Acknowledgement

In conclusion, I thank many members of the staff of the 7th Australian General Hospital both medical and clerical for their help and advice in treating these cases and preparing these notes. Also I acknowledge my gratitude to our Commanding Officer for permission to publish these case reports.

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NOTES ON FORMS OF KERATITIS PRESUMABLY DUE TO THE VIRUS OF HERPES SIMPLEX

BY

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Introduction

THE idea of writing these notes has been germinating for some considerable time but it has been brought to the surface by many facts and figures, both written and verbally communicated to me recently. Besides these intimations I have been able to make certain personal observations myself, in the Middle East, on this particular subject and these should be noted immediately.

In the *Brit. Jl. of Ophthal.* of January, 1941, I recorded a survey of superficial punctate keratitis in Tasmania over an 8½ years period. I here clearly showed from recent clinical and laboratory observations that this disease, at least, is due to the virus of herpes simplex. At the same time I indicated that superficial punctate keratitis in man was accompanied by a number of other corneal lesions, but these two facts do not yet seem to have entirely grasped the attention of my readers, nor have other important facts in my paper been appreciated. One has only to

turn to the *Arch. of Ophthalm.*, of February, 1942, and read the separate reports of Gifford and of Davis, to realise that the position, even in the U.S.A., could be clarified with advantage. The distinction between a bacterial and virus keratitis seems, in many minds, to be almost indistinguishable, and I feel this difficulty is due to the fact that a 50-year-old conception, that all external ocular infections are bacterial in origin, has taken too long to die. Further, little attempt has been made seriously to culture the conjunctiva from the virus standpoint and, when a bacterial culture is reported on as "no growth," further cultural attempts are not made to distinguish the organism. Personally, I feel that in the majority of cases a bacterial keratitis can be distinguished clinically from the virus type with ease, and I should like to detail the distinguishing points, forthwith.

When is a Keratitis due to the Virus of Herpes Simplex?

I think a virus simplex keratitis has several cardinal clinical features, which I intend again to (Hamilton, 1941) repeat and possibly enlarge upon. They are as follows:—

First, this particular type of infection often appears following a true or artificial pyrexia. That is, it may follow a pyrexia of malaria, relapsing fever, influenza or coryza, or an artificial pyrexia following T.A.B. injection. This last point has been abundantly confirmed by me in the A.I.F., and other writers have recorded attacks of herpes labialis after T.A.B. inoculations. Further, I feel even inclined to say that a sudden change from an arctic to a tropical climate is sufficient to precipitate an attack—undoubtedly the Polish Divisions, recently moved from the Russian winter to the Palestine summer, have been sorely afflicted by the disease. Gordon (1941) confirms this climatic influence. At least, marked changes in body or atmospheric temperature can be recorded in the majority of cases.

Secondly, the relapsing nature of this keratitis has impressed itself on everyone, both in Australia and in the Middle East. Not only are relapses in one eye common but also a spread to the second eye (at any time during or after the attack in the primary eye), is not an unusual feature. The short immunity to the virus of herpes simplex is recorded by Mackie & McCartney (1938). I, personally, doubt whether this particular virus produces any immunity whatsoever.

Thirdly, the total absence of acute iritis and the small amount of conjunctival discharge are both interesting features. I never use atropine for virus keratitis, except the disciform type, and have not found my judgment misplaced.

Fourthly, the protean nature of the lesions of the cornea, which may range from multiple corneal erosions to disciform keratitis (see Fig. 1). The most usual forms, however, are a superficial punctate keratitis, marginal keratitis or dendritic ulcer. Davis (1942), in the United States of America, has recently reported a superficial punctate parenchymatous keratitis, and I have lately seen a member of the Voluntary Aid Detachment with a "kaleidoscopic" keratitis varying from day to day in its configuration, commencing as a lattice form and ending with multiple erosions. I find that the canoe-shaped lesions of marginal keratitis are the most confusing to many ophthalmologists, but they respond rapidly to lid applications of silver nitrate 2 per cent.

Fifthly, lesions of the lid are not uncommon. The frequency of lid lesions I pointed out in 1941, and I attempted to explain this by suggesting that virus keratitis is a neurotrophic lesion of the ophthalmic branch of the trigeminal nerve. These skin lesions may be in the form of petechiae, vesicles or warts. Mackie & McCartney (1938) consider the virus of herpes simplex is both neurotropic and dermatropic. Since residing in the Middle East, I have been impressed with the frequency with which seborrhoeic dermatitis and pyoderma have accompanied a virus keratitis, and have pointed out this more than coincidental happening to our consulting Dermatologist; so possibly the virus is both neurotropic and dermatropic.

