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A SURVEY OF SUPERFICIAL PUNCTATE KERATITIS IN TASMANIA WITH THE RECORD OF A MILD EPIDEMIC

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HOBART

Introduction

NEAME (1937) at the conclusion of his short paper on "The Association of Dendritic Ulcer of the Cornea and of Superficial Punctate Keratitis with Herpes Facialis" says:—

"It seems almost certain, however, that one virus—modified perhaps in different localities or in different years—is capable of producing a variety of lesions of the cornea."

He makes this statement in order to clear many misconceptions that appear in the literature regarding the aetiology of such varied corneal lesions as herpes simplex corneae; superficial punctate keratitis; dendritic ulcers; disciform keratitis; neuropathic keratitis; and keratitis profunda. But it appears certain that until a better understanding of virus diseases is obtained, our exact knowledge of the aetiology and behaviour of these very interesting corneal lesions will remain somewhat obscure. According to Burnet and Williams (1939), the conception of this virus disease must be

carried still further to include, besides herpetic lesions of the face and hands, herpetic lesions of the perineum, and also such conditions as aphthous stomatitis in young children. My impression from the Tasmanian epidemic which I am about to describe, and also from the literature which I have read on the subject, is that a variety of corneal lesions due to one virus do occur, and I will take them in the order of their ascending severity.

First, multiple corneal erosions. It is pointed out by Doggart (1933), that these are very common after influenza, and also after Koch-Weeks conjunctivitis, and this I have confirmed in Tasmania. But I am of the opinion that these erosions are a manifestation of the same virus disease, and that at least in three cases, I have found multiple corneal epithelial erosions and superficial punctate keratitis associated in the same eye.

Secondly. Marginal keratitis, with or without ulceration. I have found this condition directly associated with superficial punctate keratitis in 17 cases (18·8 per cent.)

Thirdly. Frank superficial keratitis, of which I am to describe 92 cases.

Fourthly. Dendritic ulcer, which also will be considered in this paper, and was found associated with the disease under review in six instances (6·5 per cent.).

Fifthly. Disciform keratitis. Other writers such as Wright (1930) and Gruter, quoted by Doggart (1933), have found this occurring concurrently with superficial punctate keratitis, but I have not been able to associate this in my survey.

I will deal with the associated conjunctival and lid lesions later, and show that these may precede, or accompany the keratitis, and clinch or obscure the corneal diagnosis.

Case Incidence

My 92 cases of superficial punctate keratitis were culled from 6662 consecutive case records, which give a case incidence of 1·38 per cent. I cannot find any other comparable figures in the literature I have read.

Epidemiology

Superficial punctate keratitis, as an epidemic disease, has already been clearly described by Wright (1930), Ling (1932), and Doggart (1933). In this paper I want to discuss 92 cases seen in Tasmania between February 1, 1931, and June 1, 1939, in which is included a mild epidemic which commenced in the island in July, 1932, and continued with intermissions until November, 1934. Before and since then, endemic cases were seen, and these are depicted in Fig. 1.

PUNCTATE KERATITIS IN TASMANIA

GRAPH I. FIG. 1.

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GRAPHS SHEWING AGE INCIDENCE FOR 92 CASES OF SUPERFICIAL PUNCTATE

KERATITIS.

GRAPH A:— COMPARATIVE AGE INCIDENCE FOR MALES AND FEMALES.

GRAPH B:— AGE INCIDENCE-MALES AND FEMALES.

Aetiology

In spite of intensive investigation by Wright (1930) and others, the aetiology of this disease was still obscure until Burnet and Williams' (1939) clear exposition of the relationship of herpes simplex, aphthous stomatitis, and punctate corneal lesions was published (1939), which will be discussed further, under pathology. There now seems no doubt that it is a virus infection of the trigeminal nerve, for I have been able in many cases to demonstrate petechial lesions on the skin of the lid, as well as of the cornea. Neame (1937), as I have already mentioned, has noted the association of this disease with herpes facialis.

