OCULAR PEMPHIGUS

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Ocular pemphigus has been established as a clinical entity since 1858, when White Cooper, in the first volume of the Royal London Ophthalmic Hospital Reports, described a case. It is certain that prior to this date the disease occurred, but was confused with the various conjunctival degenerations known at that time, notably as conjunctival xerosis. Subsequent to this date the exact pathological differentiation of the condition occasioned dispute amongst dermatologists and ophthalmologists, a controversy which was engendered by the rarity of the disease, until von Graefe, in 1879, identified pemphigus with what had hitherto been called "essential shrinking of the conjunctiva."

Various authors (Pergens and others) have testified to the rarity of the condition; the average for eye cases is about 1 case per 20,000 and for skin cases 1 per 300 (Pusey). At Moorfields there have been four cases in the last five years.

Ocular pemphigus attacks the lids, conjunctiva, and cornea, the clinical picture often being composite. Parsons classifies the varieties of the disease as follows:—

(a) Acute, in which ocular involvement is coincident with a general eruption.

(b) Chronic, which occurs in four types.

(i) Associated with vesicles on other mucous membranes, such as the nose, pharynx, larynx, vagina, or rectum.

(ii) With vesicles on the skin.

(iii) With vesicles only on the conjunctiva.

(iv) Without history of previous vesiculation (essential shrinking).

Pathology.—As the name implies vesiculation should be a dominant factor of pemphigus (πέμφις, a blister), but it is a feature which is rarely seen in the ocular type. According to Uthoff 1/7th of ocular cases show vesiculation, due to the fact, as Franke points out, that the mobility of the globe and lids would tend to prevent vesicle formation and precipitate early rupture of them.

The disease may be said to pass through three stages, namely vesiculation, cicatrization, and the final stage of complications. The stage of vesiculation has been described by various authors (White Cooper, Pergens, Whitham, Pusey), and the size of the vesicle appears to vary from that of a pea to a bean. Such vesicles may occur either on the palpebral or bulbar conjunctiva, the site
of election being at the inner canthus and at the centre of the lower conjunctival fornix (von Michel). In other cases, shallow ulcers have been noted at these situations (James) and in still more cases no ulceration or vesiculation has been found. On the skin of the lids the distribution is varied, the lower lid tending to be attacked more than the upper lid. Vesicles have not been described as occurring on the cornea and it appears that corneal changes are secondary. Adam stresses the fact that vesiculation alone is not the important factor in the formation

![Fig. 1.](image)

**Fig. 1.**

Section of Pemphigus Conjunctivae. There is epithelial hypertrophy with vesicle formation. The sub-epithelial layer shows much fibrosis and small round-cell infiltration. (Specimen from case 5, Fig. 2).

of subsequent cicatrices, but that epithelial hypertrophy and sub-adenoid infiltration are more potent causes, whilst Castello also emphasizes the importance of sub-epithelial contracture. The section shows this sub-epithelial infiltration and epithelial hypertrophy, but beyond this there is little to distinguish it from chronic granulation tissue.

The stage of cicatriztion follows quickly on that of vesiculation. It is not so marked after an acute attack as it is after the more chronic variety. In the latter group firm bands of fibrous tissue are formed which pass from the palpebral to the bulbar conjunctiva (see Fig. 2), these eventually obliterate the fornices and impair the mobility of the globe. Later the lids and globe become firmly adherent in a mass of peri-corneal adhesions, which subsequently strangle the orifices of the lacrimal ducts and produce xerosis of the conjunctiva; ankyloblepharon is almost constant.
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The stage of complications is chiefly concerned with the state of the cornea following on xerosis. Coarse pannus frequently occurs and a xerotic plaque of fibrous tissue covered by a thin layer of epithelium invades the cornea, the lustre and transparency of the cornea thereby suffering, and blindness is the inevitable result (Fig. 3). Trichiasis and entropion may be responsible for a traumatic corneal ulcer which leads to suppurative panophthalmitis (case 2).

