rapid loss of vision during the last week. Two weeks later the ulceration of the cornea was complete in the upper half, and the upper lid was tightly attached to the surface of the cornea. The vision was fingers at 6 inches. The eye was kept closed nearly all of the time and the patient complained of great pain, which was worse at night.

Frequent examinations of the urine were always negative. A von Pirquet vaccination was made, using the crude tuberculin in solutions of 10 and 50 per cent., but this gave no evidence of tuberculous foci in the body. The Wassermann reaction was also negative.

The pain and general discomfort increased with the gradual destruction of the eyes. The condition of the nose and throat was much worse and breathing became difficult. There was free bleeding from the nose whenever the patient blew his nose or tried to remove the crusts and scales. He was unable to get about by himself, and his general health and strength had been rapidly failing, and on examination of the body, three well-formed bullæ were found over the abdominal wall. The progress of the disease in the left eye was very rapid, involving twelve weeks in all to complete the destruction.

The patient was examined by Dr. Jonathan Wright, who reported as follows: "In the nose the whole of the visible walls of the cavity is covered by what looks to be a dirty, brownish, moist, shining membrane, but which is an exudate

evidently closely incorporated with the subjacent mucosa. It does not bleed and cannot be stripped off. There is evidently associated with the process a degree of fibrosis, which is manifested first, by the firmness with which the exudate or surface structure is bound to the subjacent parts; second, by the bloodlessness of the surface, and third, by the fact that at the back of the vestibule where the internal nasal chambers proper and their mucous surfaces begin, the introitus is much narrowed by a fibrous contraction. With this fibrosis there is no appreciable amount of deep infiltration, no true ulceration, no necrosis of soft tissue or of bone. There is a somewhat analogous lesion of the conjunctiva. There is no other lesion or history pointing to syphilis. It is not the clinical picture of membranous rhinitis, diphtheria, syphilis, or rhinoscleroma. The eye lesion resembles the blebs one sees in acute herpes or pemphigus of the throat. It resembles such a lesion as I have once seen accompanying a similar one of an acute nature in the nose and throat, which I believed was pemphigus."

The first case of pemphigus of the conjunctiva was reported by Wichman in 1800, and the next one to be reported was that of White-Cooper,[4] London, in 1858. Later, Stellwag[5] described a condition of the conjunctiva which he called "syndesmitis degenerativa." Kries[6] and von Graefe, speaking of this same affection, called it "essential shrinking of the conjunctiva." They thought that this condition was analogous to pemphigus, and this opinion is accepted by many to-day.

Pemphigus of the conjunctiva has been classed under four separate headings:

1. Cases with blebs on the skin.
2. Those with blebs on the mucous membranes.
3. Those with blebs on the conjunctiva alone.
4. Essential shrinking only.

Von Graefe has pointed out that there is an essential shrinking or atrophy of the conjunctiva which has not been preceded by hypertrophy. Many writers assert that this shrinking is really due to the formation of vesicles and bullæ on the conjunctiva; this theory is supported by Pflüger, Sattler and Gelpe.[7] The vesicles and bullæ were seen in the late stage of the case reported in this paper. The appearance of bullæ is rather the exception in the cases that have been reported, and this may be explained by the fact that the epithelium of the con-

4. White-Cooper: Roy. Lond. Ophth. Hosp. Rep., 1858. i.
5. Stellwag: Lehrb. f. Augenh., 1870, p. 413.
6. Kries: Arch. f. Augenh., 1878.
7. Gelpe: Klin. Monatsbl. f. Augenh., xxiii, 191.

junctiva is so soft and delicate that it cannot, like the skin, be lifted up in broad layers by the serous exudation, but ruptures and is thrown off in the form of shreds with the areas of necrosis following.

In pemphigus affecting the eye we find that the conjunctiva is usually attacked first. It is swollen and red, and one sees spots of coagulation necrosis. The discharge is free and the edges of the lids are usually glued together, and this recurs in a very short time after they have been carefully cleansed. There is some slight degree of photophobia and lacrimation, the latter being more marked in the early stage of the disease, but after the shrinking has begun the flow of tears is very much reduced and in the very late stage they are entirely absent. The inflammatory reaction extends into the subconjunctival tissues and we have the formation of new blood-vessels which bleed at the slightest effort to examine the culdesac. These inflammatory changes are not limited to the subconjunctival tissue; at times the tarsal plate may also be thickened and misshapen. The cornea is never attacked primarily and is affected only in the later stages of the disease. In some cases that have been reported there has been ulceration of the cornea, with perforation and prolapse of the lens and vitreous. At the very last stage of this disease we may find buphthalmia, staphyloma, panophthalmitis and phthisis bulbi.