Sex and Age Incidence

According to Fuchs, quoted by Doggart (1933), the second decade of human life is the most common one in which to be affected by this disease. Doggart (1933) himself found the average age of males to be nineteen and females twenty-seven. Wright (1930) repeated that young adult males were far more commonly affected than females, but he admitted that nearly twice as many males as females attended his clinic for treatment. Despite this fact, the incidence of males was definitely higher in Madras. In my 92 cases, it will be seen that 42 were males and 50 females, which indicates that 45·65 per cent. males and 54·35 per cent. females were affected in this epidemic in Tasmania. Fig. 2 shows that the third, fifth and sixth were the most common decades for occurrence in Tasmania, when males and females were grouped together, but when the males were separated from the females, it was found that the higher incidence was in males of the third decade (which corresponds with Fuchs and Wright) and in females of the fifth and sixth decades. In other words, out of 42 male cases, 16 (38·1 per cent.), occurred between 21 and 30 years of age, and in the 50 female cases, 12 (24 per cent.) between 41 and 50 years of age, and 13 (26 per cent.) between 51 and 60 years of age.

Geographical Distribution

Fig. 3 shows in geographic form the distribution of cases of frank superficial keratitis in Tasmania. It must be understood that the majority of my patients resided in an area bounded on the north by latitude 42° and on the west by longitude 147°, and that the great proportion of the approximately 100,000 inhabitants in this area live in Hobart, or in the valleys of the Derwent and Huon rivers. In fact, 65,000 of these people reside in Hobart, *i.e.*, roughly 65 per cent., but of the 87 cases occurring within this geographical division, 67 occurred in Hobart, *i.e.*, 77 per cent. This roughly makes the city incidence 1 in 1,000, and the country 1 in 1,750.

Seasonal Variations

While Doggart (1933) considered that the disease was more common in the winter, he agreed with Fuchs that it was often accompanied by respiratory tract infection. Wright (1930) also agreed that this disease accompanied inflammation of the respiratory passages, but I was unable to find any seasonable variations in the Tasmanian epidemic (see Fig. 1), though I was able to substantiate the statement that the disease was often accompanied by respiratory tract infection, and in no less than 19 patients, and probably more, there was a definite history of influenza, colds, or other nasal and pharyngeal infections. Influenza played the greatest aetiological part.

Pathology and Bacteriology

I have nothing to add to the pathology of the condition except that with the corneal microscope, the lesions were identical with those described by Wright and Doggart. Wright (1930*a*) was unable, after much experimental work to determine the exact pathology of the lesions, and his culturings of corneal scrapings were negative, but he was successful in transmitting the disease from man to man, or rather, from human eye to human eye, and was able to determine the incubation period as between three and nine days.

Further, as shown by Burnet and Williams (1939), the condition can be produced artificially in rabbits, by scarification of their corneae with fluid from herpetic vesicles, of the human skin or mucous membrane, and that the incubation period in rabbits was two days. Further they found that a proportion of the animals developed cerebro-spinal lesions with paralysis, convulsions and death. No cerebro-spinal lesions have been recorded in human cases of superficial punctate keratitis, although they have been reported following herpes zoster ophthalmicus.

Immunity and Relapses

As far as I can determine, there is no immunity acquired to the disease in Tasmania, and 25 of the 92 patients had attacks of superficial punctate keratitis in both eyes. In six it appeared simultaneously, but in another nine there was an average interval of 78 days, the minimum being two days, and the maximum 18 months. In the other 12, the interval was indefinite. Further, 16 patients had a relapse in the same eye after intervals of from three days to four years. It therefore appears that there is no acquired immunity whatsoever to this disease. (See Fig. 4).

Burnet and Williams (1939) have also shown by their anti-body tests on chick embryo respiratory membrane, that although the acquisition of anti-bodies is high after infection with herpes

simplex, yet these anti-bodies do not provide lasting immunity to herpes simplex infection. In one of my patients herpes zoster ophthalmicus had occurred in the same eye 15 years before, so apparently herpes zoster does not produce any lasting immunity either, to herpes simplex.

FIG. 3.

FIG. 4.

Table showing comparison between cases treated with silver nitrate 2 per cent. and those not so treated.