The age incidence of this disease varies, the acute variety attacking people from 2 to 35 years of age, the chronic variety those of from 40 to 70 years, and showing a preference for butchers and those engaged in the hide trade (case 5).

Bacteriology.—As in the case of skin pemphigus, the bacteriology of this disease is obscure and differs from skin pemphigus in that secondary conjunctival infection is always present. For many years the relationship to syphilis has been noted and de St. Martin particularly stresses such a relationship. There certainly appears to be a true bill for congenital syphilitic pemphigus of the skin, but this type rarely involves the conjunctiva. On the other hand, a positive Wassermann reaction is frequently coincident with ocular pemphigus (Zentmayer). Such cases have been reported by von Maren, Holtz, Stieren, Hardy and Lamb. Radcliffe Crocker compared the appearance of the cornea to that found in neuroparalytic keratitis and suggested that the cause was the action of a toxin on nerve centres. Conjunctival culture has yielded the usual secondary infections, notably bacillus xerosis and the staphylococci, whilst those who have been fortunate enough to obtain the fluid from a vesicle have on the one hand claimed to have isolated a large diplococcus, and on the other have proved the fluid to be sterile. Dejean has failed to confirm the presence of a specific organism which would reproduce the disease in animals.

The Relationship of Ocular Pemphigus to Skin Pemphigus

Dermatologists recognize the following varieties of skin pemphigus, namely, acute and chronic vulgaris, foliaceous and vegetans; the first and second types are liable to be accompanied by ocular pemphigus.

According to Walker, Demoine has isolated a coccus from the vesicle, but “the weight of evidence” is against any bacterial cause. One difference, which is probably due to the absence of secondary infection, is that healing in skin pemphigus takes place with very little scarring, although discolouration remains. Eosinophilia occurs in skin pemphigus; in case 5 there was a blood eosinophilia of 5 per cent.

Clinical types.—Acute pemphigus is fortunately the rare type
since it is usually fatal. It attacks young people of both sexes and is said to be associated with undue exposure to sunlight. Commencing with a rigor there follows a bullous eruption in which the lids and conjunctiva become much swollen, although the cornea is rarely involved directly (Strader). With a rupture of vesicles there follows mild cicatrization in the conjunctiva, but deterioration of vision seldom results to any serious degree. Cases of this class have been reported by Martin and others.

Chronic pemphigus begins with all the usual symptoms of chronic conjunctivitis and is frequently undiagnosed, or diagnosed as trachoma or tubercle of the conjunctiva. A specific ropy discharge has been noted by a few authors. In the minority of cases vesicles give the clue to the disease, but the majority are diagnosed either by the reluctance of a conjunctivitis to clear up or by the manifest presence of cicatricial conjunctival bands. Coincidently a nasal discharge or a husky voice leads to the discovery of vesicles or ulceration in the nares, nasal pharynx, or larynx.

Differential diagnosis.—From the ocular standpoint pemphigus may be confused with extensive conjunctival burns in which the history will be of assistance, from malingering when the condition will be more likely unilateral; or with tubercle in which cicatrization of this degree rarely occurs. Trachoma may be a stumbling block (Wood), but ankyloblepharon, which is constant in pemphigus practically never occurs in trachoma, and, moreover, the lower fornix is also the site of election in pemphigus and follicles are absent. Primary xerosis of the conjunctiva does not present the same intense cicatrization as does pemphigus, and its epidemic nature and presence of night-blindness will be of assistance in determining the true cause. Syphilitic tarsitis in the later stages may occasion confusion, but here also cicatrization is not a prominent factor.

From the dermatological standpoint conjunctival vesicles, together with vesiculation of the body elsewhere, must be differentiated from erythema multiforme of the bullous type, which, however, rarely attacks the mucous membranes, from dermatitis herpetiformis in which bullae tend to occur in successive crops, and from the bullous impetigo and bullous syphilides, which occur at a much younger age than does true ocular pemphigus. Drug eruptions should also be borne in mind.