Sixthly, as is only to be expected, cultures of the conjunctival sac invariably show "no growth" or normal saprophites. I have never seen a conjunctival culture reveal any helpful evidence in a virus keratitis of the types at present being described, nor have I ever been able to persuade a bacteriologist to culture the conjunctival secretion for this particular virus.

Seventhly, if treated on correct lines the recovery of this particular keratitis is usually rapid and the visual results excellent. Recurrences may occur but are less likely if the treatment to be enumerated below is followed implicitly.

How may these Eyes be Treated

If it is primarily realised that we are really dealing with a herpes simplex (or febrilis) infection of the eye, analogous to recurring herpes febrilis (or recurrens) of the lip, we shall have burnt down the first barrier in our path, and if we appreciate that these herpetic lesions of the lip are best treated by applications of methylated spirits or tinctura iodi mitis and not by hot applications of any sort, we are over our second barrier.

Thirdly, the rationale of omitting heat is obvious once we realise that it is pyrexia which is the main precipitating factor

of all herpes simplex lesions. So, to omit local heat in any form is of the most paramount importance in treating this type of keratitis. On the other hand, ice compresses, I know, are definitely helpful and valuable.

Fourthly, having decided that local heat is inadvisable, why aggravate the condition by artificial pyrexia such as T.A.B. intravenously or milk intramuscularly? They too are strongly contra-indicated in all types of keratitis of simplex origin.

I recently saw a patient who lost the sight of his right eye following repeated T.A.B. injections for marginal keratitis. Six weeks later his left eye developed a dendritic ulcer and one application of carbolic cured that without visual loss. From this case alone it is obvious that it is not generally realised that marginal keratitis and dendritic ulcer are the same infection in different frockings. Who would think of giving T.A.B. intravenously for dendritic ulcer, so why exhibit it for marginal keratitis?

Fifthly, having discarded heat, let me next discard atropine because, with the possible exception of disciform keratitis, I never use atropine in the disease under review and have never regretted its absence. Herpes simplex virus does not cause iritis. If this observation is universally appreciated the present scarcity of atropine sulphate will be greatly relieved.

Sixthly, auto-inoculation is not practical in keratitis unless there is a vesicular skin lesion as well. Even then, I have never attempted it as I have found that simpler means of aborting an attack are at our disposal.

Seventhly, we have found that spirit or tinctura iodi mitis are efficacious in "drying up" the skin and lip lesions of herpes febrilis, and it appeared to me that a similar method would be applicable to the ocular lesions. We have, for several decades, applied pure acid carbol. to all dendritic ulcers with pronounced success, so is it unreasonable to apply a similar astringent to the other manifestation of the same disease, such as marginal keratitis or superficial punctate keratitis? Spirit did not seem indicated and tincture iodi mitis appeared to cause undue pain, I, therefore, tried an old and very dependable ocular astringent, namely, silver nitrate in 2 per cent. solution, but not 1 per cent. solution as is so often used. At first I applied it only to the palpebral conjunctiva of the upper and lower lids, and the result was dramatic. Later, I became bolder and applied it to the corneal lesions themselves, but I usually leave this last adventure for the more advanced cases. The applications are made at the first inspection, then again 36 hours later, and after that at slightly longer intervals till the cornea is healed and the eye is white. When the eye is definitely white I make an extra and final application which I find frequently prevents a recurrence. This treatment is almost

unfailing in superficial keratitis and marginal keratitis but I find it of little use in multiple corneal erosions. For this I reserve four-hourly instillation of guttae zinc sulphate and adren. chloride: grains one of zinc sulphate to the ounce of water.

For the dendritic ulcers I find nothing superior to applications of pure acid carbol. on a tooth pick, while for disciform keratitis I do not feel we have any reliable treatment except rest and patience.

The Technique of Silver Nitrate Application

I must, before leaving the application of silver nitrate, make several pertinent observations :—

(a) The eye should be well cocainised and adrenalised before the application of 2 per cent. silver nitrate. I usually make three instillations of cocaine 4 per cent. and two instillations of adrenaline chloride (1:4000) before I attempt the painting. These instillations are carried out at two minute intervals and, while I have never seen this full local anaesthetization produce any deleterious effect, it certainly maintains the patient's confidence.

(b) I also never wash out the eye immediately after the painting, and even if the whole corneal epithelium develops a "milky" hue, this is no cause for alarm and irrigation. The cornea will rapidly regain its normal lustre.

(c) After the painting I usually instil, on a glass rod, unguentum butyn & metaphen (Abbott) into the lower fornix. This procedure maintains a mild anaesthesia of the cornea and conjunctiva for an hour or more, and allows the pain of the conjunctival ischaemia to pass off relatively unnoticed.

(d) The eye should never be wrapped with pad and bandage but protected only with a flap or dark goggles.

(e) The only treatment I advise between the paintings is swabbing with lotion acid borac. 4th hourly and the application of ung. hyd. oxy. flav. 1 per cent.—thrice daily to the lid margins.