	With AgNO ₃	Without AgNO ₃
Total No. of cases - - -	74 (80·8 per cent.)	18 (19·2 per cent.)
No. of cases with relapses - -	13 (17·58 „ „)	3 (18 „ „)
No. of relapses - - - -	21	8
Average No. of relapses per case	1·6	2·6
Average duration of treatment -	7·3 days	26 days
No. of cases with final vision determined - - - -	34	11
No. of cases with visual deterioration - - - -	3 (8·8 per cent.)	2 (18·2 per cent.)
Average No. of painting with AgNO ₃ - - - -	2·2	—

Infectivity

In this epidemic, the disease did not appear to be infectious at all. In only two instances could I find any immediate relation between the patients. The first was two distant cousins, who lived miles apart, and had only seen one another once in the previous month. The other instance was one in which a mother had it in August, 1934, and her daughter, living in the same house, had it in July, 1935. Burnet and Williams (1939) found a similar position with herpes simplex.

Eyes Affected

In my 92 cases there were 60 right eyes and 57 left eyes affected, as in 25 cases both eyes were involved. Wright (1930*a*) in his first 923 cases had only 6 bilateral cases, and in his next series (1930*b*) of 1,000 cases there were 16 instances of both eyes being affected. Bilateral infection seems much more frequent in Tasmania.

Clinical Manifestation

Doggart (1933) and later Duke-Elder (1938) have given such clear descriptions of the clinical manifestation of superficial punctate keratitis, that I have nothing to add, except that I would

refer the reader to Doggart's illustrations appearing in both works. But the allied conditions in the Tasmanian epidemic seem to be of a somewhat unusual type, frequency and severity, and I will therefore pass on and describe them in some detail.

Associated Conditions

1. *Marginal Keratitis*.—This manifestation was by far the most frequent of the allied conditions. It was found in no less than 17 cases and in four instances it preceded the superficial punctate keratitis. It was characterised by small round areas of corneal infiltration, just beneath the epithelium, and just within the limbus with more intense ciliary injection at the sites of the infiltration. During the same eight 1/3 year period, I saw 43 other cases without superficial punctate keratitis, and I feel that all these cases were manifestations of this virus disease. If this is so, then the virus of herpes simplex has been the cause of a great many more cases of keratitis than the 92 cases under review indicate. (see Fig. 5).

2. *Corneal Ulceration*.—Ulcers of the cornea were indeed common in the Tasmanian epidemic, and in the 92 cases in which 117 eyes were affected, there was marginal keratitis in 17 eyes, and corneal ulceration (other than dendritic ulcers) in seven eyes also—this does not appear to be a feature of other epidemics.

3. *Disciform Keratitis*.—I have pointed out previously, that in my series there was not one case of disciform keratitis associated with superficial punctate keratitis. Coverdale (1932), in New Zealand, had a similar experience; while Wright (1930), in his epidemic considered that disciform keratitis was a malignant form of this disease under a different name.

4. *Dendritic Ulceration*.—This occurred in six out of 117 eyes affected with superficial punctate keratitis. Coverdale (1932) also found dendritic ulcers a complication of superficial punctate keratitis, and this was confirmed by Wright (1930) and Neame (1937). In Fig. 6 I give the incidence of all dendritic ulcers seen in Tasmania during the same eight 1/3 year period under review, namely, 13 cases, and in Fig. 8 the relation between all dendritic ulcers, marginal keratitis, superficial punctate keratitis, and phlyctenular disease cases seen during this same period. It must be made quite clear that only six out of these 13 cases of dendritic ulcers occurred in conjunction with superficial punctate keratitis.

5. *Iritis*.—I found superficial punctate keratitis in one patient with Neisserian iritis, but in the other 116 eyes, there is no indication whatsoever, either by slit-lamp microscopy or otherwise, that iritis was a complication of superficial punctate keratitis, and this is confirmed by Ling (1936), and Wright (1930), and Fuchs, quoted by Doggart (1933).

MONTHLY INCIDENCE CHART FOR MARGINAL KERATITIS. JAN 1931 - JUNE 1939.

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GRAPH IV. FIG. 6.