In Pergens'[8] monograph on pemphigus of the conjunctiva he gives full records of 133 cases. The ages of the patients varied from infancy to 80 years. As a rule, there is no previous history that is of any assistance in making a diagnosis. The condition usually begins in one eye and involves the other later on. As regards the frequency of this disease, it is of interest to note that Steffen has seen 1 case in 84,000; Cohn, 1 in 50,000; Scholer, 1 in 50,000; Horner, 3 in 70,000; Baumler, 7 in 97,000; Pergens, 2 in 22,000; Franke, 5 in 45,000.

Since the publication of Pergens' report in 1901, I have found the records of the following additional cases:

Salva's[9] Case.—Woman, aged 63. The disease began in 1900. First appeared in the eyes, later in the mouth and throat and then on the skin. The conjunctiva showed small round ulcerations which stained with fluorescin and methylene-

8. Pergens: Pemphigus des Auges, Berlin, 1901.
9. Salva: La Clinique Ophth., 1904, x, 235.

blue. The culdesac became smaller and smaller; there were cicatricial bands, symblepharon and trichiasis. The cornea was ulcerated; pannus crassus and blindness resulted in 1902.

JOHNSON'S[10] CASE.—Woman, aged 53. The trouble followed nervous shock; eye began to give discomfort. She was first seen when there were adhesions between the lower lid and eyeball. The conjunctiva was dry and the cornea clear. The lens was cataractous. The soft palate, pharynx and epiglottis presented eruptions of pemphigus. Antisyphilitic treatment was of no avail. The eye was lost and the conjunctiva was replaced by a hard, dry, leathery tissue.

COPPEZ'S[11] CASE.—Woman, aged 23, with pemphigus of the conjunctiva, gums, cheek and uvula. Symblepharon formed and the lower two-thirds of the cornea became opaque.

KOERBER'S[12] CASE.—Pemphigus of the palate and glans penis. The lower culdesac was narrowed and attached to the eye by bands. Both corneas were clear. Culture showed diplococcus.

BROWN'S[13] CASE.—Woman, aged 48. Blebs were seen on the cornea. Patient died one year and a half after the first eye symptoms were noted.

ANDERSON'S[14] CASE.—Woman, aged 29. There had been acute pemphigus foliaceus since August, 1903. Conjunctiva and facial manifestations were seen in November. The skin and mucous membranes showed remains of the vesicles. They were seen in the culdesac, but no mention is made of any symblepharon formation.

NETTLESHIP'S[15] CASE.—Boy, aged 8, with symblepharon and scarring of four eyelids, six months in duration; no recurrence in four years.

OGILVY'S[16] CASE.—The patient was a farmer. The first attack lasted six weeks. The eyes were then quiet for six weeks. A second attack followed at this time; the cornea became opaque and the conjunctiva became shrunken with ectropion. Lanolin was used locally.

BANE'S[17] CASE.—The patient was under observation for two years. There was ectropion of the lower lid and cicatricial contraction of the conjunctiva, and in the middle third a symblepharon was forming. A conjunctival flap failed to check the progress of the disease. A portion of conjunctiva removed from the lower culdesac was examined by Todd, who reported that the specimen consisted of cicatricial granulation tissue.

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10. Johnson, R.: Jour, Eye, Ear and Throat, 1904, p. 60.
11. Coppez: Bull. de la Soc. Belg. d'Ophth., 1905.
12. Koerber: Centralbl. f. Augenh., 1905.
13. Brown: Ann. Ophth., 1904, xiii, 535.
14. Anderson: Tr. Ophth. Soc., 1904, p. 19.
15. Nettleship: Tr. Ophth. Soc., 1904, p. 22.
16. Ogilvy: Arch. f. Ophth., 1905, p. 277.
17. Bane: Ann. Ophth., 1908, p. 405.

Sherman's[18] Case.—Man, aged 68. Patient had had eye trouble for ten weeks. There was some slight discharge; the conjunctiva was slightly thickened in the lower lid. There were several areas of denudations and the culdesac was shallow. The condition progressed. Treatment: weak solutions of silver nitrate to lids and arsenic internally.