The following cases demonstrate varieties of the disease:—

Case 1.—Female, aged 40 years, has had "sore eves" for six months. External examination shows total symblepharon below with trichiasis and corneal ulcer in the left eye.

This case had pemphigus vulgaris of the skin two years previously. Treated by epilation, guttae paroleine and thyroid; no improvement.
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Case 2.—Male, aged 65 years, has been treated at another hospital for conjunctivitis by silver applications for nine months. Both lower fornices obliterated and bilateral corneal ulceration. Treated by “Germinine,” atropine, epilation. Suppurative panophthalmitis followed on corneal ulceration and the right eye was removed.

Case 3.—Female, aged 72 years, diagnosed and treated as late trachoma for over a year. The right eye showed total symblepharon with trichiasis. Treated by argyrol, epilation and lotions. Subsequently developed extensive corneal ulceration in both eyes which were enucleated.

Case 4.—Male, aged 70 years, painter and decorator. Nine years ago “patch” appeared on the left eye. One year six months ago the right became irritable and the left eye one month later. Epilation was repeatedly carried out. There has been intermittent throat trouble, and “blisters” in the mouth were found after the onset of the eye condition. There has also been nasal discharge. No history of vesicles of the skin. No previous eye trouble. Symblepharon right and left eyes; aberrant lashes; no xerosis; corneae relatively uninvolved. There are many ulcerated areas on the fauces, gums, and lips, also a central ulcer of the hard palate. Wassermann reaction negative. Treated by vaccines. This case has not been treated by radium.

Case 5.—Male, aged 55 years, butcher. The left eye became irritable two years ago, and the right eye six months later. History of “blisters” in the mouth at the time. No recent illness; no previous skin trouble; no accident or injury to the eyes; no eye trouble in the family. No previous eye trouble. No history of conjunctival blisters. Right eye: upper and lower symblepharon; aberrant lashes. Left eye: symblepharon; pannus; aberrant lashes; no xerosis. Cultures: B xerosis; staphylococcus aureus; Wassermann reaction negative; eosinophilia 5 per cent. Treated by surface application of radium; six hours’ duration; 10 mgm. radium, 1 mm. silver screen. There have been three applications and the condition has improved.

**Treatment.**—The treatment of ocular pemphigus makes a doleful story. Almost every remedy in fashion has been employed, but the results have been consistently bad. Local collyria are of no specific avail; for the alleviation of symptoms paroleine has been found to be of greatest benefit. Surgical intervention by mucous membrane grafts has had limited success. According to Wood the most satisfactory surgical measure is tarsorrhaphy. Autohaemotherapy, turpentine injections (Gewalt) and pyretotherapy have had their day with little improvement. As a result of limited experience the author would suggest the following treatment in cases of chronic ocular pemphigus:
Local instillations of paroleine daily.

Median tarsorrhaphy.

Regular epilation.

Surface radium application.

By courtesy of Dr. Durden Smith radium treatment was carried out in case 5 at the Radium Institute, the method of application being by the use of 10 mgm. radium with 1 mm. silver screen over the closed lids for six hours' dose; this to be repeated at two monthly intervals. This case has certainly improved as a result of these measures, but whether it is due to the reduction of vascularity and redundancy of the mucosa or to true cure is doubtful. General measures have included the administration of arsenic and vaccines.

The prognosis remains today, in spite of an increased armamentarium of therapeutic measures, much as it was in the days of White Cooper. All authors are agreed on the resistance of this condition to all and every mode of treatment and to the inevitable steady progression toward blindness. Writing in 1858, White Cooper naively remarked that "to combat this condition ingenuity was severely taxed." It is a regrettable fact that in common with other methods of taxation there does not yet appear to be any estimate in the therapeutic budget which will reduce this taxation and lower the deficit of incurable diseases of which ocular pemphigus is a heavy burden.

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