(f) Ice compresses in the more severe cases are advisable four hourly but they are by no means necessary in all cases.

What proportion of cases of keratitis are due to the virus of herpes simplex?

I found that in my recent paper of superficial punctate keratitis in Tasmania (1941) I did not give figures of the various types of herpetic infiltration of the cornea that I found, but I can give these now, and a comparative table detailing those found in the A.I.F. Middle East.

These figures are presented in Table I and II :—

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TABLE I

	Tasmania	Middle East
Total Australian patients examined	6,458	3,285
No. of patients with keratitis of any type	456	164
No. of patients with keratitis due to the virus of herpes simplex,...	189	104
Percentage of patients with any type of keratitis	7.063	4.992
Percentage with keratitis due to virus herpes simplex	2.927	3.166
Percentage of total keratitis patients whose lesion is due to virus of herpes simplex	41.447	63.415

TABLE II

	Tasmania	Middle East
Corneal Erosions—multiple ...	16 (0.248%)	13 (0.395%)
Dendritic Ulcer	14 (0.217%)	12 (0.364%)
Disciform Keratitis	3 (0.046%)	4 (0.122%)
Marginal Keratitis	60 (0.929%)	40 (1.218%)
Superficial Punctate Keratitis	95 (1.471%)	34 (1.035%)
Lattice Keratitis	1 (0.015%)	1 (0.030%)
Herpes of the Lid	4 (0.062%)	3 (0.091%)

It may be argued from the above that it would be expected that the proportion of herpetic keratitis would be decidedly higher in the Middle East than in Tasmania, but I must immediately point out that in the Middle East acute respiratory infections are almost unknown amongst the troops, while their place is taken by pyrexia of malaria and relapsing fever and T.A.B. injections. Under these circumstances it is not surprising that the figures are so congruous. So we see that approximately 3 per cent. of eye disease, whether it be in Australians in Tasmania or the Middle East, are due to the virus of herpes simplex. But, owing to the fact that non-virus keratitis is decidedly less common in the Middle East than it is in Tasmania, we find that of the total cases of keratitis, 41.447 per cent. are due to this virus in Tasmania, while 63.415 per cent. are due to it in the Middle East. In brief, I find that in Australians in the Middle East no less than 2/3 of the keratitis met is of virus simplex aetiology, a fact, I feel, that is not yet realised.

FIG. 1

Multiple corneal epithelial erosions. They all stain.

Superficial Punctate Keratitis—size of K.P. but epithelial. Some may stain.

Superficial Vessels

Marginal Keratitis. Some stain and the larger ones may develop superficial vascularisation.

Dendritic Ulcer. May be multiple and always stain.

Deep Vessels

Disciform Keratitis is parenchymatous and produces deep vascularisation.

Lattice Keratitis is subepithelial. It does not stain and is transient in form.

With regard to the individual figures detailed in Table II there is little comment, except that there is an increase in every type of virus keratitis in the Middle East, with the obvious exception of superficial punctate keratitis. I do not think that any conclusion can be deduced from this, other than that a totally different climate has slightly altered the proportions of the manifestation of an infectious disease. This indeed has been observed in almost every other infection.

Summary

(1) 63 per cent. of the keratitis in Australians in the Middle East is due to the virus of herpes simplex.

(2) The majority of these cases is due to a preceding true or artificial pyrexia or gross change of climate.

(3) Repeated paintings with AgNO₃ 2 per cent. are strongly indicated in marginal and superficial punctate keratitis.

(4) Carbolicization is still the treatment par excellence for dendritic ulcer.

(5) Local heat or thermotherapy of any type is strongly contra-indicated in the treatment of any type of keratitis due to herpes simplex.

(6) Atropine is not necessary, except in disciform keratitis.

Conclusion

I must thank Colonel W. Summons, O.B.E., Commanding Officer of an Australian General Hospital, for permission to publish these figures, and I must acknowledge gratefully the assistance of the Sisters and Nursing Orderlies of this Hospital. Especially am I indebted to Sister B. Scott-Young, Sgt. K. MacFarlane and Private G. Petty, for their valuable and continuous help.

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ANNOTATION

Presence of Mind

The great Lexicographer, sometimes known as Surly Sam to differentiate him from Ben Jonson, defined presence of mind as readiness at need and quickness at expedients. It is a most useful asset, and we believe it to be a quality inborn in most people. Education may foster it but cannot produce it if it is not there. If an ophthalmic surgeon begins a cataract operation and finds, when he has completed his puncture and counter-puncture, that he has inserted the Graefe knife upside down, we believe the best thing to do is to withdraw the knife at once and postpone the operation for a day or two until the punctures have healed. Presence of mind will not as a rule enable one to rotate the knife through half a circle