Adams'[19] Case.—Woman, aged 57. There was a free eruption and ulceration of the pharynx besides the conjunctival manifestation. Treatment consisted in the use of arsenic, atoxyl and fibrolysin. Transplantation in the culdesac was tried. The case ended fatally through rupture of pharyngeal eruptions.

Quint's[20] Case.—Patient, aged 16, had typical eruptions of pemphigus on the conjunctiva. There was a complete symblepharon in the left eye and partial in the right. The mucous membrane of the nose and throat presented similar eruptions.

Shumway's[21] Case.—Man, aged 40 (?). Besides the conjunctival eruption there was a general involvement of the skin and mucous membranes; broad symblepharon involving the inner third of the lower lid and a gradual extension of opaque tissue over the cornea. Bullæ were noted during the progress of the disease. No operation was attempted. The patient was under treatment for seven months.

Wollner's[22] Case.—The eruption was localized to the conjunctiva. The patient was under observation for three years.

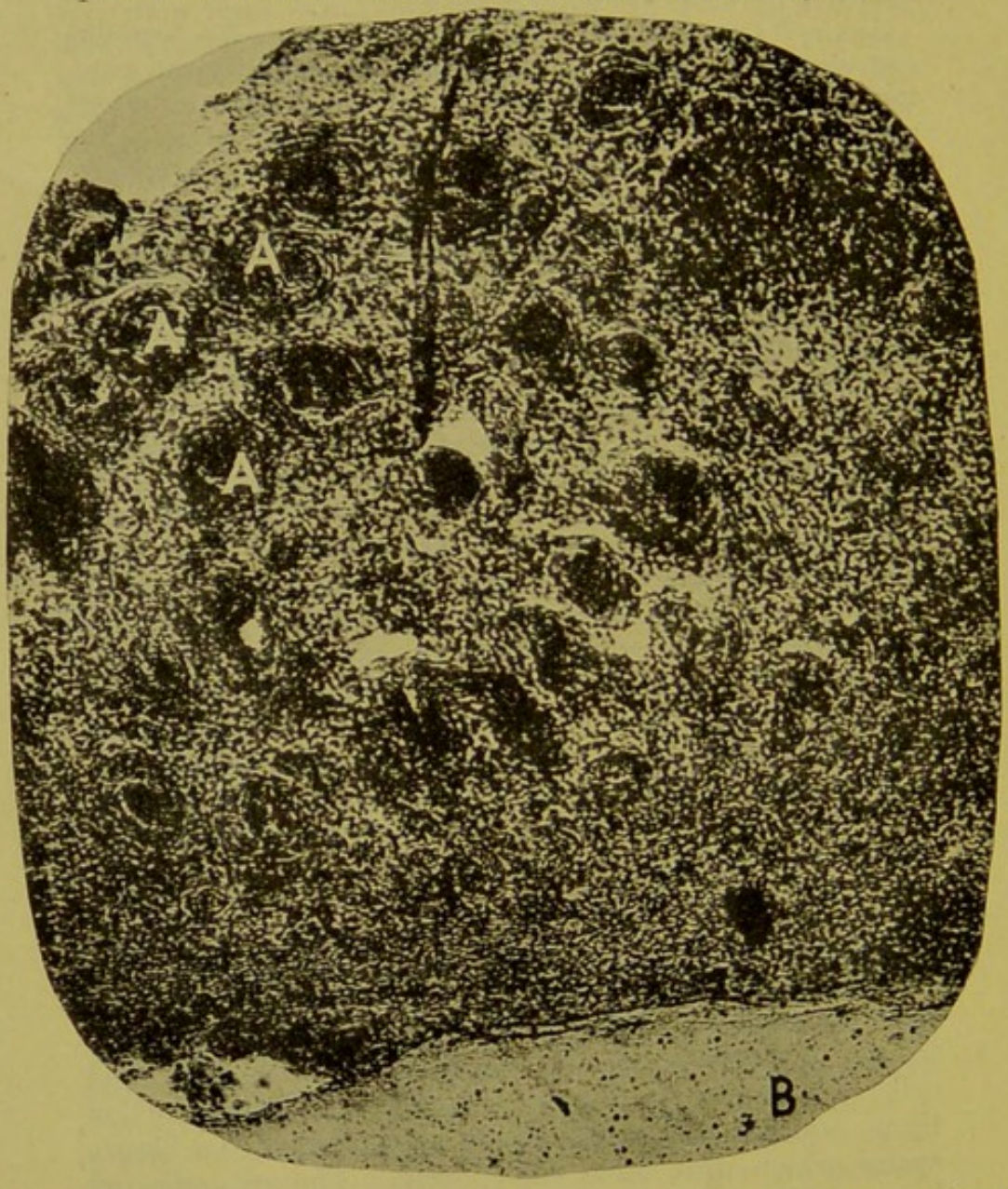
Landolt's[23] Case.—Man, aged 41. Previous history of trachoma (?). Left eye was completely involved and the right partially. Three years after onset there was total symblepharon in the right eye with xerosis, and only slight perception of light. Transplantation of skin from face and lids, with good results, lasting four years. Left eye was enucleated later because of discomfort.