MONTHLY INCIDENCE CHART FOR PHLYCTENS.
JAN. 1931 - JUNE 1932

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GRAPH VI, FIG. 8

6. *Phlyctens*.—During this eight 1/3 year period, I had three cases of superficial punctate keratitis accompanied by phlyctens, out of a total of 38 cases of phlyctens seen during that time (Fig. 7). Fig. 8 shows the monthly relation of all phlyctenular cases to superficial punctate keratitis, and dendritic ulcers and marginal keratitis during that period. It is apparent that unlike marginal keratitis and dendritic ulceration, phlyctens do not appear to be a manifestation of the disease under review, but a separate concurrent lesion. My opinion Hamilton (1938), that phlyctens are a manifestation of tuberculous toxæmia (but not actual tubercles), is confirmed by Coverdale (1938).

7. *Folds in Descemet's Membrane*.—This was apparent in one case in the Tasmanian epidemic, and Wright quotes cases as having occurred in the Madras epidemic in 1928-29.

8. *Hordeolum*.—I found stytes in five cases of superficial punctate keratitis during the Tasmanian epidemic, and Coverdale (1932) also found them a complication in New Zealand. Stytes occurred in three of the five cases before the superficial punctate keratitis appeared.

9. *Herpes Facialis*.—Wright (1930) found no cases of this in the Madras epidemic, but I have found petechial spots frequently on the skin surface of the lower lid. Occasionally patients who have reported with red eyes, demonstrated no corneal lesion at all, but the spots on the face were characteristic, and made a diagnosis of virus infection of the trigeminal nerve, easy. Actual herpes on the lids was seen in two cases, but I think Neame (1937), has conclusively proved the close relation of superficial punctate keratitis and herpes facialis, without further stressing it.

10. *Conjunctivitis*.—Ling (1932), reported that at least 50 per cent. of the 52 cases in the Nanking epidemic, had swimming-pool conjunctivitis, but as there is only one swimming pool in Hobart, it is natural that swimming-pool conjunctivitis was not found in Southern Tasmania, although acute conjunctivitis was an accompaniment of 14 of the cases.

11. *Warts of the Lid*.—I have two recorded examples of this condition associated with superficial punctate keratitis. In one the wart ran an acute course, and by the time the keratitis had subsided, the wart had practically disappeared altogether, although at the height of the keratitis its increasing dimensions were alarming. Roth (1939) in reporting ten cases of conjunctivitis and keratitis due to warts on the lids, is of the opinion that in at least one case the keratitis closely resembled the disease I am reviewing. The second of my cases had recurrent corneal ulceration, accompanied by two warts on the upper lid of the same side. I removed the warts and nine months later she developed superficial punctate keratitis in the same eye.

Diagnosis

The diagnosis of superficial punctate keratitis, can, in a majority of cases be made with a monocular loupe, but it is advisable in every case to survey the stained cornea of each eye, as well as the anterior chamber, with the slit-lamp and the corneal microscope. If a corneal microscope is not at hand, a great help is to dilate the pupil, for quite often a few early spots can be defined when they are seen against the black pupil, while they remain invisible against the grey iris. Another aid to the diagnosis, already mentioned, is the petechial spots on the face, and I think these should always be looked for if the disease is suspected. In my 92 cases, I find that 15 patients reported with red eyes without any obvious superficial punctate keratitis, and it was only after an interval of days that the corneal lesions developed their normal proportions. In these 15 cases the patient first came complaining of the following diseases.

Corneal Ulcers (other than Dendritic Ulcers)	...	1
Acute Conjunctivitis		6
Dendritic Ulcers		3
Multiple Corneal Epithelial Erosions		1
Marginal Keratitis		4
Hordeolum		3
Warts		1

(As two of the marginal keratitis and one of the acute conjunctivitis cases had styes as well, before any superficial punctate keratitis was detected, and one acute conjunctivitis had dendritic ulcers, the total number of cases included in the list is only 15).

The history of a recurrent red and watery eye, with photophobia and little discharge, and no deep seated pain, accompanied by a slight blurring of the vision, is most typical. It will be apparent from the above that many cases of superficial punctate keratitis, must be missed, unless continuous and careful observation be made, and it shows the importance of completing the examination of the cornea with the slit-lamp in every case of recurrent red eyes.

Differential Diagnosis

This should not be difficult when a corneal microscope is available. The conditions with which it might be confused are acute conjunctivitis; multiple minute erosions of the cornea; commencing interstitial keratitis; dendritic ulcers and incipient disciform keratitis, while acute iritis in its early stages must be excluded. The slit-lamp can easily differentiate these conditions.