## PATHOLOGY

The pathology of this disease is still obscure. Sattler[24] reports the microscopic findings in one case. He observed that the swelling of the conjunctiva bulbi was not due to the infiltration of the conjunctiva with lymphoid cells, but partly to a great swelling of the connective tissue bundles, and partly to the expansion of the fissure spaces which were filled with liquid. The subepithelial layer of the conjunctiva bulbi formed a special modified membrane about 40 microns broad, more turbid than the

18. Sherman: Arch. f. Ophth., 1909, p. 140.
19. Adams: Berl. Ophth. Gesellsch., 1909.
20. Quint: Klin. Monatsbl. f. Augenh., 1909.
21. Shumway: Ann. Ophth., 1910.
22. Wollner: Klin. Monatsbl. f. Augenh., 1911.
23. Landolt: Arch. d'Ophth., 1910, xxx, 337.
24. Sattler: Quoted by Morris and Robert in Brit. Jour. Dermat., 1888, p. 180.

rest of the tissue, being almost opaque and running parallel with the surface of the conjunctiva and covering the greater part of the cornea. This subepithelial turbid layer might easily be mistaken at first sight for the epithelium itself. The entire stroma of this layer was




A section of conjunctiva from the lower culdesac, showing round-cell and leukocytic infiltration, new "blood-paths" or channels (A) and hemorrhagic area (B) below. × 90.

pervaded by granular bodies, which did not stain with Bismarck brown or hematoxylin. The blood-vessels of the conjunctiva were numerous and much congested. They were not, however, apparent on superficial view of the conjunctiva, being concealed by the condition of the

epithelium. This epithelium had lost totally its normal character. From the deepest layers to the most superficial it consisted of horny cells. It was 30 microns thick and separated easily from the underlying conjunctiva.

Baumler[25] reports a case and gives about the same findings except that he mentions a hypertrophy and a papillary formation of the epithelium.

Collins[26] has made a contribution to our knowledge of this disease by reporting the macroscopic and microscopic findings of two cases of pemphigus of the conjunctiva. In the first case he found from the macroscopic study that the cornea showed a great convexity and that on the anterior surface of the cornea there was a layer of tissue quite different from the normal epithelium. The iris was atrophied and attached to the posterior surface of the cornea. The lens was shrunken and adherent to the cornea. The vitreous fluid and retina were *in situ*. There was cupping of the optic nerve head. Microscopically viewed, he found the epithelial layer of the cornea thickened and a number of finger-like processes dipping down into the fibrous layer of the cornea, several areas of round-cell infiltration, and a number of new blood-vessels. Descemet's membrane was absent in places. In the second case the findings were very much the same.

Microscopic examination of a small portion of the conjunctiva excised from the lower culdesac of the right eye of my case revealed the following: The specimen was hardened in formaldehyd solution and the gradual increasing alcohols, and stained in hematoxylin and eosin. The outer portion of the specimen was made up of round cells in great abundance and blood-vessels, making a partial capsule around the central fibrinous material. In the outer edge of the specimen were seen necrotic changes in the cellular proliferation. This outer limiting edge showed some flat cells and some tendency to hornification. There was great invasion of leukocytes throughout, more or less centralized in spots. At places eosinophils were seen. There was a most remarkable increase of blood-vessels; these should more properly be called blood-paths, as they did not have well-formed vessel walls. Some of the larger ones had a well-formed wall of cells without the formation of the different coats. These blood-paths were well filled with red blood-corpuscles. The leukocytes, which made up the greater portion of the section, presented all the different stages of cell division. In the center of the section there was a mass which

25. Baumler, Zeh: Klin. Monatsbl. f. Augenh., 1885, xxiii, 337.
26. Collins: Tr. Ophth. Soc. U. Kingdom, 1890. p. 62.

took the eosin stain only and consisted of red corpuscles and fibrin. This was the hemorrhagic portion of the specimen and was the result of the dissection of the tissue from the culdesac. A few leukocytes could also be seen in this hemorrhagic area. There was no attempt to form any connective tissue or any new form of specialized tissue growth. The polymorphonuclear leukocytes predominated.

### BACTERIOLOGY

Considerable work has been done along bacteriologic lines of study of pemphigus of the conjunctiva. Elaborate studies have been made of the secretions and discharges found in eyes so affected, but no real importance can be attached to the results.

Gelpe found in a case reported in 1885, the presence of micrococci, diplococci, and on making a culture of another case, he was able to show streptococci. Sachsalber[27] later found the presence of the diplococcus, the streptococcus, tetragenus, and comma vibrans. Bellecontre[28] demonstrated streptococci and staphylococci, and Franke,[29] from a culture, found the pseudodiphtheritic bacillus and the staphylococcus.

Lipschutz,[30] from his microscopic studies, advances two theories in regard to the etiology of this disease, the neuropathic and the bacterial or parasitic. By some investigators the contents of the blisters or vesicles have been found sterile, but others have found that they contain strepto- and staphylococci. Lipschutz further claimed to have found something characteristic in the plasma which he called cytoplasma.

Bacteriologic study of the case reported in this paper showed the following: a smear made of the secretion from the right eye showed the presence of pus-producing organisms only; in a culture using agar as the medium for growth, the presence of streptococci and pseudo Klebs-Loeffler bacilli was demonstrated.

### TREATMENT

As regards the treatment of pemphigus of the conjunctiva, there is not much that can be offered that is new or of any great value. Arsenic, in all of its forms, has been used most generally, and when used, it should be pushed to its physiologic limit. It is of

27. Sachsalber: Klin. Monatsbl. f. Augenh., 1894. p. 241.
28. Bellecontre: Quoted by Pergens, Pemphigus des Auges, Berlin, 1901.
29. Franke: Der Pemphigus und die essentielle Schrumpfung der Bindehaut des Auges, Wiesbaden, 1900.
30. Lipschutz: Centralbl. f. Bakteriol., May, 1910.

interest to know the different forms of treatment used in such a disease from time to time. Cooper, in the treatment of his case in 1858, used cold compresses, opened the bullæ and applied silver nitrate. Hassen[31] tried zinc sulphate in varying strengths, and Sattler and Pflugler used milk and oils. Barthelen and Sachsalber recommended lanolin and glycerin. Bellecontre, after his microscopic studies, made experimental use of anti-diphtheritic serum injection. There were no especial improvements noted, but he asserts that it helped to check the progress of the disease.

Transplantation of conjunctival tissue, mucous membranes and skin have been tried at different times, but the results have not been eminently successful. The difficulty seems to be in getting the grafts of tissue to grow, notwithstanding the great vascularity of the conjunctiva. Not being satisfied with the results of Sattler's experiments in the surgery of this condition, von Graefe tried the transplantation of mucous membrane from a dog and also from the mouth of a man with no better results. Sachs,[32] in his cases, used the skin from the prepuce, but did not have great success as a reward for his efforts. None of these men had what might be called even fair results, as none of them succeeded in stopping the progress of the atrophy and symblepharon formation. Marple reports a case in which he used the skin from the inner side of the arm near the axilla. The graft took well and he was able to stop the progress of the disease. Four years after the operation the condition had not advanced and the disease was quiescent. Operative measures have also been employed in the hope of checking the deformity of the lids, and these also have been most unsatisfactory.

The treatment employed in my own case was a boric acid wash four times a day to keep the lids clean, and gentle applications of silver nitrate and the copper stick. Olei ricini was used three times a day to relieve the dryness of the conjunctiva and at other times this was alternated with liquid petrolatum. Arsenious acid was given over a long period of time, in gradually increasing doses. It did not seem to improve the patient's general

31. Hassen: Quoted by Pergens, Pemphigus des Auges, Berlin, 1901.
32. Sachs: Wien. klin. Wchnschr., 1899, p. 671.

health or have any especial action in the eye condition. The patient was urged to come into the hospital, but this was refused on account of his religious scruples. Operative measures were suggested for relief of the disease and the rapidly increasing destruction, but this was also refused.

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