Treatment

Doggart (1933), Duke-Elder (1938), Wright (1930), and Graves in Behrens (1936), and especially the first named, were sceptical about treatment, but Cowan (1938) reports the successful use of

1 per cent. iodine solution drops and Pregl's solution packs. Gifford (1937) also suggests saturated iodine or trichloroacetic acid as counter irritants, giving relief when locally applied to each spot. Wright does admit that at the later stages of the disease, dionin drops are useful. I found that in the early stages of the epidemic, cases lingered on for weeks, when mild lotions and drops, with or without heat, were used, and Wright (1930*a*) admitted that in the Madras epidemic, some of the cases continued for 12 months. Doggart (1933) has seen them persist for two years; Harrison Butler (1927) for 18 months, while Neame (1937) reports one instance of a year's duration. In December, 1931, I had a patient who for eight weeks had bilateral superficial punctate keratitis with marked photophobia and lacrymation, necessitating hospitalization. As the disease seemed to make no response to bland lotions, disinfectant drops or heat, I painted the conjunctival surface of her lids with 2 per cent. silver nitrate, with dramatic results. Since then, almost all cases have been treated by applications of silver nitrate 2 per cent. to the conjunctival surface of the lids, with great success, and the average duration of treatment since silver nitrate 2 per cent. has been used, has been 7.3 days, as compared to 26 days without its exhibition. In all, 74 patients have received paintings and the average number applied was 2.2. I also found that if a final application of silver nitrate 2 per cent. was made to the lids after all the corneal lesions had departed, and the eye looked satisfactorily white, relapses were diminished. It has been pointed out by many that the disease cleared rapidly on its own initiative, but it will be seen that in certain cases, the disease may be prolonged almost indefinitely with palliative treatment. The severity of the disease in Tasmania has been such as to prevent the patients continuing their occupations on account of lacrymation and pain. It became economically imperative that the disease should be cleared as rapidly as possible. With the silver nitrate treatment not one patient has had to be admitted to hospital, or even confined to bed on account of their disease. (See Fig. 4.)

Silver nitrate, when applied to the conjunctival surface of the lid, does itself produce multiple corneal erosions, which last for some time. I have noticed frequently after it has been applied for superficial punctate keratitis, that when the superficial punctate keratitis has completely disappeared, multiple corneal erosions linger for some little time without any discomfort to the patient. Two per cent. silver nitrate applied to the lids in dendritic ulcers seems to be ineffective, and carbolic is always indicated. So it is apparent that the exhibition of 2 per cent. silver nitrate is most suited to those frank cases of superficial punctate keratitis, and not to the milder or more severe manifestations of this disease.

Kentgens (1938) considers that definite benefit is to be derived from treating herpetic conditions of the cornea (including superficial

punctate keratitis), with vitamin A preparations, both locally and generally, but he was unable to prove from chemical analysis of the blood that avitaminosis A was confined only to these patients in his clinic. He found 72 patients requiring refraction had an average of 3.5 international units of vitamin A in 10 c.c. of serum, while patients with herpetic corneal lesions averaged 3.2. The difference in these figures, to my mind, is of little significance, but what is significant, is that the duration of treatment of herpetic cases treated with vitamin A therapy was 10 days, and those without 30 days. This aspect of the treatment of infections of the cornea could be explored further with advantage.

Prognosis

Since the institution of silver nitrate 2 per cent. paintings, the prognosis given is that the eye will return to normal within a fortnight, and as mentioned previously, the actual duration of treatment has been 7.3 days. In one or two cases I find this has not been substantiated, but it is definitely so in the majority, to the great satisfaction of the patients and myself. Unfortunately, the final visual result was only determined in 45 cases (Fig. 4), and in five of these there was mild deterioration of vision, but superficial punctate keratitis does not appear to have any relation at all to the causes of blindness in Tasmania, either directly or indirectly. (Hamilton and Counsell, 1939).

Conclusion

I must thank the Australian Commonwealth National Health and Medical Research Council for their assistance in the form of a grant, in making this and other surveys of eye diseases in Tasmania possible.

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